Doctoral Dissertation

Development of Oxidative Functionalization Using Hypervalent Iodines with Controlled Reactivity by Modified Carbon Framework

Masaki Fujie

January 2023

Department of Applied Chemistry

Graduate School of Engineering

Osaka University

Preface and Acknowledgements

This thesis has been performed from 2017 to 2023 under the guidance of Prof. Dr. Makoto Yasuda at the Department of Applied Chemistry, Graduate School of Engineering, Osaka University. The thesis describes the modification of carbon framework on hypervalent iodines for oxidative functionalization.

I would like to express my deepest appreciation to Prof. Dr. Makoto Yasuda for his precise guidance, helpful suggestions, and hearty encouragement throughout this work. His enthusiasm for chemistry has always motivated me. He also gave me a lot of invaluable experiences. I really appreciate him for supervising me. I would also like to thank Professors Dr. Ikuya Shibata and Dr. Yutaka Ie for their helpful advice and kind assistance. I gratefully express acknowledgement to Associate Prof. Dr. Yoshihiro Nishimoto for his intimate assistance, helpful suggestion, and stimulating discussion. I really wish to make a grateful acknowledgement to Assistant Prof. Dr. Akihito Konishi for his sharp comments and kind encouragement. I am grateful to Associate Prof. Dr. Shuntaro Tsubaki for helpful discussions.

I am deeply thankful to Ms. Yoshimi Shinomiya and Ms. Tomoko Shimizu for giving me their grateful support and heartwarming kindness. I have had the great support of Mr. Hiroshi Moriguchi, Dr. Nobuko Kanehisa, Dr. Hiroaki Tanaka, Dr. Kyoko Inoue, Mr. Kunihiko Kamon, and Mr. Hiromi Ohi with analytic assistance at the analytical instrumentation facility.

I express my appreciation to all members of the Yasuda group. I am deeply indebted to my colleagues since I joined the Yasuda group in 2017. Especially, I would like to express my appreciation to our pioneer of hypervalent iodine chemistry, Mr. Junki Hara, for the development of this chemistry in early days. I also appreciate my disciple, Mr. Kyohei Mizufune, for his active discussion and hard work to create our hypervalent iodine chemistry together. I gratefully wish to thank Dr. Naoto Esumi, Dr. Yuji Kita, Dr. Yohei Minami, Dr. Kyoungmin Kang, Dr. Kensuke Suzuki, Dr. Shuichi Nakao, Dr. Fei Wang, Mr. Naoki Sugihara, and Mr. Yuya Tsutsui for their worthwhile advice and active discussion. I would also wish to express my gratitude to Dr. Koki Horii, Dr. Tetsuji Yata, and Dr. Daiki Tanaka for their active discussion and encouragement to work hard in the doctor course.

Professor Yasuda also assisted me to visit Technische Universität München, Germany for three and a half months from April 2022. I would like to thank Prof. Dr. Shigeyoshi Inoue for allowing me to study his fascinating chemistry. I am also grateful to all members of AK Inoue for their kind support during my stay.

Finally, I would like to express my gratitude to my parents, Yasuhiro Fujie and Naoko Fujie, for their understanding my work, constant assistance, and financial support. I would also like to thank my older brothers, Ryosuke Fujie and Akinori Fujie, for understanding my work.

January, 2023

Masaki Fujie

Department of Applied Chemistry
Graduate School of Engineering
Osaka University
2-1 Yamadaoka, Suita, Osaka 565-0871, JAPAN

List of Publications

1) **Effect of Noncovalent Interactions in Ion Pairs on Hypervalent Iodines: Inversion of Regioselectivity in Sulfonyloxylactonization**
   Y. Nishimoto, M. Fujie, J. Hara, M. Yasuda
   Org. Chem. Front. **2021**, *8*, 3695–3704.

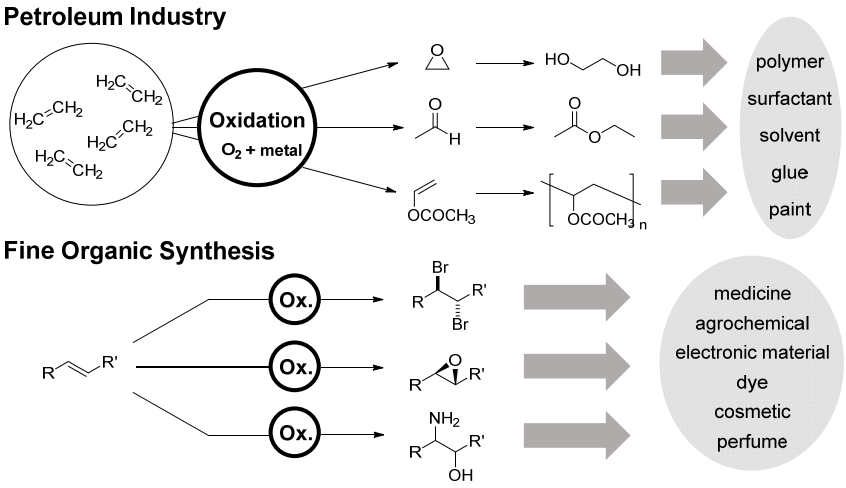
2) **1-Fluoro-1-sulfonyloxylation of Alkenes by Sterically and Electronically Tuned Hypervalent Iodine: Regression Analysis toward 1,1-Heterodifunctionalization**
   M. Fujie, K. Mizufune, Y. Nishimoto, M. Yasuda
   Org. Lett. **2023**, *25*, 766-770.

3) **Sulfonyloxylation and Acetoxylation of Aryl C–H Proximal to λ^3-Iodanediyl Group on Biaryl Structures**
   M. Fujie, K. Mizufune, Y. Nishimoto, M. Yasuda
   Chem. Lett. **2023**, *52*, 79-83.

Contents

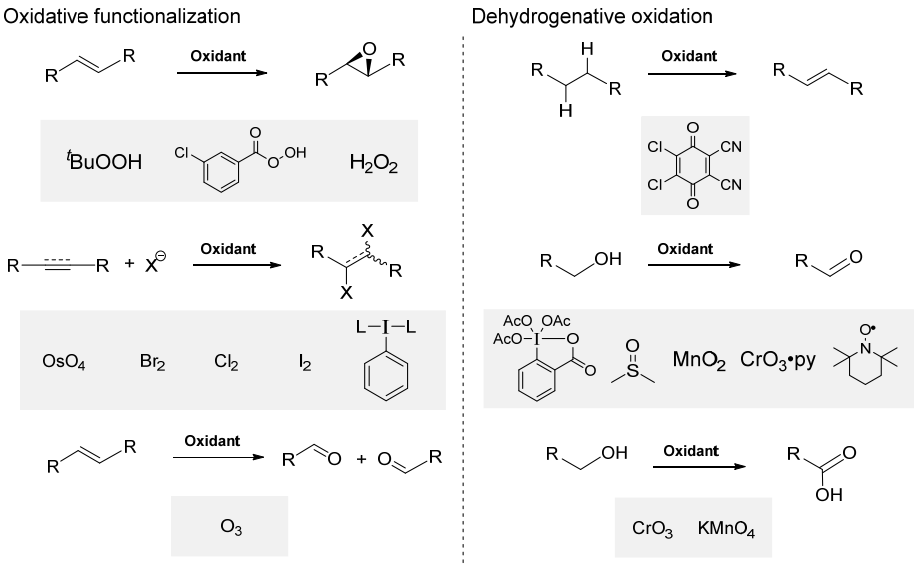
General Introduction

Oxidation is one of the most fundamental and important reactions because it has played an important role in organic synthesis. For example, in petroleum industry, ethylene is oxidized by oxygen in appropriate reaction conditions to give ethylene oxide, acetaldehyde and vinyl acetate in mass production (Scheme 1, top). These compounds are further converted to basic chemical products which underpin industry.



Scheme 1. Oxidation in petroleum industry and fine organic synthesis.

Oxidation reaction is a powerful tool for fine organic synthesis which produces highly functionalized chemicals such as pharmaceutical compounds and electronic materials (Scheme 1, bottom). To accomplish the fine organic synthesis, various kinds of oxidants are required. Many types of oxidants have been developed for oxidative functionalization and dehydrogenative oxidation (Scheme 2). It is noted that organic hypervalent iodines have distinctive advantages over the others because their reactivities are tuned by modifications of their carbon frameworks.



Scheme 2. Representative oxidation modes by oxidants.

Hypervalent iodines are oxidants whose iodine atom has formally contains more than the 8 electrons in the valence shell required for the octet rule, because an iodine has a large atomic radius, weak electron negativity and easily polarizes to give hypervalent state (Figure 1).[1] In iodine(III) molecules RIL_2, the interaction of the filled 5p orbital of the central iodine atom and the half-filled orbitals of the two ligands L leads to formation of three molecular orbitals: bonding, nonbonding and antibonding orbitals. Because the highest occupied molecular orbital (HOMO) includes a node at the iodine center, the hypervalent bonds exhibit a highly polarized nature; hence, the axial positions are tended to be occupied by more electronegative atoms due to the interaction of the orbitals of three collinear atoms. The carbon substituent R is bound by a normal covalent bond and the molecule RIL_2 has a distorted trigonal bipyramid geometry with two heteroatom ligands L occupying the apical positions and the least electronegative carbon ligand R and both electron pairs are located in equatorial positions. Iodine can form polyvalent states, I(III), I(V) and I(VII), as organic and inorganic hypervalent iodines. In particular, organic hypervalent iodine(III) is easy to handle among other hypervalent iodines due to its stability.

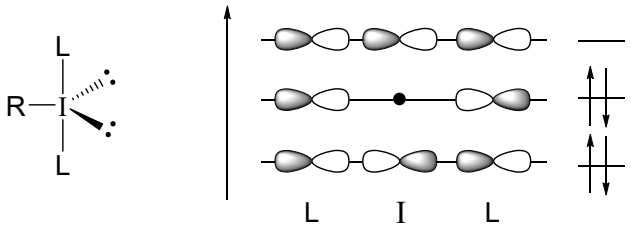
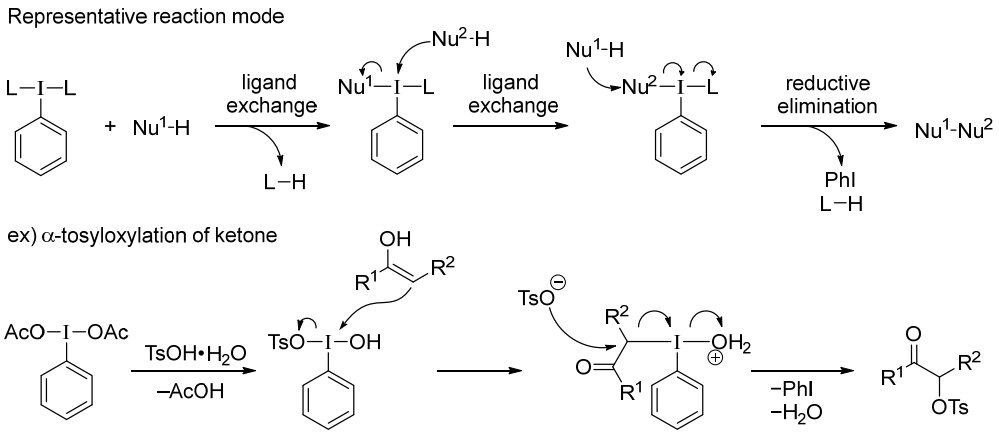


Figure 1. Molecular orbital description of the three-center-four-electron bond in hypervalent iodine(III) molecules RIL_2.

Hypervalent iodines act as oxidants exhibiting an electrophilic character and a leaving ability. Most reactions of λ^3-iodanes $PhIL_2$ involve the ligand exchange on an iodine atom with an external nucleophile followed by elimination of iodobenzene (Scheme 3, top). For example, in α-tosyloxylation of ketones, ligand exchange of $PhI(OAc)_2$ with TsOH and ligand exchange of PhI(OH)OTs with an enol derived from a ketone produces an alkyliodonium intermediate, which on S_N2 displacement by tosylate gives a product with liberation of iodobenzene (Scheme 3, bottom).



Scheme 3. Representative reaction mode of λ^3-iodanes $PhIL_2$.

Modification of the carbon framework on organic hypervalent iodines is an efficient methodology to control the reactivity (Figure 2). Chelation with a ligand to stabilize hypervalent iodines has provided bench-stable and easy-handling hypervalent iodine reagents (Scheme 4a).[2] These hypervalent iodines stabilized by chelating effect can be used as electrophilic group transfer reagents. Togni *et al.* firstly reported the trifluoromethylbenziodoxolone as a CF_3^+ equivalent for electrophilic trifluoromethylation reagent (Scheme 4b)[2a,2c,2d,2f]. Waser *et al.* demonstrated the practical usage of ethynylbenziodoxolone and other types of benziodoxolone reagents (Scheme 4c).[2b,2e]

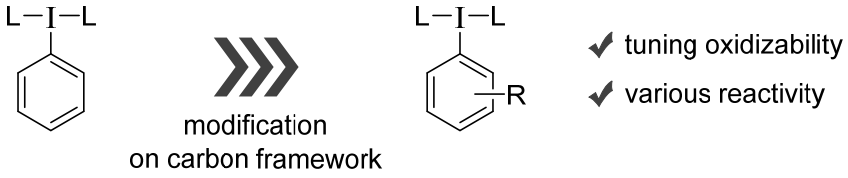
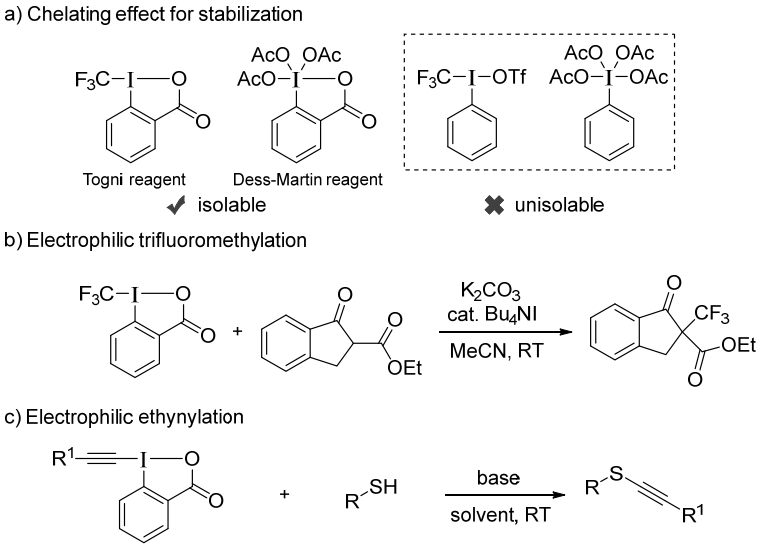
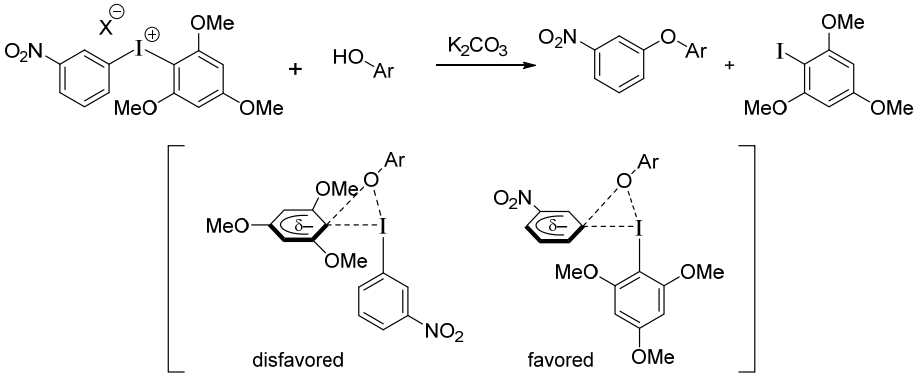


Figure 2. Modification on carbon framework of hypervalent iodine(III).



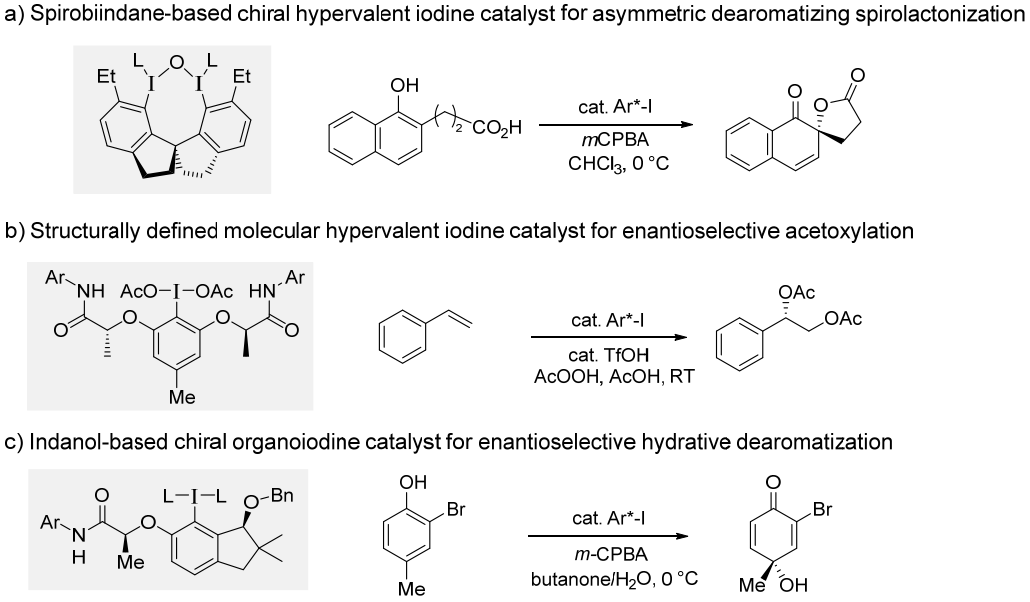
Scheme 4. Chelating effect for stabilization of hypervalent iodine and their application for electrophilic group transfer reagent.

Inductive effect with substituents has made hypervalent iodines more efficient reagents, especially diaryliodonium salts. For example, unsymmetrical diaryliodonium salts with trimethoxybenzene-derived auxiliary provide high levels of aryl transfer selectivity (Scheme 5).[3] Electronic effects favor the transfer of the most electron-poor aryl group because of the stabilization on the *ipso*-carbon atom in the ligand-coupling step.



Scheme 5. Inductive effect on diaryliodonium salt for selective arylation

Incorporation of chiral auxiliary on carbon framework allows enantioselective oxidative functionalization in high efficiency (Scheme 6).[4] Dohi and Kita *et al.* demonstrated the spirobiindane-based chiral hypervalent iodine catalyst for high efficient asymmetric dearomatizing spirolactonization (Scheme 6a).[4a] Muñiz and Ishihara *et al.* reported the asymmetric diacetoxylation of alkenes by the bislactamide-based hypervalent iodine catalyst (Scheme 6b).[4b] Hashimoto and Maruoka *et al.* showed the indanol-based chiral organoiodine catalyst for enantioselective hydrative dearomatization (Scheme 6c).[4c]

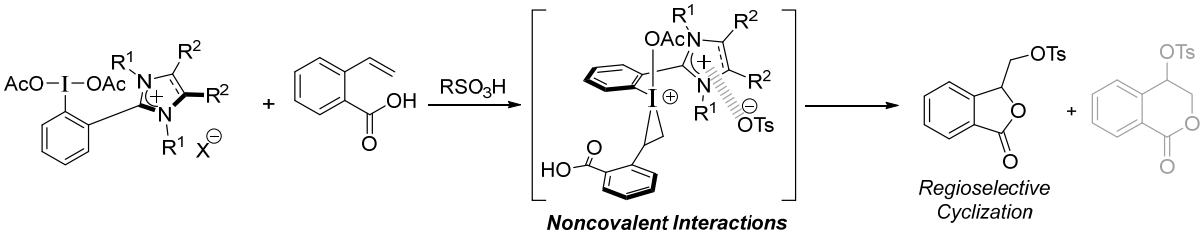


Scheme 6. Representative chiral organoiodine catalysts and their application for enantioselective oxidative functionalizations.

The modification method on the carbon framework of hypervalent iodines has much potential for novel oxidative functionalizations.

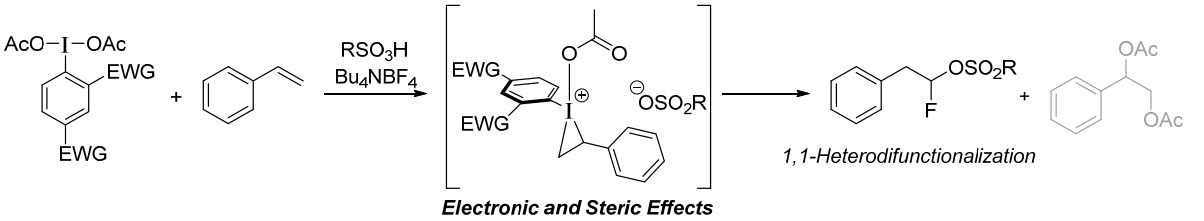
In chapter 1, noncovalent interactions in ion pairs on hypervalent iodines was used to developed a novel oxidative functionalization of alkenes. The hypervalent iodine with a benzimidazolium moiety allowed unique selectivity upon sulfonyloxylactonization of 2-vinylbenzoic acids (Scheme 7). According to the results of the experiments and theoretical calculation, it was revealed that noncovalent interactions between

the imidazolium moiety and sulfonyloxy group were important for regioselectivity.



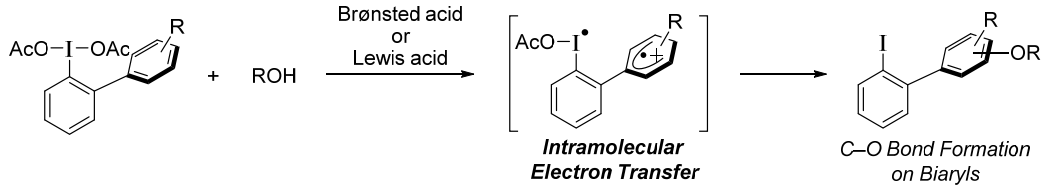
Scheme 7. Regioselective oxidative cyclization by hypervalent iodine with cationic moiety.

In chapter 2, 1,1-heterodifunctionalization of alkenes by optimized hypervalent iodines was developed (Scheme 8). Regression analysis of substituents on carbon framework revealed the importance of the bulkiness and electron withdrawing character for selective 1,1-heterodifunctionalization. Synergistic substituent effects further improved the efficiency.



Scheme 8. 1,1-heterodifunctionalization of alkenes by optimized hypervalent iodines.

In chapter 3, C–O bond formation on biaryls with hypervalent iodine moieties was developed (Scheme 9). Sulfonyloxylation and acetoxylation were carried out with appropriate Brønsted acids or Lewis acids. Experimental studies revealed that intramolecular electron transfer was an important key step for functionalizations.



Scheme 9. C–O bond formation on biaryls with hypervalent iodine moiety.

References

[1] a) *Iodine Catalysis in Organic Synthesis* (Eds.: K. Ishihara, K. Muñiz), Wiley-VCH, Weinheim, **2022**; b) *PATAI's Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds* (Eds.: B. Olofsson, I. Marek, Z. Rappoport) Wiley-Blackwell, **2019**; c) A. Yoshimura, V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328; d) T. Wirth, *Hypervalent Iodine Chemistry (Topics in Current Chemistry, 373)*, Springer, **2016**.

[2] selected papers; a) P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579; b) R. Frei, J. Waser, *J. Am. Chem. Soc.* **2013**, *135*, 9620; selected review; c) J. Charpentier, N. Früh, A. Togni, *Chem. Rev.* **2015**, *115*, 650; d) J.-Y. Chen, J. Huang, K. Sun, W.-M. He, *Org. Chem. Front.* **2022**, *9*, 1152; e)

D. P. Hari, P. Caramenti, J. Waser, *Acc. Chem. Res.* **2018**, *51*, 3212; f) X. Wang, A. Studer, *Acc. Chem. Res.* **2017**, *50*, 1712; g) K. Kiyokawa, S. Minakata, *Synlett* **2020**, *31*, 845.

[3] selected papers; a) T. L. Seidl, S. K. Sundalam, B. McCullough, D. R. Stuart, *J. Org. Chem.* **2016**, *81*, 1998; b) J. Malmgren, S. Santoro, N. Jalalian, F. Himo, B. Olofsson, *Chem. Eur. J.* **2013**, *19*, 10334; reviews; c) E. A. Merritt, B. Olofsson, *Angew. Chem. Int. Ed.* **2009**, *48*, 9052; d) N. Takenaga, R. Kumar, T. Dohi, *Front. Chem.* **2020**, *8*, 599026.

[4] selected papers; a) T. Dohi, N. Takenaga, T. Nakae, Y. Toyoda, M. Yamasaki, M. Shiro, H. Fujioka, A. Maruyama, Y. Kita, *J. Am. Chem. Soc.* **2013**, *135*, 4558; b) S. Haubenreisser, T. H. Wöste, C. Martinez, K. Ishihara, K. Muñiz, *Angew. Chem. Int. Ed.* **2016**, *55*, 413; c) T. Hashimoto, Y. Shimazaki, Y. Omatsu, K. Maruoka, *Angew. Chem. Int. Ed.* **2018**, *57*, 7200; selected review; d) A. Parra, *Chem. Rev.* **2019**, *119*, 12033.

Chapter 1: Effect of Noncovalent Interactions in Ion Pairs on Hypervalent Iodines: Inversion of Regioselectivity in Sulfonyloxylactonization

1-1. Introduction

Organic hypervalent iodine compounds are utilized as efficient oxidants and perform unique oxidative functionalizations of various substrates such as alkenes, ketones, and alkanes.[1] Modifications of the carbon backbones in organic hypervalent iodines strongly improve their properties such as stability, reactivity, and selectivity. Typically, the inductive effect of substituents tunes the oxidizability (Figure 1.1a).[1] The coordination of functional groups to an iodine center enhances stability and solubility of hypervalent iodines (Figure 1.1b).[2,3] The asymmetric induction effect by various types of chiral auxiliaries or chiral organic backbones has accomplished enantioselective oxidative reactions (Figure 1.1c).[1,4] For example, Ishihara and Muñiz reported that an effective reaction field for an asymmetric oxidation of alkenes is generated by the hydrogen bond between an amide NH group in a chiral auxiliary and an AcO group located at the iodine center.[5] Recently, Jacobsen, Sigman, Houk, and Xue revealed that multiple attractive non-covalent interactions, including CH-π and π-π interactions, between styrene substrates and the hypervalent iodine framework contributed to asymmetric induction in difluorinations of styrenes (Figure 1.1d).[6] As described above, hypervalent iodine chemistry has progressed with the establishment of control methods of the properties and reaction fields. Therefore, to pioneer a novel area in tactics for the accomplishment of selective reactions with hypervalent iodine reagents has been of great significance even now. Recently, the

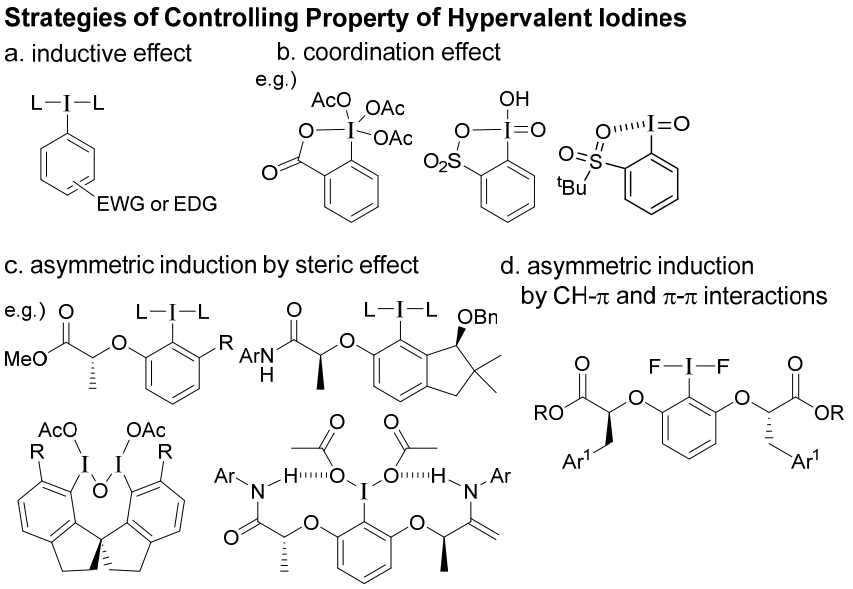


Figure 1.1. Control of reaction fields on hypervalent iodines.

control of regio- or stereoselectivity via noncovalent interactions in designed ion pairs has made amazing successes in various fields such as transition metal catalysis,[7] phase-transfer catalysis,[8] counteranion-directed catalysis,[9] and ion-paring catalysis[10] with the noncovalent attractive forces in ion pairs which are mainly constructed by electrostatic and induction interactions to be considerably long-range and strong by

comparison with other noncovalent forces.[11] In hypervalent iodine chemistry, only a C-H chlorination of steroids catalyzed by an ion-paired template was reported by Breslow (Figure 1.2a), wherein a regioselective chlorination is accelerated by the generation of ion pairs between ammonium and sulfonate moieties attached on steroids and hypervalent iodines.[12] Despite a large potential indicated by Breslow, other reaction systems

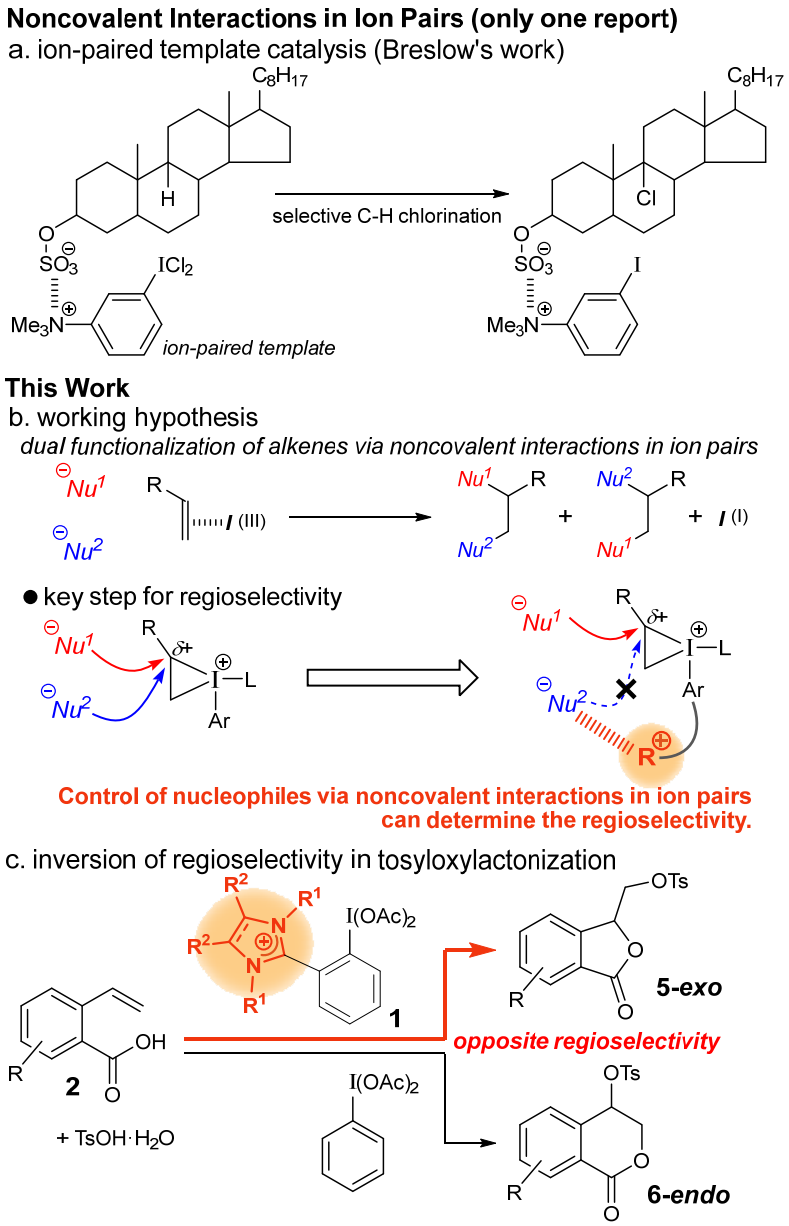


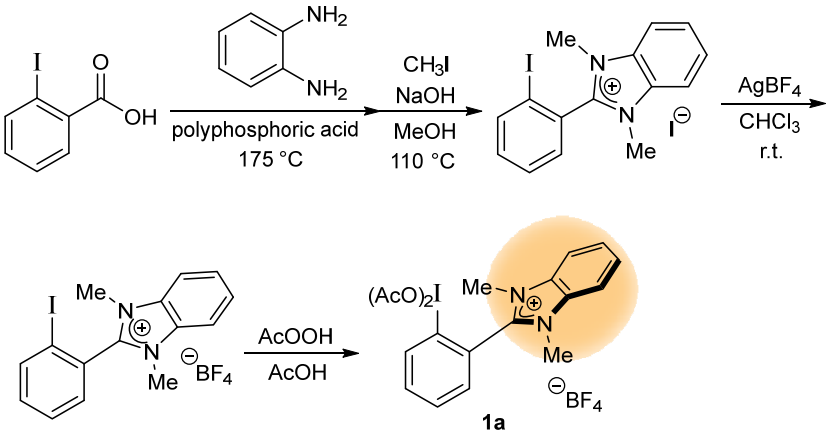
Figure 1.2. Noncovalent interactions in ion pairs in hypervalent iodines.

via noncovalent attractive forces in ion pairs has been scarcely reported. Thus, we envisioned the application of the noncovalent interactions in ion pairs to a dual functionalization of alkenes using two different nucleophiles (Nu^1 and Nu^2) which is a significant reaction in hypervalent iodine chemistry (Figure 1.2b).[1,4] The control of regioselectivity in the addition of nucleophiles to iodonium intermediates is a vital issue for the success of a selective double functionalization (Figure 1.2b, key step for regioselectivity).[13] In our working hypothesis, noncovalent interactions between anionic nucleophiles (Nu^2) and the cationic

substituents (R^+) on hypervalent iodine molecules affect the nucleophilicity in order to control regioselectivity. Herein, we report the synthesis of novel λ^3-iodanes (**1**) bearing cationic nitrogen-containing heterocyclic moieties nearby the iodine(III) center (Figure 1.2c). These hypervalent iodines and $PhI(OAc)_2$ exhibited an opposite regioselectivity in the sulfonyloxylactonization of 2-vinylbenzoic acids (**2**). This is the first report of the control of regioselectivity by noncovalent interactions in dual functionalization of alkenes with hypervalent iodine reagents, which has enormous implications in terms of revealing the role of noncovalent interactions in hypervalent iodine-mediated reaction systems.

1-2. Results and Discussion

Imidazolium structures as cationic moieties were chosen because of the tolerance to oxidative conditions using hypervalent iodines.[14] Targeted $ArI(OAc)_2$ (**1a**) bearing an imidazolium moiety at the *ortho*-position in the ArI structure was prepared from commercially available 2-iodobenzoic acid by conventional methods (Scheme 1.1).[14] X-ray diffraction analysis of **1a** (Figure 1.3) shows that the structure around the iodine atom adopts a T-shaped geometry with the benzene ring, which is located in a plane of the trigonal bipyramidal structure that occupies an equatorial position. AcO groups occupy apical positions and both carbonyl oxygens coordinate to the iodine center *trans* to each other. BF_4^- is located near the imidazolium moiety in a solid state. The imidazolium plane is almost perpendicular to the benzene ring.



Scheme 1.1. Synthetic route of **1a** bearing imidazolium moiety at *ortho*-position.

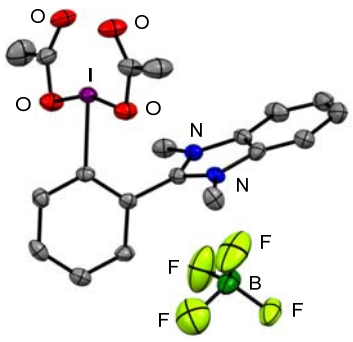
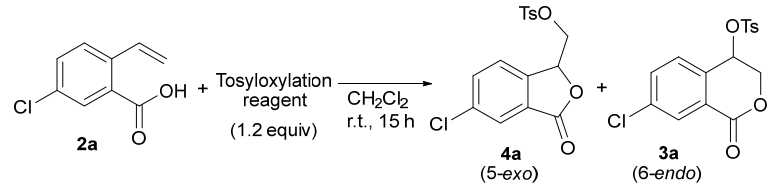


Figure 1.3. ORTEP drawing of **1a**.

By investigating various oxidative functionalizations using **1a**, we discovered that **1a** exhibited an interesting regio-divergence in tosyloxylactonization of 2-vinylbenzoic acids (Table 1.1). Fujita reported that asymmetric lactonization using *p*-toluenesulfonic acid (TsOH) and chiral iodoarene diacetate proceeded in a 6-*endo* cyclization fashion.[15] Tosyloxylactonization was performed using $PhI(OAc)_2$ and TsOH to preferentially obtain the 6-*endo* product (**3a**), which is similar to that of Fujita's reagent (**4a**/**3a** = 17:83) (entry 1). Generally, ArI(OTs)OH generated in situ is considered an intermediate in tosyloxylation using TsOH and iodoarene diacetates.[16] Examining Koser's reagent PhI(OTs)OH, the same regioselectivity as $PhI(OAc)_2$/TsOH was observed (entry 2).[17] To our delight, the synthesized hypervalent iodine (**1a**) exhibited a regioselectivity that was quite different from common hypervalent iodines to produce 5-*exo* product (**4a**) in high selectively (**4a**/**3a** = 91:9) (entry 3).[18] Even when $CHCl_3$, PhCl, $ClCH_2CH_2Cl$, or CH_3CN instead of CH_2Cl_2 was used as solvents, **1a** and $PhI(OAc)_2$ showed the high level of 5-*exo* selectivity and 6-*endo* selectivity, respectively, regardless of the permittivity (Scheme 1.S16 in Chapter 1-4). In addition, the isomerization between 5-*exo* (**4a**) and 6-*endo* (**3a**) did not occur under tosyloxylactonization conditions (Scheme 1.S18 in Chapter 1-4). 1-Butyl-3-methylimidazolium tetrafluoroborate was used as an additive in the tosyloxylation of **2a** using PhI(OTs)OH, and preferentially afforded 6-*endo* (**3a**) (entry 4). The selectivity (**4a**/**3a** = 14:86) approximated that in a no-additive examination (entry 2),thus, an outer-sphere cationic unit is ineffective and the change in regioselectivity is influenced by the intramolecular imidazolium moiety.

Table 1.1. Comparison of **1a** with common hypervalent iodine reagents on the regioselectivity of tosyloxylactonization of 2-vinyl benzoic acid (**2a**)[a].

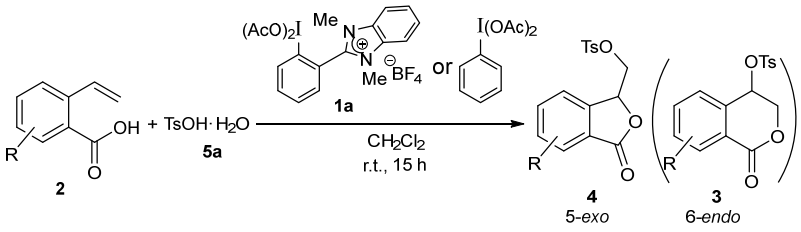


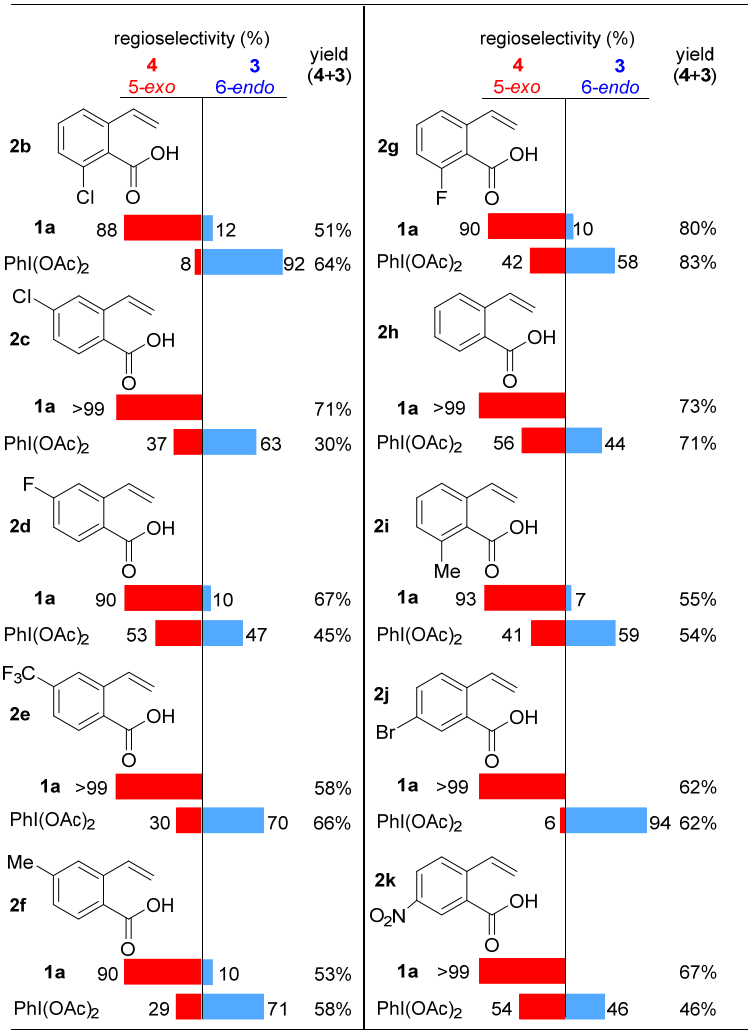
entry	Tosyloxylation reagent	regioselectivity (%) 4a 5-*exo*	3a 6-*endo*	yield (**4a**+**3a**)
1[b]	AcO−I(Ph)−OAc + TsOH•H_2O **5a**	17	83	60%
2[c]	TsO−I(Ph)−OH	4	96	69%
3[d]	$(AcO)_2I$, Me, N, N, Me, BF_4 **1a** + TsOH•H_2O **5a**	**91**	9	64%
4[e]	TsO−I(Ph)−OH + MeN, NBu, BF_4	14	86	38%

[a]**2a** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h. [b]$PhI(OAc)_2$ (0.18 mmol), TsOH·H_2O (**5a**) (0.15 mmol). [c]PhI(OTs)OH (0.18 mmol). [d]**1a** (0.18 mmol), TsOH·H_2O (**5a**) (0.15 mmol). [e]PhI(OTs)OH (0.18 mmol), *N*-butyl-*N*-methylimidazolium tetrafluoroborate (0.65 mmol).

Tosyloxylactonization of various 2-vinylbonzoic acids (**2**) using **1a** gave 5-*exo* products (**4**) with high selectivity (Table 1.2). The present 5-*exo* cyclization was compatible to functional groups as demonstrated for fluoro (**2d** and **2g**), chloro (**2b** and **2c**), bromo (**2j**), trifluoromethyl (**2e**), and nitro (**2k**) ones. The cyclization of electron-neutral (**2h**), electron-rich (**2f** and **2i**), and electron-deficient substrates (for example, **2e** and **2k**) proceeded with high 5-*exo* selectivity in moderate to high yields. When $PhI(OAc)_2$ was applied to the tosyloxylation of these substrates (**2b**-**2k**), the cyclization did not exhibit high 5-*exo* selectivity but resulted either in 6-*endo* or in no selectivity.

Table 1.2. Scope of 2-vinyl benzoic acids in 5-*exo* tosyloxylactonization using **1a**[a].

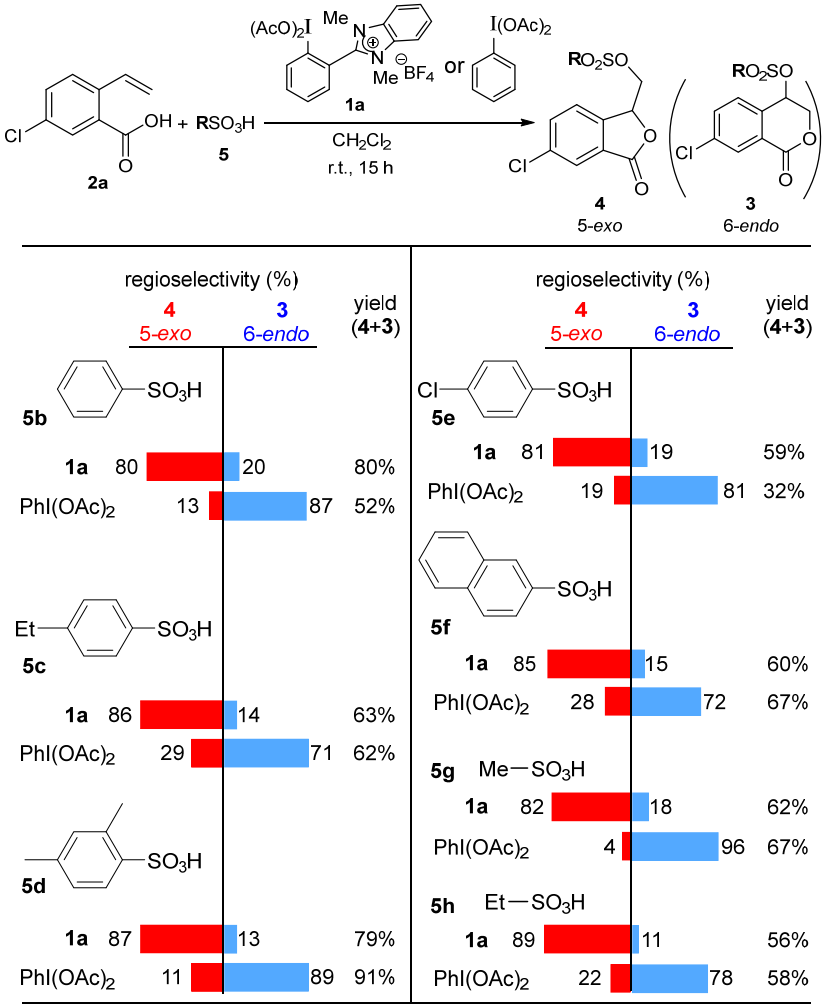




[a]Method with **1a**: **2** (0.15 mmol), **1a** (0.18 mmol), **5a** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h. Method with $PhI(OAc)_2$: **2** (0.15 mmol), $PhI(OAc)_2$ (0.18 mmol), **5a** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h.

The generality of sulfonic acids in 5-*exo* cyclization using **1a** was examined (Table 1.3). Benzene-, *p*-ethylbenzene-, *m*-xylene-, 4-chlorobenzene-, naphthalenesulfonic acids (**5b**, **5c**, **5d**, **5e**, and **5f**) as well as TsOH selectively gave the corresponding 5-*exo* products (**4**). Alkanesulfonic acids (**5g** and **5h**) were applicable to 5-*exo* selective cyclization. It is noted that $PhI(OAc)_2$ selectively led to 6-*endo* products in reactions using these sulfonic acids in contrast to **1a** in all cases.

Table 1.3. Scope of sulfonic acids in 5-*exo* sulfonyloxylactonization using **1a**[a].

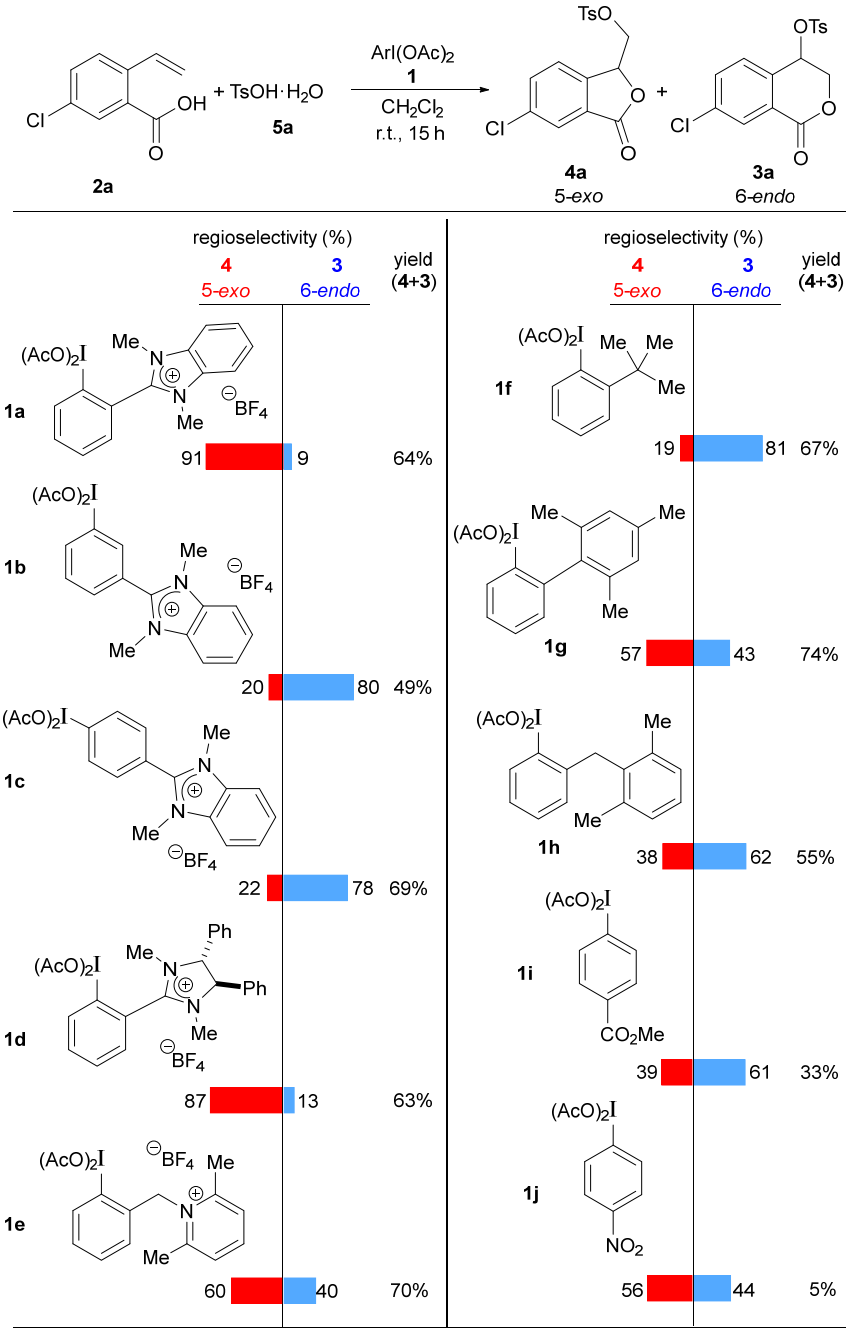


[a]Method with **1a**: **2** (0.15 mmol), **1a** (0.18 mmol), **5** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h. Method with $PhI(OAc)_2$: **2** (0.15 mmol), $PhI(OAc)_2$ (0.18 mmol), **5** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h.

To reveal the effect that the imidazolium moiety exerts on regioselectivity, various types of $ArI(OAc)_2$ were applied to the tosyloxylactonization (Table 1.4). In contrast to **1a**, regioisomers (**1b** and **1c**) bearing an imidazolium unit at *meta*- and *para*-positions, respectively, exhibited 6-*endo* selectivity. These results indicate that the structural arrangement between the iodine atom and the imidazolium moiety is an important factor for regioselectivity. $ArI(OAc)_2$ with imidazolidinium moiety (**1d**) also worked as a trigger to lead to 5-*exo* selectivity. $ArI(OAc)_2$ with a 2,6-dimethylpyridinium moiety at the *ortho*-position via a methylene spacer (**1e**) afforded 5-*exo* product (**4a**) although the selectivity was slightly decreased. The imidazolium

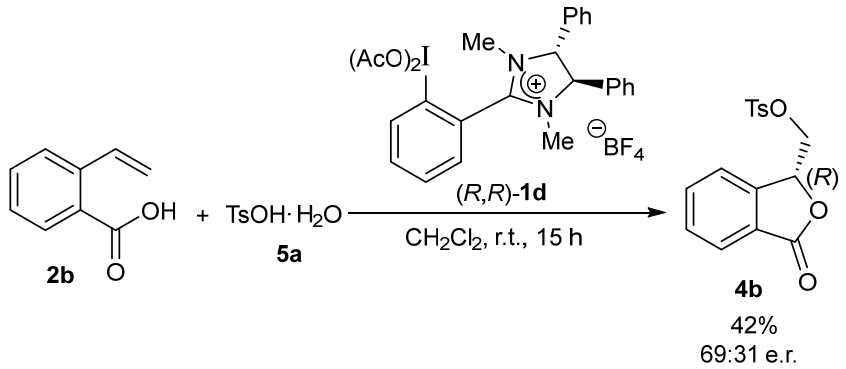
moiety could be recognized as bulky and electron-withdrawing, and thus steric and inductive effects were investigated. $ArI(OAc)_2$ (**1f**) gave 6-*endo* selectivity that was the same as that of $PhI(OAc)_2$ in spite of the steric hindrance of *t*Bu group. *ortho*-Mesityl-substituted $ArI(OAc)_2$ (**1g**) afforded 5-*exo* product (**4a**) in slightly preference to 6-*endo* (**3a**), and the selectivity was quite low. A 2,6-dimethylpyridinium moiety (**1e**) was compared with a 2,6-dimethylphenyl moiety (**1h**) connected by a methylene spacer, and the regioselectivities were divergent despite having the same steric hindrance; **1e** and **1h** exhibited 5-*exo* and 6-

Table 1.4. Effects of substituents on the benzene skeleton of $ArI(OAc)_2$[a].



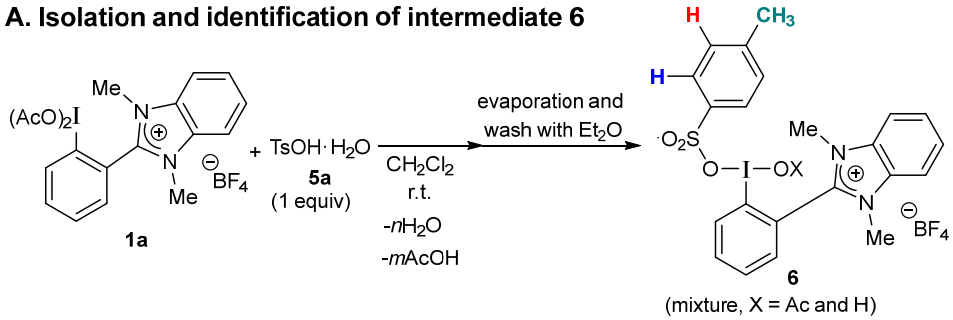
[a]**2a** (0.15 mmol), **1** (0.18 mmol), **5a** (0.15 mmol), CH_2Cl_2 (0.5 M), room temperature, 15 h.

endo selectivity, respectively. Thus, the steric hindrance is not a critical factor in 5-*exo* selectivity. *para*-Substituents were investigated to verify electron-withdrawing effects, in which the *para*-position was adopted to avoid steric and coordination effects on the iodine center. The main product of *para*-(MeO)CO-substituted ArI(OAc)$_2$ (**1i**) was 6-*endo* product (**3a**). The examination of NO_2 group-substituted ArI(OAc)$_2$ **1j** resulted in a very low yield with no regioselectivity. Therefore, we established that the electron-withdrawing substituents on a phenyliodane backbone do not lead to effective 5-*exo* selectivity. These results suggested the importance of cationic moieties near the iodine(III) center in a manifestation of 5-*exo* cyclization. 2-Vinyl benzoic acid (**2b**) was subjected to the reaction conditions with optically active hypervalent iodine (*R*,*R*)-**1d** (Scheme 1.2). The corresponding 5-*exo* product (**4b**) was obtained in 69:31 e.r., which suggested the cationic nitrogen-containing heterocycle in **1d** worked as a chiral auxiliary.



Scheme 1.2. Enantioselective tosyloxylactonization using optically active hypervalent iodine (*R,R*)-**1d**.

The reaction of ArI(OAc)$_2$ with TsOH·H_2O generally produces ArI(OTs)OX (X = Ac or H) species that serve as intermediates in various reactions.[1] When **1a** and TsOH·H_2O were mixed in CH_2Cl_2, the generation of AcOH was confirmed by in situ ^{1}H NMR (Scheme 1.S1 in Chapter 1-4). After evaporation of the volatiles and washing with Et_2O, the mixture of ArI(OTs)OH and ArI(OTs)OAc (= ArI(OTs)OX (**6**)) was isolated (Figure 1.4A). The comparison of ArI(OTs)OX (**6**) with **1a** and PhI(OTs)OX in ^{1}H NMR spectra (Figure 1.4B) showed that chemical shifts of the Ts signals in **6** differed from those of TsOH but were quite similar to those of PhI(OTs)OH. According to the spectra comparison, ArI(OTs)OX (**6**) is considered an intermediate. In fact, the tosyloxylation of **2a** using isolated **6** afforded almost the same result as that of the **1a**/TsOH·H_2O system (Figure 1.4C and Scheme 1.S3 in Chapter 1-4).[19]



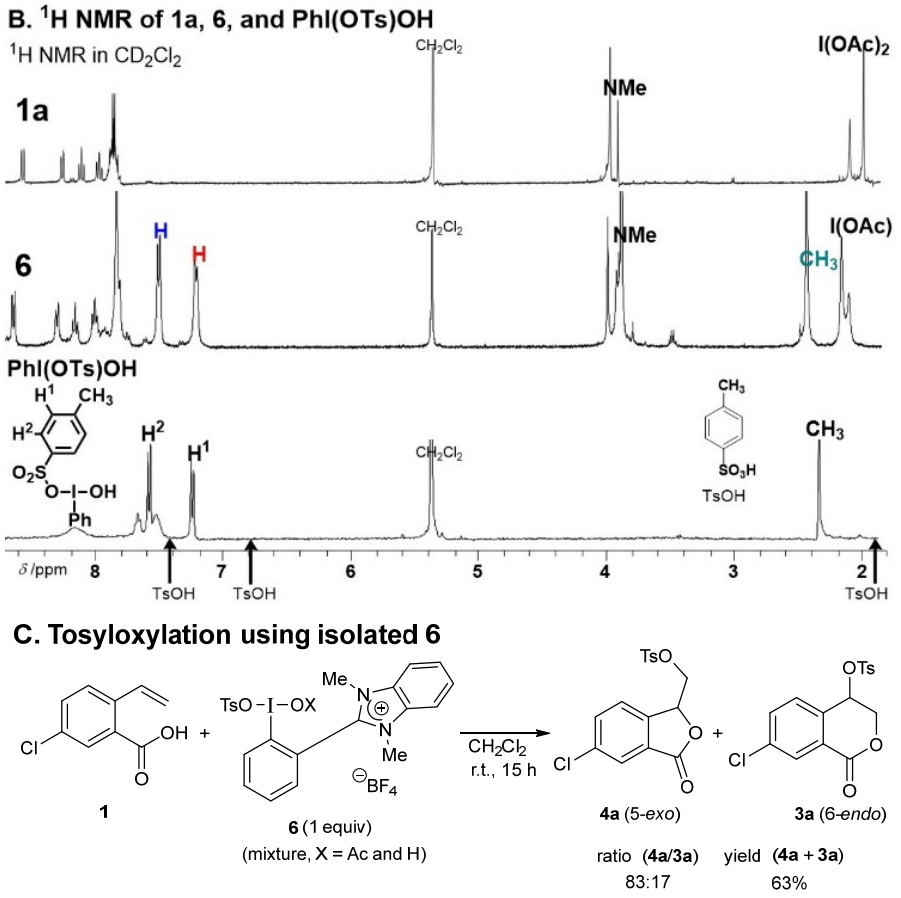


Figure 1.4. Observation, isolation and reactivity of intermediate **6**.

To gain insights into intermediate **6**, a density functional theory study (see Chapter 1-4 for full details) was performed with ArI(OH)OSO$_2$Ph (***o*-7**) (Ar = 2-benzoimidazoliumylphenyl) used as a model of **6** (Figure 1.5A). The ***o*-7** has two energetic local minimums, and conformer ***o*-7-A** is more stable than ***o*-7-B** by 3.57 kcal/mol. Noncovalent interaction analysis[20] shows that in ***o*-7-A** the Me group of the imidazolium moiety and the phenyl ring of the PhSO$_3$ group generates a cation–π interaction surface.[21,22,23] In addition, the same Me group forms an effective cation-oxygen interaction[10] with the oxygen atom of the PhSO$_3$ group, which is evident from the large isosurface. In minor conformer ***o*-7-B**, the π–π interaction of the PhSO$_3$ group with the iodobenzene framework helps stabilize the conformation. Notably, the I-O^1 bond of ***o*-7-A** (2.222 Å) is elongated by comparison with that of ***o*-7-B** (2.208 Å), which suggests that the iodine center in ***o*-7-A** is activated via the noncovalent interactions between the imidazolium moiety and the PhSO$_3$ group. In contrast to ***o*-7**, the most stable conformers of other regioisomers, *meta*-substituted ***m*-7** and *para*- substituted ***p*-7**, are the structures involving a π–π interaction like ***o*-7-B** (Schemes 1.S25, 1.S26, and 1.S30 in Chapter 1-4). This type of π–π interaction is a main factor in stabilizing the conformation of Koser-type reagents supported by crystalline structures,[24] and calculation studies.[25] Additionally, we calculated the conformation of mesityl-substituted **8**, which has almost the same steric demand around the iodine atom as that of ***o*-7** (Figure 1.5B). A local-minimum conformer possessing efficient interactions of mesityl and PhSO$_3$ groups like **8-A** was not found, and the optimized conformer **8-B** includes a π–π interaction like ***o*-7-B**. Thus, it is quite unusual that

***o*-7-A** would be a more stable conformer than ***o*-7-B** with a π–π interaction, which indicates that only the imidazolium moiety at the *ortho* position favorably attracts the $PhSO_3$ group via cation–π and cation-oxygen interactions.[26] When ArI(OAc)(*p*-$EtC_6H_4SO_3$) (**9**), which was generated from the reaction of **1a** with 4-$EtC_6H_4SO_3H$[27], was observed by ^1H NMR spectroscopy, the two Me groups on nitrogen atoms are anisochronous and each of singlet signals appear at 3.44 and 3.83 ppm (Scheme 1.3).[28] The signal of Me^A group interacting with *p*-$EtC_6H_4SO_3$ group would shift upfield compared with that of Me^B group due to cation-π interactions.[29]

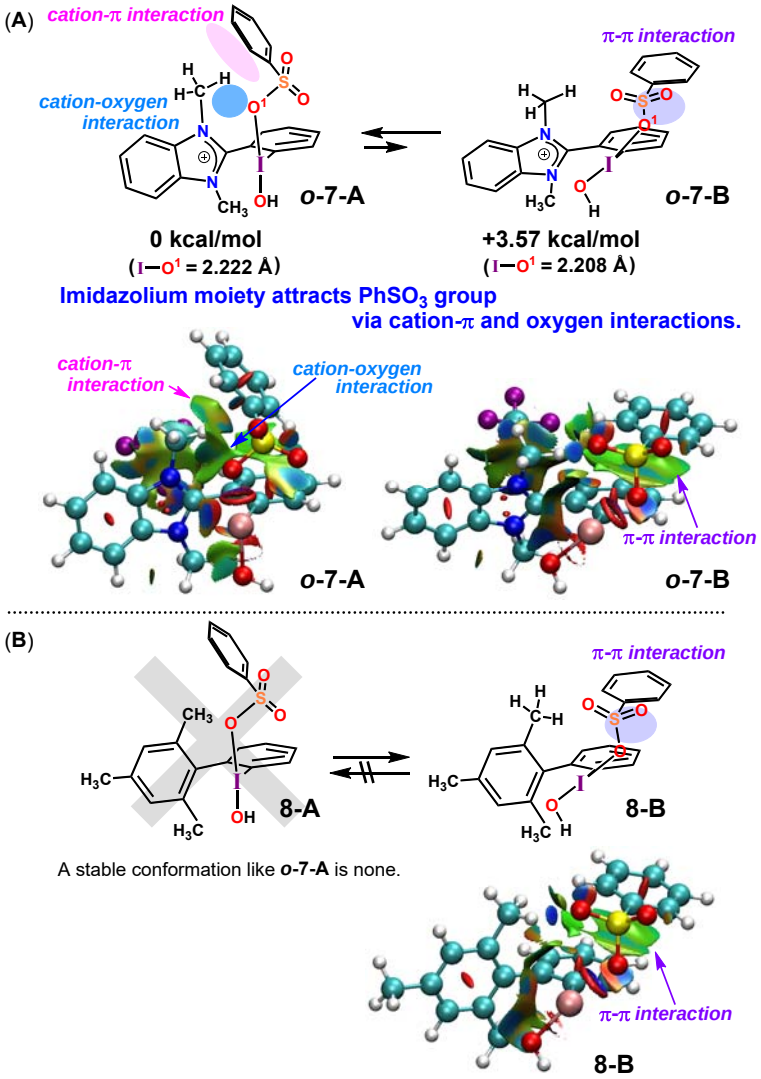
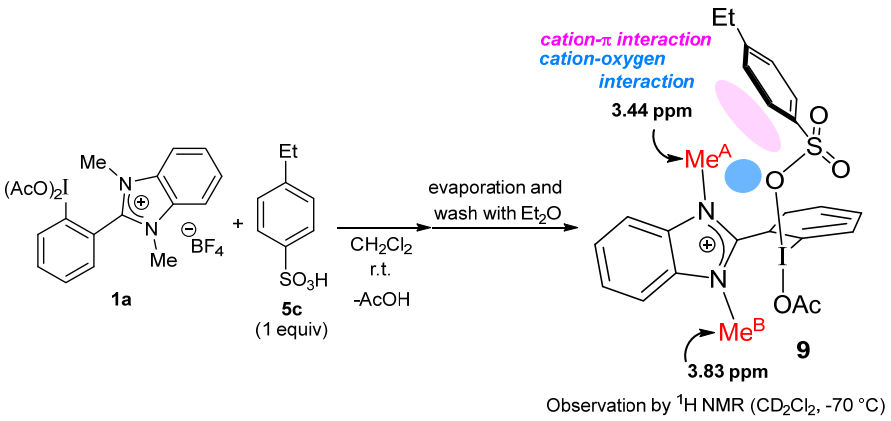


Figure 1.5. Noncovalent interaction analysis for selected conformers of $ArI(OH)OSO_2Ph$ **7**, **8**, and **9**. Color code for NCI analysis: red, repulsive; blue, attractive.



Scheme 1.3. Anisochronous two Me groups of **9** in ^{1}H NMR spectroscopy.

Tsuzuki revealed that strong noncovalent attractive forces in ion pairs such as imidazolium trifluoromethanesulfonate by ab initio calculation, and found that electrostatic and induction interactions were contributors.[10] Thus, we thought, in the present sulfonyloxylactonization, the sulfonyloxy anion dissociating from the iodine atom and acting as a nucleophile was restrained by noncovalent interactions with the imidazolium moiety. Generally, sulfonyloxy groups on iodine(III) atoms are kicked out either by intramolecular coordinative functional groups or by external ligands.[30] Thus, when adding γ-pyrone (**10**) as an external ligand, the behavior of the 4-Et$C_6H_4SO_3$ group of **9** by using ^{1}H NMR spectroscopy was observed (Figure 1.6A). Imidazolium sulfonate (**12**) was used as a reference compound to evaluate the interaction of the imidazolium cation with 4-Et$C_6H_4SO_3^-$ because two kinds of protons of the benzene ring of the 4-Et$C_6H_4SO_3$ group in **12** appear at a more upfield than those in Bu_4N salt (**13**) (Figure 1.6B, Charts A and B).[31,32] The treatment of **9** (Chart D) with γ-pyrone (**10**) as an external ligand caused a downfield shift of signals of **10**, which shows that the carbonyl oxygen coordinated to the iodine center (Chart C).[33] More importantly, signals of the 4-Et$C_6H_4SO_3$ group appeared in a more upfield compared with those of **9**, and the chemical shift values approximated those of **12**.[34] Therefore, these results suggest that 4-Et$C_6H_4SO_3^-$ is kicked out and trapped by noncovalent interactions with the imidazolium moiety, which generates **11**.[30d,35]

We propose a plausible reaction mechanism based on mechanistic studies (Scheme 1.4A). Ar$I(OAc)_2$ (**1a**) reacts with TsOH·H_2O to give ArI(OTs)OX (**6**) (X = H or Ac) (step I).[36] Notably, the imidazolium moiety strongly attracts the TsO group via cation-π and cation-oxygen interactions in **6** (Figure 1.5A). The noncovalent attractive interactions lead to abstraction and effective trap of TsO^- by the imidazolium moiety to generate the more electrophilic species **14** with trapped TsO^- (step II), and disturb the generation of **14′** with naked TsO^-. The electrophilic addition of **14** to the alkene moiety of **2b** gives iodonium intermediate **15** (step III).[37] A nucleophilic attack of the carboxyl group prior to TsO^- occurs at the benzylic carbon atom to afford **16** (step IV) because TsO^- is trapped by noncovalent attractive forces of the imidazolium moiety, which is supported by the experimental results shown in Figure 1.6. Finally, a substitution of the iodine atom by TsO^- produces 5-*exo* product (**4b**) (step V). In the case of step IV', a substitution of the iodine atom by the TsO^- in **15** gives intermediate **17**, and 6-*endo* product (**3b**) is afforded as a minor product (step V'). On the other hand, a path involving species **14′** with naked TsO^- could be also possible, giving 6-*endo* product

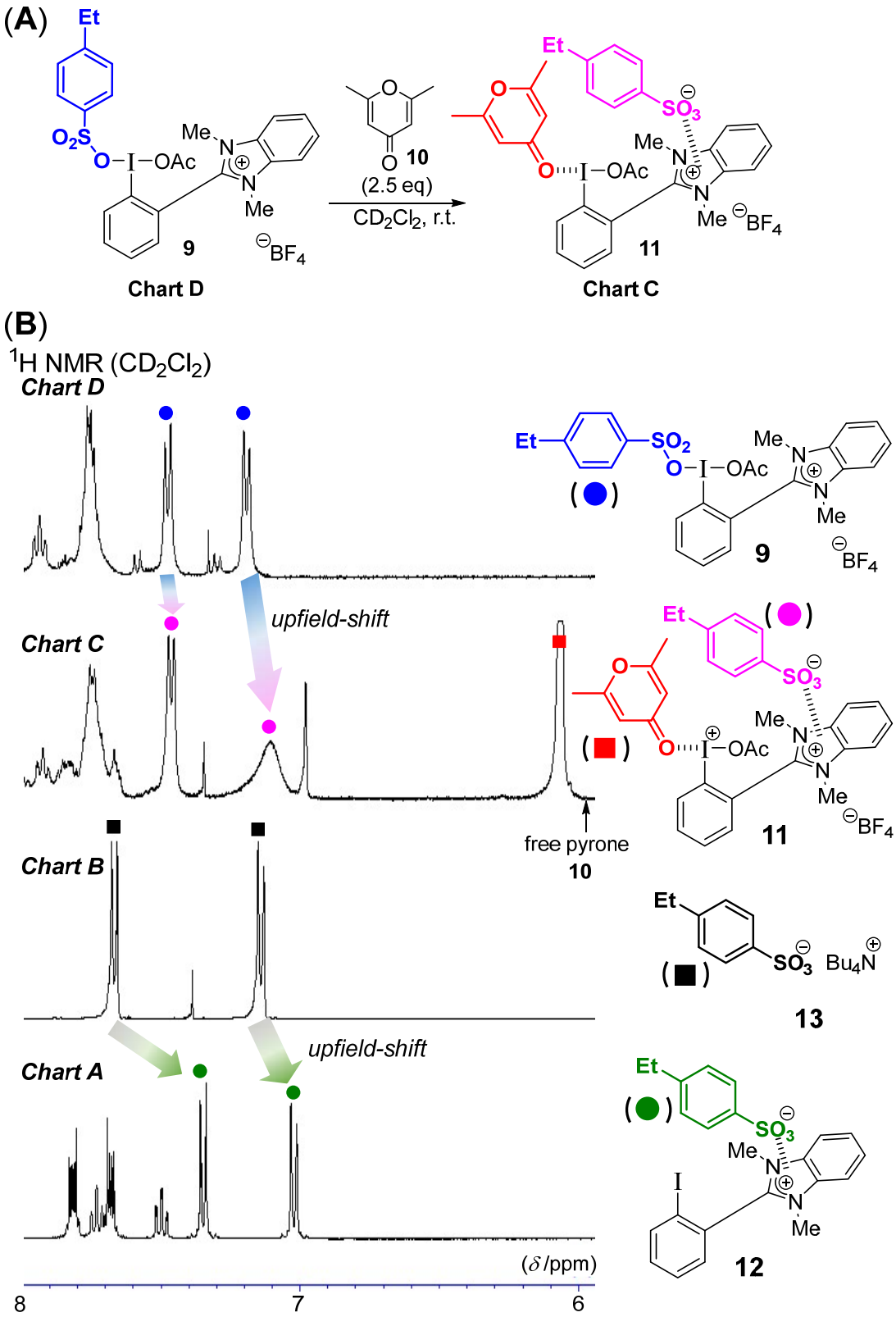
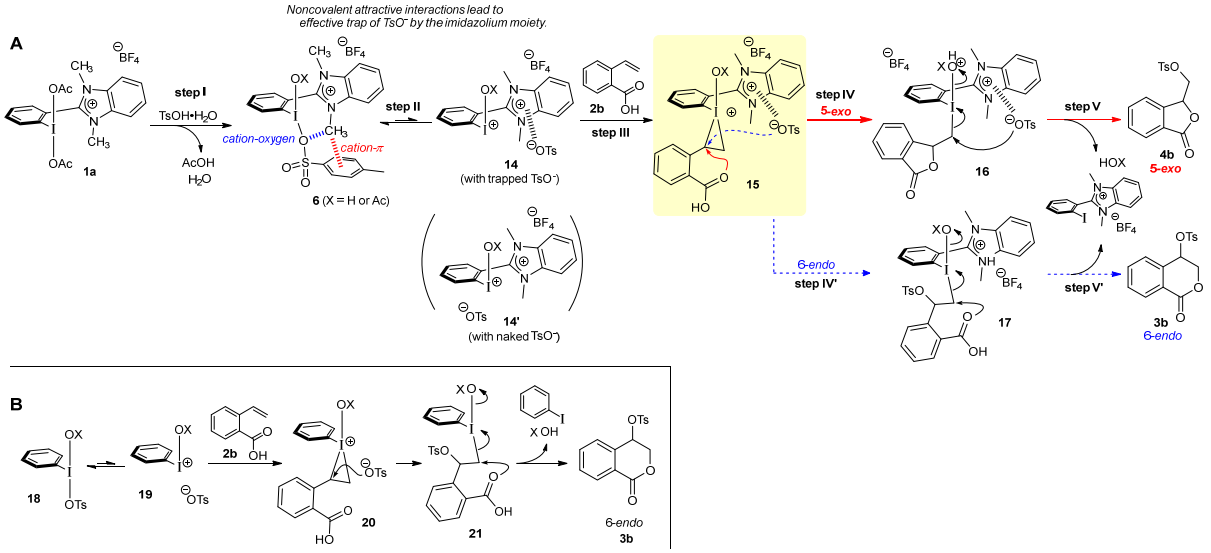


Figure 1.6. (A) Reaction of **9** with γ-pyrone **10** to give complex **11**. (B) Chart A: Bu_4N·4-$EtPhSO_3$ **13**. Chart B: Imidazolium 4-ethylbenzenesulfonate **12**. Chart C: Complex **11** generated from **9** with γ-pyrone **10**. Chart D: $ArI(OAc)OSO_2Ph$ **9**.

(**3b**) because naked TsO^- in prior to the carboxyl group can attack iodonium intermediate **15**. But, the noncovalent attractive interactions in **6** lead to effective trap of TsO^- to disturb the generation of **14′**. Therefore, the noncovalent attractive interactions between TsO and imidazolium moieties in **6** is critical to the regioselectivity. In the present sulfonyloxylactonization, carboxylic acids with electron-withdrawing groups gives excellent regioselectivity, and the regioselectivity in the reactions using carboxylic acids with electron-donating groups is slightly decreased (Table 1.2). Electron-donating groups in carboxylic acids enhance the stability of the corresponding iodonium intermediate to increase the rate of steps IV and IV′ so the regioselectivity slightly deteriorates. In the case of PhI(OTs)OX (**18**) (Scheme 1.4B), naked TsO^- preferentially attacks the iodonium moiety in intermediate **20** to give 6-*endo* product (**3b**). Therefore, the trapping of TsO^- by noncovalent interaction with the cationic imidazolium moiety significantly changes the reaction course.



Scheme 1.4. Proposed reaction mechanisms.

1-3. Conclusion

In conclusion, we discovered that the noncovalent interaction between the sulfonyloxy group and the cationic nitrogen-containing heterocyclic moiety substituted in the hypervalent iodines caused specific regioselectivity in the sulfonyloxylactonization of 2-vinyl benzoic acids. Hypervalent iodines bearing an imidazolium moiety exhibited 5-*exo* cyclization selectivity in contrast to the 6-*endo* selectivity shown by $PhI(OAc)_2$. ^1H NMR spectroscopy established **6** as the intermediate and DFT studies clarified the trapping of the sulfonyloxy group by the imidazolium moiety via noncovalent interactions such as cation-π and cation-oxygen interactions, which allowed a significant change in regioselectivity.

1-4. Experimantal Section

General

NMR spectra were recorded on JEOL JNM-400 (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR)

spectrometer. Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 for ^{1}H NMR) and residual $CHCl_3$ (δ = 77.16 for ^{13}C NMR) as an internal reference. New compounds were characterized by ^{1}H, ^{13}C, ^{13}C off-resonance techniques, COSY, HMQC, and HMBC. Infrared (IR) spectra were recorded on a JASCO FT/IR-6200 Fourier transform infrared spectrophotometer or METTLER TOLEDO ReactIR15. Column chromatography was performed with silica gel. Purification by recycle HPLC was performed on SHIMADZU recycle HPLC system (SPD-20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) and Japan Analytical Industry Co. (NEXT recycling preparative HPLC). Reactions were carried out in dry solvents under nitrogen atmosphere, unless otherwise stated. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), Wako Pure Chemical Industries, Ltd., and used after purification by distillation or used without purification for solid substrates. X-ray diffraction analysis was carried out by Rigaku XtaLAB Synergy with Hypix-6000HE.

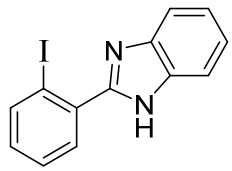
Materials

Dehydrated solvents were purchased from Wako Pure Chemical Industries and used as obtained. All sulfonic acids, *p*-TsOH•H_2O (**5a**), $PhSO_3H$ (**5b**), 4-ethylbenzenesulfonic acid (**5c**), *m*-xylenesulfonic acid (**5d**), *p*-chlorobenzenesulfonic acid (**5e**), 2-naphthalenesulfonic acid (hydrate) (**5f**), methanesulfonic acid (**5g**), ethanesulfonic acid (**5h**) were purchased and used as obtained. $PhI(OAc)_2$, PhI(OH)OTs, 1-butyl-3-methylimidazolium tetrafluoroborate, and pyrone (**10**) were purchased and used as obtained.
The preparation and characterization of new compounds were described below. Carboxylic acids **2d** (S. Ram, S. Shankar, K. Ajay, A. S. Chauhan, P. Das, *Chem. Commun.* **2020**, *56*, 10674.), **2e** (T. Ishida, M. Iwasaki, Y. Kazao, Y. Nishihara, *Org. Lett.* **2020**, *22*, 7343.), and **2i** (P. Dydio, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2013**, *52*, 3878.) were reported compounds.

Synthesis of Hypervalent Iodines $ArI(OAc)_2$

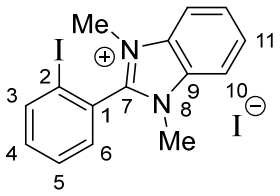
$ArI(OAc)_2$ (1a)

(S1) 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazole



This manipulation was carried out according to the reported method (I. H. Lee, E. H. Jeoung, M. M. Kreevoy, *J. Am. Chem. Soc.* **1997**, *119*, 2722). To the round-bottom flask was added polyphosphoric acid (81.6 g), 2-iodobenzoic acid (25.1 g, 101 mmol) and *o*-phenylenediamine (11.0 g, 102 mmol). The mixture was allowed to warm to 175-180 °C and stirred for 4 h. After cooling to room temperature, the reaction mixture was neutralized by 1 M NaOH aq to pH about 7. Then the solid was collected with Büchner funnel and washed with water. The collected solid was dried with an oven to give the titled product as a light brown solid (31.3 g, 97%). The spectral data was agreement with the reported data (Y. A. Vlasenko, P. S. Postnikov, M. E. Trusova, A. Shafir, V. V. Zhdankin, A. Yoshimura, M. S. Yusubov, *J. Org. Chem*. **2018**, *83*, 12056.).
^{1}H NMR (DMSO-d_6): 12.75 (br s, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.63-7.62 (m, 3H), 7.55 (t, J = 7.8 Hz, 1H), 7.29-7.23 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 152.5, 139.7, 139.6, 136.54, 131.40, 131.36, 131.29, 131.24, 131.16, 128.17, 128.12, 122.1, 97.4; HRMS (EI, 70 eV) Calculated ($C_{13}H_9N_2I$) 319.9811, Found: 319.9808

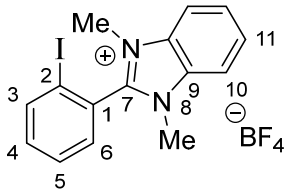
(S2) 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide



This manipulation was carried out according to the reported method (I. H. Lee, E. H. Jeoung, M. M. Kreevoy, *J. Am. Chem. Soc.* **1997**, *119*, 2722). To the microwave vial (20 mL volume) with a stirrer bar was added 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazole (2.56 g, 8.23 mmol) and methanol (8 mL). Iodomethane (2 mL) and NaOH powder (0.342 g, 8.55 mmol) were added to the reaction mixture, and then the vial was capped. The mixture was heated at 110 °C for 2 h by microwave irradiation. The precipitated solid was washed with ethanol to give a light brown color solid. The product was used at the next step without further purification (3.15 g, 83%).

mp: This compound was not melted and not decomposed at 300 °C.; IR: (KBr) 3025, 1485, 760 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 8.25 (d, J = 7.7 Hz, 1H, 3-H), 8.23-8.18 (m, 2H, 10-H), 7.89 (dd, J = 7.7, 1.4 Hz, 1H, 6-H), 7.85-7.80 (m, 3H, 5-H and 11-H), 7.61 (td, J = 7.7, 1.4 Hz, 1H, 4-H), 3.83 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, DMSO-d_6): 150.8 (s, C-7), 139.4 (d, C-3), 134.8 (d, C-4), 132.4 (d, C-6), 131.4 (s, C-9), 129.3 (d, C-5), 127.3 (d, C-11), 126.8 (s, C-2), 113.8 (d, C-10), 99.1 (s, C-1), 32.6 (q, CH_3 x 2); Analysis: $C_{15}H_{14}I_2N_2$ (476.10) Calcd: C, 37.84; H, 2.96; N, 5.88, Found: C, 37.58; H, 2.86; N, 5.81

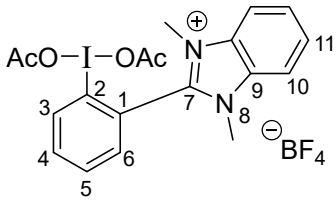
(S3) 2-(2-iodophenyl)-1,3-dimethyl-1H-benzo[d]imidazol-3-ium tetrafluoroborate



This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952-955.). To the solution of 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide (2.02 g, 4.23 mmol) in chloroform (45 mL) was added silver tetrafluoroborate (0.945 g, 4.85 mmol). The mixture was stirred at room temperature overnight. The reaction mixture was filtrated off and the obtained solid was extracted with hot chloroform. The obtained chloroform solution was evaporated to give a pale red solid. The product was used at the next step without further purification (1.88 g, 99%).

mp: 221-226 °C (decomposed); IR: (KBr) 3357, 3080, 1525, 1139 cm^{-1}; ^1H NMR (400 MHz, CD_3CN): 8.22 (d, J = 7.9 Hz, 1H, 3-H), 7.98-7.94 (m, 2H, 10-H), 7.83-7.77 (m, 3H, 5-H and 11-H), 7.65 (dd, J = 7.9, 1.9 Hz, 1H, 6-H), 7.59 (td, J = 7.9, 1.9 Hz, 1H, 4-H), 3.81 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, CD_3CN): 151.9 (s, C-7), 141.0 (d, C-3), 135.8 (d, C-4), 133.2 (d, C-6), 132.6 (s, C-2), 130.5 (d, C-5), 128.5 (d, C-11), 127.8 (s, C-9), 114.4 (d, C-10), 98.0 (s, C-1), 33.5 (q, CH_3 x 2); ^{19}F NMR (377 MHz, CD_3CN, external standard: TFA in D_2O): -151.8; HRMS: (EI, 70 eV) Calculated ($C_{15}H_{14}N_2I$): 349.2002 ($[M - BF_4]^+$), Found: 349.0197; Analysis: $C_{15}H_{14}BF_4IN_2$, Calcd: C, 41.32; H, 3.24; N, 6.43, Found: C, 40.99; H, 3.30; N, 6.32

(1a) 2-(2-(diacetoxy-λ^3-iodaneyl)phenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate



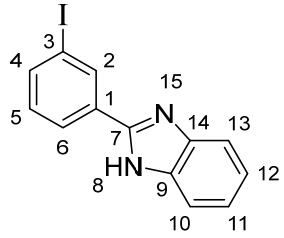
This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate (1.32 g, 3.2 mmol) and 9% peracetic acid (12 mL). The reaction mixture was stirred at 45 ºC for 12 h. After cooling to room temperature, the solvent was evaporated. Then, the precipitated solid was washed with acetic acid over 3 times. The solid was washed with diethyl ether (anhydrous) to remove acetic acid. The volatiles were evaporated to give the product as a white solid (1.17 g, 70%). The structure was determined by X-ray crystallography.

mp: 207-209 °C (decomposed); IR: (KBr) 1645, 1369, 1278, 1064 cm^{-1}; ^1H NMR (400 MHz, CD_3CN): 8.67 (d, J = 8.0 Hz, 1H, 3-H), 8.09 (t, J = 8.0 Hz, 1H, 5-H), 8.01 (t, J = 8.0 Hz, 1H, 4-H), 7.99-7.92 (3H, m, 6-H and 10-H), 7.86-7.78 (2H, m, 11-H), 3.88 (6H, s, Me x 2), 1.88 (6H, s, OAc x 2); ^{13}C NMR (100 MHz, CD_3CN): 177.8 (s, *C*OCH_3 x 2), 149.4 (s, C-7), 139.5 (d, C-3), 136.9 (d, C-4), 134.8 (d), 134.2 (d), 133.0 (s,

C-9), 128.8 (d, C-11), 125.9 (s, C-2), 123.7 (s, C-1), 114.7 (d, C-10), 34.2 (q, Me x 2), 20.3 (q, OAc x 2); ^{19}F NMR (377 MHz, CD_3CN, external standard: TFA in D_2O): -151.8; HRMS: (ESI) Calculated ($C_{19}H_{20}N_2O_4I$) 467.04623 ([M - BF_4]$^+$), Found: 467.04656; X-ray crystallographic data have been deposited at the Cambridge Crystallographic Centre: CCDC 2044394.

ArI(OAc)$_2$ (1b)

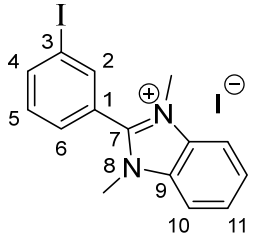
(S4) 2-(3-iodophenyl)-1*H*-benzo[*d*]imidazole



This manipulation was carried out according to the reported method (I. H. Lee, E. H. Jeoung, M. M. Kreevoy, *J. Am. Chem. Soc.* **1997**, *119*, 2722). To a round-bottom flask was added 3-iodobenzoic acid (1 mmol, 0.25 g), *o*-phenylenediamine (1 mmol, 0.11 g) and polyphosphoric acid (3.7 g). The mixture was stirred for 1.5 h at 175-180 ºC. The reaction mixture was allowed to room temperature and neutralized by 6% NaOH aqueous solution. After neutralizing viscous mixture, the precipitated solid was washed with water and dried to give the soil color product (0.298 g, 93%).

mp: 262-264 °C; IR: (KBr) 2913, 1439, 744 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 13.04 (br s, 1H, 8-H), 8.55 (s, 1H, 2-H), 8.19 (d, *J* = 7.9 Hz, 1H, 6-H), 7.85 (d, *J* = 7.9 Hz, 1H, 4-H), 7.67 (d, *J* = 7.7 Hz, 1H, 10-H or 13-H), 7.54 (d, *J* = 7.2 Hz, 1H, 10-H or 13-H), 7.36 (t, *J* = 7.9 Hz, 1H, 5-H), 7.28-7.16 (m, 2H, 11-H and 12-H); ^{13}C NMR (100 MHz, DMSO-d_6): 149.6 (s, C-7), 143.7 (s, C-9 or C-14), 138.3 (d, C-4), 135.0 (s, C-9 or C-14), 134.6 (d, C-2), 132.2 (s, C-1), 131.2 (d, C-5), 125.7 (d, C-6), 122.9 (d, C-11 or C-12), 122.0 (d, C-11 or C-12), 119.1 (d, C-10 or C-13), 111.6 (d, C-10 or C-13), 95.4 (s, C-3); HRMS: (EI, 70 eV) Calculated ($C_{13}H_9N_2I$) 319.9811, Found: 319.9806

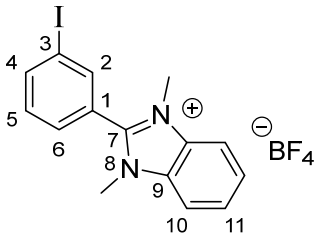
(S5) 2-(3-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide



This manipulation was carried out according to the reported method (I. H. Lee, E. H. Jeoung, M. M. Kreevoy, *J. Am. Chem. Soc.* **1997**, *119*, 2722). To the microwave vial (5 mL volume) with a stirrer bar was added 2-(3-iodophenyl)-1*H*-benzo[*d*]imidazole (0.300 g, 0.937 mmol) and methanol (1 mL). Iodomethane (0.45 mL) and NaOH powder (0.060 g, 1.5 mmol) were added to the reaction mixture, and then the vial was capped. The mixture was heated at 110 °C for 2 h by microwave irradiation. The precipitated solid was washed with ethanol to give a light brown color solid. The product was used at the next step without further purification (0.345 g, 77%).

mp: 298-299 °C; IR: (KBr) 1519, 1483, 1455 cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): 8.31 (s, 1H, 2-H), 8.21 (d, *J* = 8.0 Hz, 1H, 4-H), 8.14 (dd, *J* = 5.9, 3.0 Hz, 2H, 10-H), 7.94 (d, *J* = 8.0 Hz, 1H, 6-H), 7.77 (dd, *J* = 5.9, 3.0 Hz, 2H, 11-H), 7.58 (t, *J* = 8.0 Hz, 1H, 5-H), 3.89 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, DMSO-d_6): 148.7 (s, C-7), 141.5 (d, C-4), 138.5 (d, C-2), 131.6 (s, C-9), 131.2 (d, C-5), 130.1 (d, C-6), 126.7 (d, C-11), 123.0 (s, C-3), 113.4 (d, C-10), 95.8 (s, C-1), 32.8 (q, CH_3 x 2); HRMS: (EI, 70 eV) Calculated ($C_{15}H_{14}N_2I$) 349.0202 ([M - I]$^+$), Found: 349.0199

(S6) 2-(3-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate

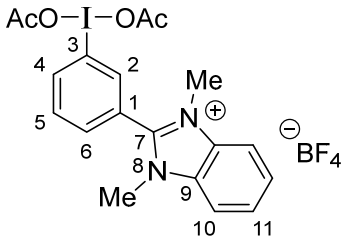


This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952-955.). To the solution of 2-(3-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide (0.959 g, 2.01 mmol) in $CHCl_3$ (20 mL) was added silver tetrafluoroborate (0.440 g, 2.26 mmol). The mixture was stirred at room temperature overnight. The reaction mixture was filtrated off and the obtained solid was extracted with hot chloroform. The obtained chloroform solution

was evaporated to give a white solid The product was used at the next step without further purification (0.665 g, 76%).

mp: 230-234 °C; IR: (KBr) 1520, 1486, 1057 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD): 8.25-8.23 (m, 2H, 2-H and 6-H), 8.04-7.98 (m, 2H, 10-H), 7.84 (dt, *J* = 8.1, 1.3 Hz, 1H, 4-H), 7.81-7.76 (m, 2H, 11-H), 7.57 (t, *J* = 8.1 Hz, 1H, 5-H), 3.96 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, CD_3OD): 150.3 (s, C-7), 143.6 (d), 140.0 (d), 133.5 (s, C-9), 132.5 (d, C-5), 131.0 (d, C-4), 128.4 (d, C-11), 124.3 (s, C-1), 114.2 (d, C-10), 95.7 (s, C-3), 33.3 (q, CH_3 x 2); ^{19}F NMR (377 MHz, CD_3OD, external standard: TFA in D_2O): -154.9; HRMS: (EI, 70 eV) Calculated ($C_{15}H_{14}N_2I$): 349.2002 ($[M - BF_4]^+$), Found: 349.0196; Analysis: $C_{15}H_{14}BF_4IN_2$, Calcd: C, 41.32; H, 3.24; N, 6.43, Found: C, 41.21; H, 3.21; N, 6.41

(1b) 2-(3-(diacetoxy-λ^3-iodaneyl)phenyl)-1,3-dimethyl-1H-benzo[d]imidazol-3-ium tetrafluoroborate

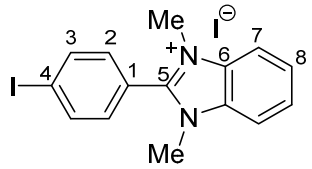


This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added 2-(3-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate (0.418 g, 0.959 mmol) and 9% peracetic acid (4 mL). The reaction mixture was stirred at 45 ºC for 12 h. After cooling to room temperature, the solvent was evaporated. Then, the precipitated solid was washed with acetic acid over 3 times. The solid was washed with diethyl ether (anhydrous) to remove acetic acid. The remained ether was evaporated to give the product as a white solid (0.355 g, 67%).

mp: 221-224 °C; IR: (KBr) 1643, 1274, 1056 cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN): 8.56-8.53 (m, 1H, 4-H), 8.49 (t, *J* = 1.7 Hz, 1H, 2-H), 8.00 (dt, *J* = 7.9, 1.7 Hz, 1H, 6-H), 7.96-7.92 (m, 3H, 5-H and 10-H), 7.78 (dd, *J* = 6.3, 3.4 Hz, 2H, 11-H), 3.90 (s, 6H, 8-Me x 2), 1.98 (s, 6H, $COCH_3$ x 2); ^{13}C NMR (100 MHz, CD_3CN): 177.6 (s, *C*OCH_3 x 2), 149.3 (s, C-7), 140.0 (d, C-4), 137.8 (d, C-2), 135.0 (d, C-6), 133.1 (d, C-5), 133.1 (s, C-9), 128.4 (d, C-11), 124.1 (s, C-1), 122.0 (s, C-3), 114.2 (d, C-10), 33.9 (q, 8-Me x 2), 20.4 (q, CO*C*H_3 x 2); ^{19}F NMR (377 MHz, CD_3CN, external standard: TFA in D_2O): -151.3; HRMS: (ESI) Calculated ($C_{19}H_{20}N_2O_4I$) 467.0462 ($[M - BF_4]^+$), Found: 467.0448

ArI(OAc)$_2$ (1c)

(S7) 2-(4-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide

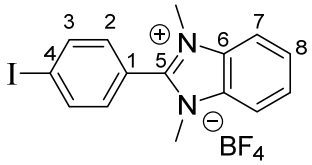


This manipulation was carried out according to the reported method (I. H. Lee, E. H. Jeoung, M. M. Kreevoy, *J. Am. Chem. Soc.* **1997**, *119*, 2722). To the vial (5 mL volume) with a stirrer bar was added 2-(4-iodophenyl)-1*H*-benzo[*d*]imidazole (0.785 g, 2.45 mmol) and methanol (3 mL). Iodomethane (0.6 mL) and NaOH powder (0.130 g, 3.25 mmol) were added to the reaction mixture, and then the vial was capped. The mixture was heated at 110 °C for 8 h by microwave irradiation. The precipitated solid was washed with ethanol to give a light brown color solid. The product was used at the next step without further purification (0.833 g, 71%).

Caution: Dimethyl ether (b.p. -24 °C) is generated during the reaction. Be careful to the pressure in a vial.

mp: This compound does not melt and not decompose at 300 °C., IR: (KBr) 1593, 1463, 766 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): 8.18 (d, *J* = 8.2 Hz, 2H, 3-H), 8.13 (dd, *J* = 6.3, 3.4 Hz, 2H, 7-H), 7.77 (dd, *J* = 6.3, 3.4 Hz, 2H, 8-H), 7.68 (d, *J* = 8.2 Hz, 2H, 2-H), 3.89 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, DMSO-d_6): 149.7 (s, C-5), 138.3 (d, C-3), 132.4 (d, C-2), 131.7 (s, C-6), 126.7 (d, C-8), 120.4 (s, C-1), 113.4 (d, C-7), 101.7 (s, C-4), 32.8 (q, CH_3 x 2); HRMS: (FAB) Calculated ($C_{15}H_{14}N_2I$): 349.2002 ($[M - I]^+$), Found: 349.0198

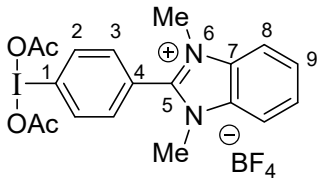
(S8) 2-(4-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate



This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952-955.). To the solution of 2-(4-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide (1.42 g, 2.98 mmol) in CH_3CN (30 mL) was added silver tetrafluoroborate (0.641 g, 3.29 mmol). The mixture was stirred at room temperature overnight. The reaction mixture was filtrated off, and additionally the obtained solid was extracted with CH_3CN. The combined CH_3CN solution was evaporated to give a grey solid. The obtained product was used at the next step without further purification (1.11 g, 85%).

mp: This compound does not melt and not decompose at 300 °C.; IR: (KBr) 1486, 1070, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 8.19 (d, J = 8.5 Hz, 2H, 3-H), 8.13 (dd, J = 6.0, 3.1 Hz, 2H, 7-H), 7.77 (dd, J = 6.0, 3.1 Hz, 2H, 8-H), 7.68 (d, J = 8.5 Hz, 2H, 2-H), 3.89 (s, 6H, Me x 2); ^{13}C NMR (100 Hz, DMSO-d_6): 149.7 (s, C-5), 138.4 (d, C-3), 132.4 (d, C-2), 131.8 (s, C-6), 126.7 (d, C-8), 120.4 (s, C-1), 113.4 (d, C-7), 101.6 (s, C-4), 32.7 (q, Me); ^{19}F NMR (377 MHz, DMSO-d_6, external standard: TFA in D_2O): -148.4; HRMS: (EI, 70 eV) Calculated ($C_{15}H_{14}N_2I$): 349.2002 ($[M - BF_4]^+$), Found: 349.0206; Analysis: $C_{15}H_{14}BF_4IN_2$, Calcd: C, 41.32; H, 3.24; N, 6.43, Found: C, 41.24; H, 3.14; N, 6.44

(1c) 2-(4-(diacetoxy-λ^3-iodaneyl)phenyl)-1,3-dimethyl-1H-benzo[d]imidazol-3-ium tetrafluoroborate

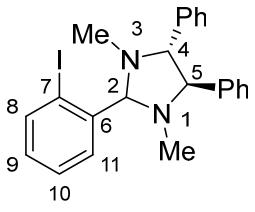


This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added 2-(4-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium tetrafluoroborate (0.172 g, 0.393 mmol) and 9% peracetic acid (1.5 mL). The reaction mixture was stirred at 45 ºC for 12 h. After cooling to room temperature, the solvent was evaporated. Then, the precipitated solid was washed with acetic acid over 3 times. The solid was washed with diethyl ether (anhydrous) to remove acetic acid. The remained ether was evaporated to give the product as a white solid (0.100 g, 46%).

mp: 289-293 °C; IR: (KBr) 1644, 1276, 1062 cm^{-1}; ^1H NMR (400 MHz, CD_3CN): 8.51 (d, J = 8.6 Hz, 2H, 2-H), 7.93 (dd, J = 6.3, 3.1 Hz, 2H, 8-H), 7.89 (d, J = 8.6 Hz, 2H, 3-H), 7.78 (dd, J = 6.3, 3.1 Hz, 2H, 9-H), 3.89 (s, 6H, 6-Me x 2), 1.99 (s, 6H, $COCH_3$ x 2); ^{13}C NMR (100 MHz, CD_3CN): 177.7 (s, *C*OCH_3 x 2), 149.7 (s, C-5), 137.1 (d, C-2), 133.9 (d, C-3), 133.1 (s, C-7), 128.4 (d, C-9), 126.1 (s, C-4), 125.1 (s, C-1), 114.2 (d, C-8), 33.9 (q, 6-Me x 2), 20.5 (q, CO*C*H_3 x 2); ^{19}F NMR (377 MHz, CD_3CN, external standard: TFA in D_2O): -151.8; HRMS: (ESI) Calculated ($C_{19}H_{20}N_2O_4I$): 467.0462 ($[M - BF_4]^+$), Found: 467.0464

ArI(OAc)$_2$ ((R,R)-1d)

(S9) (*4R*,*5R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine

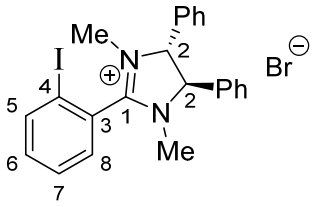


This manipulation was carried out according to the reported method (V. Jurčík, R. Wilhelm, *Tetrahedron: Asymmetry* **2006**, *17*, 801.). The mixture of 2-iodobenzaldehyde (1.06 g, 4.57 mmol) and (*1R*,*2R*)-N,N-dimethyl-1,2-diphenylethanediamine (1.10 g, 4.57 mmol) was grinded with spatula for 10 min. The mixture exothermically became solid. The reaction mixture was purified by flash column chromatography (hexane/EtOAc) to give a white solid containing 2-iodobenzaldehyde (1.12 g). This mixture was used next reaction without further purification. The further purification was carried out for the characterization.

mp: 148-149 °C; IR: (KBr) 2790, 1602, 1008, 748, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.92 (dd, 1H, J = 7.8 Hz, 11-H), 7.88 (dd, 1H, J = 7.8 Hz, 8-H), 7.47 (t, 1H, J = 7.8 Hz, 10-H), 7.29-7.19 (m, 10H, Ph x 2), 7.06 (td, 1H, J = 7.8 Hz, 9-H), 5.13 (s, 1H, 2-H), 3.87 (d, 1H, J = 8.7 Hz), 3.61 (d, 1H, J = 8.7 Hz), 2.16 (s,

3H, NMe), 1.91 (s, 3H, NMe); ^{13}C NMR (100 MHz, $CDCl_3$): 141.5 (s, C-6), 140.1 (s), 139.6 (d, C-8), 139.4 (s), 131.1 (d, C-9), 130.1 (d, C-11), 128.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.5 (d), 102.2 (s, C-7), 90.8 (d, C-2), 77.9 (d), 77.3 (d), 37.6 (q, NMe), 36.3 (q, NMe); $[\alpha]_D^{20}$ = +84.9 (c = 0.62, $CHCl_3$); HRMS: (CI, 70 eV) Calculated ($C_{23}H_{24}N_2I$) : 455.0984 ([M + H]), Found: 455.0989

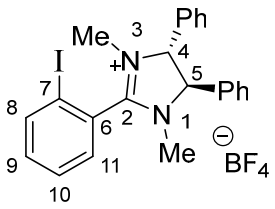
(S10) (4*R*,5*R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium bromide



This manipulation was carried out according to the reported method (V. Jurčík, R. Wilhelm, *Tetrahedron: Asymmetry* **2006**, *17*, 801.). To the solution of (*4R*,*5R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine (3.56 g, 7.84 mmol) in DME (23 mL) was added N-bromoacetamide (1.09 g, 7.90 mmol). The reaction mixture was stirred at room temperature overnight. After diethyl ether was added to the reaction mixture, a white solid was precipitated. The supernatant solution was removed and the precipitated solid was washed with diethyl ether. The solid was dried under reduced pressure to give a product as a white solid (4.14 g, 99%).

mp: 145-150 °C (sublimation); IR: (KBr) 3404, 1602, 760, 703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.81 (dd, *J* = 7.7, 1.4 Hz, 1H, 8-H), 8.03 (d, *J* = 8.2 Hz, 1H, 5-H), 7.87 (d, *J* = 6.8 Hz, 2H), 7.76 (t, *J* = 7.7 Hz, 1H, 7-H), 7.51-7.40 (m, 9H), 5.92 (d, *J* = 13.3 Hz, 1H, 2-H), 5.04 (d, *J* = 13.3 Hz, 1H, 2-H), 2.99 (s, 3H, NMe), 2.78 (s, 3H, NMe); ^{13}C NMR (100 MHz, $CDCl_3$): 167.0 (s, C-1), 139.4 (d, C-5), 134.3 (s, C-3), 134.2 (d, C-6), 133.0 (d, C-8), 132.5 (s), 130.4 (d), 130.3 (d), 130.1 (d), 129.8 (d), 129.7 (d), 128.6 (d), 128.3 (s), 93.9 (s, C-4), 76.6 (d, C-2), 74.7 (d, C-2), 33.8 (q, Me), 32.8 (q, Me); $[\alpha]_D^{20}$ = +93.7 (c = 0.54, $CHCl_3$); HRMS: (FAB+, 70 eV) Calculated ($C_{23}H_{22}N_2I$) 453.0828 ([M - Br]$^+$), Found: 453.0834

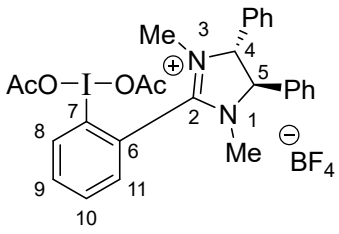
(S11) (*4R*,*5R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium



This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952-955.). To the solution of (*4R*,*5R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium bromide (0.853 g, 1.60 mmol) in chloroform (16 mL) was added silver tetrafluoroborate (0.411 g, 2.11 mmol). The mixture was stirred at room temperature overnight. The resulting residue was filtrated off and the solution was evaporated. After the evaporation, the crude product was purified by silica gel chromatography (MeOH) to give a white solid (0.617 g, 72%).

mp: 169-172 °C; IR (KBr): 1607, 1059 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.13 (dd, *J* = 7.6, 1.4 Hz, 1H, 11-H), 8.05 (d, *J* = 7.2 Hz, 1H, 8-H), 7.74 (t, *J* = 7.6 Hz, 1H, 10-H), 7.60 (d, *J* = 7.7 Hz, 2H, Ph-*o*), 7.52-7.40 (m, 9H, 9-H, Ph-*m* and *p*), 5.56 (d, *J* = 12.8 Hz, 1H), 5.02 (d, *J* = 12.8 Hz, 1H), 2.85 (s, 3H, NMe), 2.76 (s, 3H, NMe); ^{13}C NMR (100 MHz, $CDCl_3$): 166.9 (s, C-2), 139.6 (d, C-8), 134.32 (d), 134.28 (s, Ph-*i*), 132.7 (s, Ph-*i*), 131.6 (d, C-11), 130.5 (d), 130.4 (d), 130.2 (d), 129.9 (d), 129.8 (d), 128.9 (d), 128.5 (d), 128.3 (s, C-6), 93.4 (s, C-7), 76.2 (d), 74.5 (d), 33.0 (q, NMe), 32.7 (q, NMe); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -152.0; $[\alpha]_D^{20}$ = +91.1 (c = 2.35, $CHCl_3$); HRMS: (FAB+, 70 eV) Calculated ($C_{23}H_{22}N_2I$): 453.0828 ([M - BF_4]$^+$), Found: 453.0823; Analysis: $C_{23}H_{22}BF_4IN_2$, Calcd: C, 51.14; H, 4.11; N, 5.19, Found: C, 51.02; H, 4.06; N, 5.15

((*R*,*R*)-1d) (*4R*,*5R*)-2-(2-(diacetoxy-λ^3-iodaneyl)phenyl)-1,3-dimethyl-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium tetrafluoroborate

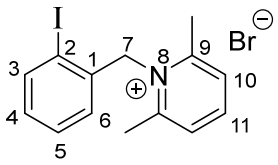


This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added (*4R*,*5R*)-2-(2-iodophenyl)-1,3-dimethyl-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium tetrafluoroborate (0.541 g, 1.00 mmol) and 9% peracetic acid (5 mL). The reaction mixture was stirred at 45 ºC for 12 h under N_2. After cooling to room temperature, the solvent was evaporated. Then, the precipitated solid was washed with diethyl ether (anhydrous) under N_2. The solid was further washed with anhydrous diethyl ether in a glove box. Remained ether was evaporated to give the product as a white solid (0.585 g). The hypervalent iodine included a small amount of starting material.

mp: 101-103 °C; IR: (KBr) 3425, 1602, 1056 cm^{-1}; $[\alpha]_D^{20}$ = +79.2 (c = 0.68, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): 8.57 (d, *J* = 7.7 Hz, 1H, 11-H), 8.48 (d, *J* = 7.7 Hz, 1H, 8-H), 8.07 (t, *J* = 7.7 Hz, 1H, 10-H), 7.84 (t, *J* = 7.7 Hz, 1H, 9-H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.53-7.41 (m, 6H), 7.32 (t, *J* = 3.4 Hz, 2H), 5.58 (d, *J* = 12.8 Hz, 1H), 5.05 (d, *J* = 12.8 Hz, 1H), 2.91 (s, 3H, NMe), 2.77 (s, 3H, NMe), 1.93 (broadening singlet, 6H, OAc x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 177.1 (s, *C*OCH_3), 165.1 (s, C-2), 138.3 (d, C-8), 135.3 (d, C-9), 134.6 (d, C-10), 133.9 (s), 132.8 (d, C-11), 132.1 (s), 130.7 (d), 130.5 (d), 130.10 (d), 130.07 (d), 129.1 (d), 128.3 (d), 126.3 (s, C-7), 120.3 (s, C-6), 76.1 (d), 75.0 (d), 34.1 (q, NMe), 33.3 (q, NMe), 20.3 (q, CO*C*H_3); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -151.6; HRMS: (ESI+) Calculated ($C_{27}H_{28}IN_2O_4$) 571.1088 ($[M - BF_4]^+$), Found: 571.1059

ArI(OAc)₂ (1e)

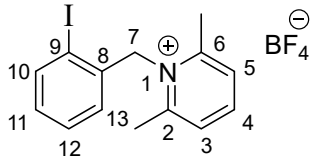
(S12) 1-(2-iodobenzyl)-2,6-dimethylpyridin-1-ium bromide



This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952.). To the solution of 1-(bromomethyl)-2-iodobenzene (1.19 g, 4.01 mmol) in CH_3CN (2 mL) was added 2,6-lutidine (0.504 g, 4.70 mmol). The reaction mixture was stirred at reflux temperature for 28 h. After cooling to room temperature, to the reaction mixture was added ether and the precipitated solid was washed with ether to give the product as a pale red solid (0.714 g, 44%).

mp: The product was sublimated during 260-274 °C.; IR: (KBr) 2978, 1619, 1489, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.51 (t, *J* = 7.7 Hz, 1H, 11-H), 8.10 (d, *J* = 7.7 Hz, 2H, 10-H), 8.00 (d, *J* = 7.7 Hz, 1H, 3-H), 7.30 (t, *J* = 7.7 Hz, 1H, 5-H), 7.11 (t, *J* = 7.7 Hz, 1H, 4-H), 6.11 (d, *J* = 7.7 Hz, 1H, 6-H), 5.82 (s, 2H, 7-H_2), 2.89 (s, 6H, 9-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 156.5 (s, C-9), 146.1 (d, C-11), 140.9 (d, C-3), 133.4 (s, C-2), 130.7 (d, C-4), 129.5 (d, C-5), 129.1 (d, C-10), 124.5 (d, C-6), 97.2 (s, C-1), 62.5 (t, C-7), 22.3 (q, 9-Me); HRMS: (EI, 70 eV) Calculated ($C_{14}H_{14}IN$): 323.0171 ($[M - H - Br]^+$), Found: 323.0167

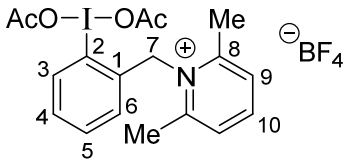
(S13) 1-(2-iodobenzyl)-2,6-dimethylpyridin-1-ium tetrafluoroborate



This manipulation was carried out according to the reported method (W. Qian, E. Jin, W. Bao, Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952-955.). To a solution of 1-(2-iodobenzyl)-2,6-dimethylpyridin-1-ium bromide (1.50 mmol, 0.606 g) in chloroform (15 mL) was added silver tetrafluoroborate (1.6 mmol, 0.311 g). The mixture was stirred at room temperature for 12 h. After the reaction, black precipitates were filtered off and the solvent was evaporated to give the product as white solid (0.577 g, 94%).

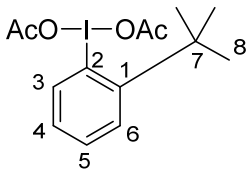
mp: 188-190 °C; IR: (KBr) 1621, 1494, 1083 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) 8.34 (t, 1H, 4-H), 7.99 (d, 1H, 10-H), 7.85 (d, 2H, 3-H and 5-H), 7.31 (t, 1H, 12-H), 7.10 (t, 1H, 11-H), 6.08 (d, 1H, 13-H), 5.68 (s, 2H, 7-H_2), 2.74 (s, 6H, 2-Me and 6-Me); ^{13}C NMR: (100 MHz, $CDCl_3$) 156.4 (s, C-2 and C-6), 145.9 (d, C-4), 140.8 (d, C-10), 133.5 (s, C-8), 130.7 (d, C-11), 129.7 (d, C-12), 128.6 (d, C-3), 124.4 (d, C-13), 97.0 (s, C-9), 61.7 (t, C-7), 21.5 (q, 2-Me and 6-Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -153.7; HRMS: (FAB+) Calculated ($C_{14}H_{15}NI$): 324.0249 ($[M - BF_4]^+$), Found: 324.0248; Analysis: $C_{14}H_{15}BF_4IN$ (410.99) Calcd: C, 40.91; H, 3.68; N, 3.41, Found: C, 40.63; H, 3.62; N, 3.44

(1e) 1-(2-(diacetoxy-λ^3-iodaneyl)benzyl)-2,6-dimethylpyridin-1-ium tetrafluoroborate



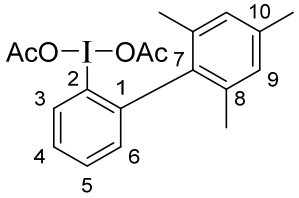
This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added 1-(2-iodobenzyl)-2,6-dimethylpyridin-1-ium tetrafluoroborate (0.290 g, 0.704 mmol) and 9% peracetic acid (3 mL). The reaction mixture was stirred at room temperature overnight. After the reaction, the solvent was evaporated. Then, the precipitated solid was washed with acetic acid briefly. The solid was washed with diethyl ether (anhydrous) to remove acetic acid. Remained ether was evaporated to give the product as a white solid (0.322 g, 87%). The structure was determined by X-ray crystallography.
mp: 121-124 ºC; IR (KBr): 3421, 1565, 1084 cm^{-1}; ^1H NMR (400 MHz, CD_3CN): 8.41 (m, 2H, 3-H and 10-H), 7.90 (d, J = 7.7 Hz, 2H, 9-H), 7.61-7.53 (m, 2H, 4-H and 5-H), 6.46 (d, J = 7.2 Hz, 1H, 6-H), 6.13 (s, 2H, 7-H), 2.70 (s, 6H, 8-Me x 2), 1.96 (s, 6H, OAc x 2); ^{13}C NMR (100 MHz, CD_3CN): 177.3 (s, *C*OCH_3), 158.0 (s, C-8), 147.1 (d), 139.2 (d), 134.7 (d), 133.7 (s, C-2), 132.4 (d), 129.7 (d, C-9), 126.2 (d, C-6), 124.0 (s, C-1), 59.6 (t, C-7), 21.7 (q, 8-Me), 20.3 (q, CO*C*H_3); ^{19}F NMR (377 MHz, CD_3CN, external standard: TFA in D_2O): -151.8; HRMS: (ESI) Calculated ($C_{18}H_{21}NO_4I$): 442.05098 ($[M - BF_4]^+$), Found: 442.04964; X-ray crystallographic data was deposited at the Cambridge Crystallographic Centre: CCDC 2044652

(1f) (2-(*tert*-butyl)phenyl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 1-(*tert*-butyl)-2-iodobenzene (0.212 g, 0.815 mmol) and 9% peracetic acid (3.5 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated and the sluggish liquid was washed with hexane briefly to give the product as a white solid (0.188 g, 61%).
mp: 91-95 °C; IR: (KBr) 1650, 1366, 1287, 1262 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.44 (d, J = 7.7 Hz, 1H, 3-H), 7.74 (d, J = 7.7 Hz, 1H, 6-H), 7.59 (t, J = 7.7 Hz, 1H, 5-H), 7.26 (t, J = 7.7 Hz, 1H, 4-H), 1.98 (s, 6H, $COCH_3$ x 2), 1.54 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 176.6 (s, *C*OCH_3), 150.2 (s, C-1), 142.9 (d, C-3), 132.6 (d, C-5), 129.2 (d, C-4), 128.8 (d, C-6), 122.5 (s, C-2), 38.0 (s, *C*$(CH_3)_3$), 31.6 (q, C(*C*$H_3)_3$), 20.6 (q, CO*C*H_3); HRMS: (ESI) Calculated ($C_{14}H_{19}O_4NaI$) 401.0220 ($[M + Na]^+$), Found: 401.0224

(1g) (2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate

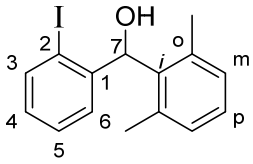


To 2'-iodo-2,4,6-trimethyl-1,1'-biphenyl (0.346 g, 1.07 g) was added 9% peracetic acid (4 mL) and stirred at room temperature overnight. AcOH was evaporated under vacuum condition, then the resulting solid was washed with ether and dried to give a white solid (0.285 g, 60%).
mp: 154-156 °C; IR: (KBr) 1644, 1269, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.39 (dd, J = 8.5, 1.2 Hz, 1H, 3-H), 7.70 (td, J = 7.5, 1.2 Hz, 1H, 5-H), 7.47-7.42 (m, 2H, 4-H and 6-H), 6.92 (s, 2H, 9-H), 2.34 (s, 3H, 10-Me), 2.01 (s, 6H, 8-Me x 2), 1.92 (s, 6H, $COCH_3$ x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 176.4 (s, *C*OCH_3), 145.2 (s, C-2), 138.6 (s, C-10), 138.2 (d, C-3), 138.0 (s, C-7), 136.5 (s, C-8), 132.9 (d, C-5), 131.2 (d, C-4 or C-6), 129.6 (d, C-4 or C-6), 128.4 (d, C-

9), 127.0 (s, C-1), 21.3 (q, 8-Me), 20.6 (q), 20.4 (q); HRMS: (ESI) Calculated ($C_{19}H_{21}O_4INa$) 463.0377 ([M + Na]$^+$), Found: 463.0394

ArI(OAc)$_2$ (1h)

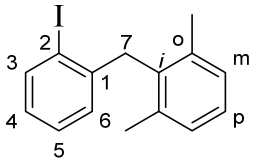
(S14) (2,6-dimethylphenyl)(2-iodophenyl)methanol



Magnesium turnings (6.7 mmol, 0.18 g) was placed into a three-necked flask equipped with a dropping funnel. The flask was flame-dried under reduced pressure and filled with N_2. THF (8 mL) was added to the flask and the solution of 2-bromo-*m*-xylene (6.7 mmol, 1.28 g) in THF (3.6 mL) was added dropwise over 20 min. Additional THF was added to the flask and the reaction mixture was stirred for 1 h at room temperature. Then, the flask was cooled to 0 °C and 2-iodobenzaldehyde (6.7 mmol, 1.28 g) in THF (2.4 mL) was added dropwise over 16 min. The reaction mixture was allowed to room temperature and stirred for 2.5 h. Then, the reaction was quenched by saturated aqueous Na_2CO_3 and the aqueous layer was extracted with diethyl ether. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (1.42 g, 84%).

mp: 92-93 °C; IR: (KBr) 3308 (OH) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.88 (d, *J* = 7.7 Hz, 1H, 6-H), 7.30-7.21 (m, 2H, 3-H and 4-H), 7.14 (t, *J* = 7.7 Hz, 1H, *p*), 7.04 (d, *J* = 7.7 Hz, 2H, *m*), 6.97 (td, *J* = 7.7, 2.4 Hz, 1H, 5-H), 6.20 (d, *J* = 4.7 Hz, 1H, 7-H), 2.49 (d, *J* = 4.7 Hz, 1H, OH), 2.28 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 144.0 (s, C-1), 140.2 (d, C-6), 137.4 (s, *o*), 137.0 (s, *i*), 129.6 (d, *m*), 129.5 (d), 129.2 (d), 128.3 (d), 127.9 (d), 99.3 (s, C-2), 76.5 (d, C-7), 21.7 (q, CH_3 x 2); HRMS: (EI, 70 eV) Calculated ($C_{15}H_{15}OI$) 338.0168, Found 338.0162

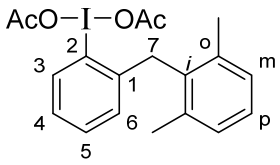
(S15) 2-(2-iodobenzyl)-1,3-dimethylbenzene



This manipulation was carried out according to the reported method (M. Yasuda, Y. Onishi, M. Ueba, T. Miyai, A. Baba, *J. Org. Chem.* **2001**, *66*, 7741.). To a solution of (2,6-dimethylphenyl)(2-iodophenyl)methanol (1.0 mmol, 0.337 g) in dichloromethane (1 mL) was added indium trichloride (0.16 mmol, 0.0371 g) and chlorodiphenylsilane (2 mmol, 0.41 mL). The mixture was stirred at room temperature for 2 h. Then, the reaction mixture was diluted by diethyl ether and water. The mixture was extracted with diethyl ether. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The crude product was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 26 mm silica gel) to give the titled product as a white solid (0.265 g, 83%).

mp: 60-65 °C, IR: (KBr) 2946, 1467, 1011, 775 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.88 (dd, *J* = 7.7, 1.0 Hz, 1H, 6-H), 7.15-7.07 (m, 4H, 4-H, *m* and *p*), 6.88 (t, 1H, *J* = 7.7 Hz, 5-H), 6.50 (d, 1H, *J* = 7.7 Hz, 3-H), 3.97 (s, 2H, 7-H_2), 2.17 (s, 6H, CH_3 x 2); ^{13}C NMR (100 MHz, $CDCl_3$) 142.0 (s, C-1), 139.3 (d, C-6), 137.5 (s), 136.6 (s), 128.5 (d, *p*), 128.3 (d, *m*), 127.9 (d), 127.8, (d), 126.8 (d), 102.0 (s, C-2), 41.5 (t, C-7), 20.2 (q, CH_3 x 2); HRMS: (FAB) Calculated ($C_{15}H_{15}I$) 322.0219, Found: 322.0128

(1h) (2-(2,6-dimethylbenzyl)phenyl)-λ^3-iodanediyl diacetate



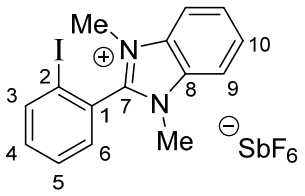
To the flame-dried flask was added 2-(2-iodobenzyl)-1,3-dimethylbenzene (0.974 g, 3.02 mmol) and 9% peracetic acid (10 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated and the precipitated solid was washed with hexane. The remained hexane was evaporated to give the product as a white solid (1.21 g, 91%).

mp: 126-129 °C; IR: (KBr) 1654 (C=O), 1278, 666 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$): 8.24 (d, *J* = 7.6 Hz, 1H, 3-H), 7.40 (t, *J* = 7.6 Hz, 1H, 5-H), 7.27 (t, *J* = 7.6 Hz, 1H, 4-H), 7.17 (t, *J* = 7.2 Hz, 1H, *p*), 7.11 (d, *J* = 7.2 Hz, 2H, *m*), 6.76 (d, *J* = 7.6 Hz, 1H, 6-H), 4.37 (s, 2H, C-7), 2.21 (s, 6H, *o*-Me x 2), 2.02 (s, 6H, $COCH_3$ x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 176.5 (s, *C*OCH_3), 141.3 (s, C-2), 137.6 (s, C-1), 137.5 (d, C-3), 134.8 (s, C-*o*), 132.9 (d, C-5), 128.9 (d), 128.52 (d), 128.48 (d), 127.8 (s, C-*i*), 127.2 (d), 38.3 (t, C-7), 20.4 (q, CO*C*H_3), 20.1 (q, *o*-Me); HRMS: (ESI) Calculated ($C_{19}H_{21}IO_4Na$): 463.03767 ([M + Na]$^+$) Found: 463.03639

ArI(OAc)$_2$ (1k)

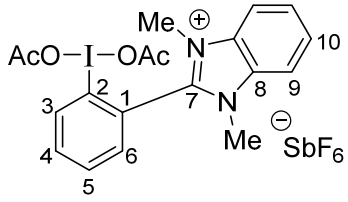
(S16) 2-(2-iodophenyl)-1,3-dimethyl-1H-benzo[d]imidazol-3-ium hexafluoroantimonate



To the solution of 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide (0.946 g, 1.99 mmol) in chloroform (20 mL) was added silver hexafluoroantimonate (0.815 g, 2.37 mmol). The mixture was stirred at room temperature overnight. The reaction mixture was filtrated off and the obtained solid was extracted with hot chloroform. The obtained chloroform solution was evaporated to give a pale yellow solid. The product was used at the next step without further purification (1.12 g, 96%).

mp: 175-182 °C; IR: (KBr) 1524, 1487, 1452, 756 cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN): 8.22 (d, *J* = 8.2 Hz, 1H, 3-H), 7.96 (dd, *J* = 6.3, 3.4 Hz, 2H, 9-H), 7.83-7.77 (m, 3H, 5-H and 10-H), 7.66 (dd, *J* = 8.2, 1.4 Hz, 1H, 6-H), 7.59 (td, *J* = 8.2, 1.4 Hz, 1H, 4-H), 3.81 (s, 6H, Me x 2); ^{13}C NMR (100 MHz, CD_3CN): 152.0 (s, C-7), 141.1 (d, C-3), 135.8 (d, C-4), 133.2 (d, C-6), 132.7 (s, C-8), 130.6 (d, C-5), 128.6 (d, C-10), 127.8 (s, C-1), 114.5 (d, C-9), 98.0 (s, C-2), 33.6 (q, Me); HRMS: (FAB, 70 eV) Calculated ($C_{15}H_{14}N_2I$): 349.2002 ([M - SbF_6]$^+$), Found: 349.0198

(1k) 2-(2-(diacetoxy-λ^3-iodaneyl)phenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium hexafluoroantimonate

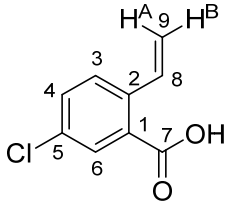


This manipulation was carried out according to the reported method (M. Uyanik, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2013**, *52*, 9215.). To the flame-dried flask was added 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium hexafluoroantimonate (0.879 g, 1.50 mmol) and 9% peracetic acid (7 mL). The reaction mixture was stirred at 45 ºC over 12 h. After cooling to room temperature, the solvent was evaporated. Then, the precipitated solid was washed with acetic acid over 3 times. The solid was washed with diethyl ether (anhydrous) to remove acetic acid. Remained ether was evaporated to give the product as a white solid (0.661 g, 63%).

mp: 117-132 °C (decomposed); IR: (KBr) 1646 (C=O), 1274, 658 cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN): 8.66 (d, *J* = 7.7, 1.3 Hz, 1H, 3-H), 8.08 (td, *J* = 7.7, 1.3 Hz, 1H, 5-H), 8.01 (td, *J* = 7.7, 1.8 Hz, 1H, 4-H), 7.97-7.93 (m, 3H, 6-H and 9-H), 7.83-7.79 (m, 2H, 10-H), 3.87 (s, 6H, NMe x 2), 1.89 (s, 6H, OAc x 2); ^{13}C NMR (100 MHz, CD_3CN): 177.8 (s, *C*OCH_3), 149.4 (s, C-7), 139.5 (d, C-3), 136.9 (d, C-4), 134.8 (d, C-5), 134.2 (d, C-6), 133.0 (s, C-8), 128.8 (d, C-10), 125.9 (s, C-2), 123.7 (s, C-1), 114.7 (d, C-9), 34.2 (q, NMe), 20.3 (q, CO*C*H_3); HRMS: (ESI) Calculated ($C_{19}H_{20}N_2O_4I$): 467.0462 ([M - BF_4]$^+$), Found: 467.0476

Synthesis of 2-Vinylbenzoic Acids (2)

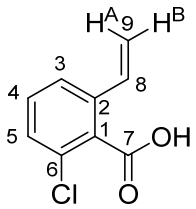
(2a) 5-chrolo-2-vinylbenzoic acid



To a solution of methyl 5-chrolo-2-vinylbenzoate (0.195 g, 0.99 mmol) in a THF/MeOH/H_2O (4:1:1) mixture (6 mL) was added LiOH (0.0806 g, 3.37 mmol). The reaction mixture was stirred at 70 °C overnight. After cooled to room temperature, the mixture was diluted by water. Then, THF and MeOH were removed under a reduced pressure. The aqueous layer was washed by CH_2Cl_2 and acidified by 1 M HCl aq, and then, the target benzoic acid was precipitated. The resulting solid was extracted by CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated to give a white solid (0.158 g, 88%). This is known compound and spectroscopic data were identical with those from the reported literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$): 11.85 (br s, 1H, COOH), 8.03 (d, J = 2.2 Hz, 1H, 6-H), 7.58-7.47 (m, 3H), 5.67 (d, J = 17.4 Hz, 1H, 9-H^A), 5.42 (d, J = 11.1 Hz, 1H, 9-H^B); ^{13}C NMR (100 MHz, $CDCl_3$): 172.0, 139.2, 135.0, 133.5, 133.4, 131.3, 129.1, 128.3, 117.7; HRMS: (EI, 70 eV) Calculated ($C_9H_7ClO_2$): 182.0135; Found: 182.0131

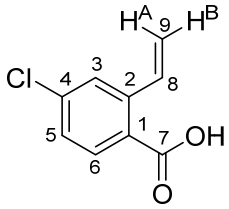
(2b) 6-chloro-2-vinylbenzoic acid



To a solution of methyl 6-chloro-2-vinylbenzoate (0.278 g, 1.41 mmol) in a THF/MeOH/H_2O (4:1:1) mixture (6.4 mL) was added LiOH (0.0962 g, 4.02 mmol). The reaction mixture was stirred at 70 °C overnight. After cooled to room temperature, the mixture was diluted by water. Then, THF and MeOH were removed under a reduced pressure. The aqueous layer was washed by CH_2Cl_2 and acidified by 1 M HCl aq, and then, the target benzoic acid was precipitated. The resulting solid was extracted by CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated to give a white solid (0.124 g, 48%).

mp: 99-101 °C; IR: (KBr) 3018 (O-H), 1705 (C=O), 1282 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 11.72 (br s, 1H, COOH), 7.54-7.50 (m, 1H, 4-H), 7.39-7.34 (m, 2H, 3-H and 5-H), 6.88 (dd, J = 17.3, 11.0 Hz, 1H, 8-H), 5.82 (d, J = 17.3 Hz, 1H, 9-H^A), 5.47 (d, J = 11.0 Hz, 1H, 9-H^B); ^{13}C NMR (100 MHz, $CDCl_3$): 172.9 (s, C-7), 137.2 (s, C-2), 132.8 (d, C-8), 131.3 (s), 131.03 (s), 130.96 (d), 128.8 (d), 124.0 (d, C-4), 118.9 (t, C-9); HRMS: (EI, 70 eV) Calculated ($C_9H_7ClO_2$) 182.0135, Found: 182.0134

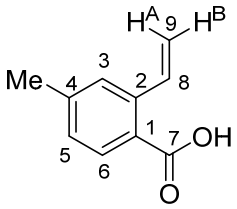
(2c) 4-chloro-2-vinylbenzoic acid



A sealable reactor vessel was charged with methyl 4-chloro-2-vinylbenzoate (0.551 g, 2.80 mmol), lithium hydroxide (0.186 g, 7.78 mmol), a THF/methanol/water (4:1:1) mixture (10 ml), sealed and stirred at 70 °C overnight. The reaction mixture was diluted with water, followed by evaporation of THF and methanol under reduced pressure. Then, the water phase residue was washed with DCM, acidified with 1M HCl to pH = 3, and extracted with DCM. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under vacuum, yielding 0.451 g (89%) of the titled product. This procedure was referred to the reported literature.[2]

mp: 152-153 °C; IR: (KBr) 2817 (OH), 1685 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.00 (d, J = 8.4 Hz, 1H, 6-H), 7.58-7.51 (m, 2H, 3-H and 8-H), 7.34 (dd, J = 8.4, 2.2 Hz, 1H, 5-H), 5.69 (d, J = 17.4 Hz, 1H, 9-H^A), 5.44 (d, J = 10.6 Hz, 1H, 9-H^B); ^{13}C NMR (100 MHz, $CDCl_3$): 172.0 (s, C-7), 142.6 (s, C-2), 139.7 (s, C-4), 135.1 (d, C-8), 133.0 (d, C-6), 127.85 (d), 127.80 (d), 125.4 (s, C-1), 118.2 (t, C-9); HRMS: (EI, 70 eV) Calculated ($C_9H_7ClO_2$): 182.0135; Found: 182.0132

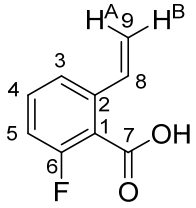
(2f) 4-methyl-2-vinylbenzoic acid



To a solution of methyl 5-chrolo-2-vinylbenzoate (0.124 g, 0.70 mmol) in a THF/MeOH/H_2O (4:1:1) mixture (4 mL) was added LiOH (0.0539 g, 2.25 mmol). The reaction mixture was stirred at 70 °C overnight. After cooled to room temperature, the mixture was diluted by water. Then, THF and MeOH were removed under a reduced pressure. The aqueous layer was washed by CH_2Cl_2 and acidified by 1 M HCl aq, and then, the target benzoic acid was precipitated. The resulting solid was extracted by CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated to give a white solid (0.103 g, 90%). This is known compound and spectroscopic data were identical with those from literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$): 12.46 (br s, 1H, COOH), 7.97 (d, J = 8.3 Hz, 1H), 7.60 (dd, J = 17.4, 10.9 Hz, 1H, 8-H), 7.41 (s, 1H, 3-H), 7.18 (d, J = 8.3 Hz, 1H), 5.66 (d, J = 17.4 Hz, 1H, 9-H^A), 5.37 (d, J = 10.9 Hz, 1H, 9-H^B), 2.43 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): 173.1, 144.0, 140.9, 136.5, 131.7, 128.5, 128.5, 124.4, 116.6, 21.8; HRMS: (EI, 70 eV) Calculated ($C_{10}H_{10}O_2$) 162.0681, Found: 162.0677

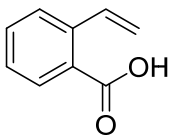
(2g) 6-fluoro-2-vinylbenzoic acid



To a solution of methyl 6-fluoro-2-vinylbenzoate (0.402 g, 2.04 mmol) in a THF/MeOH/H_2O (4:1:1) mixture (4 mL) was added LiOH (0.132 g, 5.52 mmol). The reaction mixture was stirred at 70 °C overnight. After cooled to room temperature, the mixture was diluted by water. Then, THF and MeOH were removed under a reduced pressure. The aqueous layer was washed by CH_2Cl_2 and acidified by 1 M HCl aq, and then, the target benzoic acid was precipitated. The resulting solid was extracted by CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated to give a white solid (0.337 g, 99%).

mp: 126-127 °C; IR: (KBr) 2998 (OH), 1707 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.47-7.39 (m, 2H, 3-H and 4-H), 7.11-7.02 (m, 2H, 8-H and 5-H), 5.78 (d, J = 17.4 Hz, 1H, 9-H^A), 5.44 (d, J = 10.6 Hz, 1H, 9-H^B); ^{13}C NMR (100 MHz, $CDCl_3$): 170.5 (s, C-7), 160.6 (s, d, $^1J_{CF}$ = 253 Hz, C-6), 139.5 (s, C-2), 133.5 (d, d, $^4J_{CF}$ = 2.5 Hz, C-8), 132.5 (d, d, $^3J_{CF}$ = 9.0 Hz, C-4), 122.0 (d, d, $^4J_{CF}$ = 3.3 Hz, C-3), 118.9 (s, $^2J_{CF}$ = 14.7 Hz, C-1), 118.6 (t, C-9), 115.3 (d, d, $^2J_{CF}$ = 22.1 Hz, C-5); ^{19}F NMR (377 MHz, $CDCl_3$, external standard:TFA in D_2O): -115.36; HRMS: (EI, 70 eV) Calculated ($C_9H_7FO_2$) 166.0430, Found: 166.0428

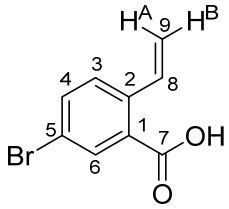
(2h) 2-vinylbenzoic acid



To a dried 100 mL three necked round bottom flask equipped with a reflux condenser and a dropping funnel was added magnesium metal turnings (0.378 g, 16 mmol). THF (30 mL) was added to the flask. The solution of 2-bromostyrene (2.76 g, 15 mmol) in THF was added dropwise by dropping funnel into the flask at room temperature. After exothermic reaction, the mixture was stirred at 70 °C for 2 h. Then, the mixture was allowed to room temperature and poured onto dry ice in a beaker. The mixture was washed with ether, and then, water was added poured into the beaker. The water phase was acidified to pH ~ 1 with 1 N HCl aq and extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure to yield 2-vinylbenzoic acid (1.54 g, 69%). The spectral data accorded with reference data.[3]

^{1}H NMR (400 MHz, $CDCl_3$): 11.93 (br s, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.63-7.54 (m, 3H), 7.38 (t, J = 7.6 Hz, 1H), 5.68 (dd, J = 17.4, 1.3 Hz, 1H), 5.40 (dd, J = 11.0, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.3, 140.8, 136.2, 133.3, 131.5, 127.8, 127.7, 127.2, 117.0; HRMS: (EI, 70 eV) Calculated ($C_9H_8O_2$): 148.0524, Found: 148.0522

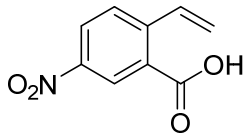
(2j) 5-bromo-2-vinylbenzoic acid



A sealable reactor vessel was charged with methyl 5-bromo-2-vinylbenzoate (0.125 g, 0.518 mmol), lithium hydroxide (0.0435 g, 1.82 mmol), a THF/methanol/water (4:1:1) mixture (3 ml), sealed and stirred at 70 °C overnight. The reaction mixture was diluted with water, followed by evaporation of THF and methanol under reduced pressure. Then, the water phase residue was washed with DCM, acidified with 1M HCl to pH = 3, and extracted with DCM. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under vacuum, yielding 0.105 g (89%) of the titled product. This procedure was referred by the reported literature.[2]

mp: 134-135 °C; IR: (KBr) 2995 (OH), 1698 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.18 (d, J = 1.9 Hz, 1H, 6-H), 7.66 (dd, J = 8.7, 1.9 Hz, 1H, 4-H), 7.54-7.47 (m, 2H, 3-H and 8-H), 5.68 (d, J = 17.4 Hz, 1H, 9-H^A), 5.42 (d, J = 11.1 Hz, 1H, 9-H^B); ^{13}C NMR (100 MHz, $CDCl_3$): 171.9 (s, C-7), 139.7 (s, C-2), 136.3 (d, C-4), 135.1 (d, C-8), 134.2 (d, C-6), 129.3 (d, C-3), 128.7 (s, C-1), 121.4 (s, C-5), 117.8 (t, C-9); HRMS: (EI, 70 eV) Calculated ($C_9H_7BrO_2$): 225.9629, Found: 225.9630

(2k) 5-nitro-2-vinylbenzoic acid

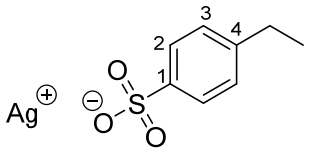


A sealable reactor vessel was charged with methyl 5-nitro-2-vinylbenzoate (0.603 g, 2.9 mmol), lithium hydroxide (0.817 g, 34 mmol), a THF/methanol/water (4:1:1) mixture (10 ml), sealed and stirred at rt overnight. The reaction mixture was diluted with water, followed by evaporation of THF and methanol under reduced pressure. Then, the water phase residue was washed with DCM, acidified with 1M HCl to pH = 3, and extracted with DCM. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under vacuum, yielding 0.519 g (92%) of the titled product. This procedure was referred to the following literature and the NMR data were agreement with the reported data.[2]

^1H NMR (400 MHz, $CDCl_3$): 8.92 (d, J = 2.4 Hz, 1H), 8.39 (dd, J = 8.7, 2.4 Hz, 1H), 7.80 (d, J = 8.7 Hz, 1H), 7.64 (dd, J = 17.3, 11.4 Hz, 1H), 5.86 (d, J = 17.3 Hz, 1H), 5.63 (d, J = 11.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 170.9, 146.9, 146.7, 134.4, 129.0, 127.9, 127.7, 126.9, 121.2; HRMS: (EI, 70 eV) Calculated ($C_9H_7NO_4$): 193.0375, Found: 193.0371

Syntheses of ethylbenzenesulfonate salts 12 and 13

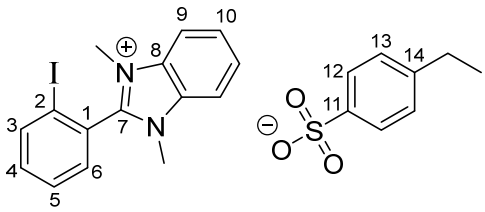
silver 4-ethylbenzenesulfonate



To a solution of 4-ethylbenzenesulfonic acid (2.08 g, 11.2 mmol) in deionized H_2O (16 mL) was added $AgNO_3$ (1.96 g, 11.5 mmol). The mixture was stirred over night at room temperature. H_2O in the reaction mixture was evaporated and the precipitated solid was washed with small amount of deionized water. Then the solid was dried with dried N_2 flow to give a white solid (1.25 g, 37%). This procedure was referred by the following report.[4]

mp: This compound was decomposed and did not melt during 200-297 °C; IR: (KBr) 2894, 1406, 1189, 1038, 1011 cm^{-1}; ^1H NMR (400 MHz, D_2O): 7.75 (d, J = 7.5 Hz, 2H, 2-H), 7.42 (d, J = 7.5 Hz, 2H, 3-H), 2.72 (q, J = 7.6 Hz, 2H, CH_2CH_3), 1.23 (t, J = 7.6 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, D_2O): 165.9 (s, C-1), 156.8 (s, C-4), 145.4 (d, C-3), 142.6 (d, C-2), 45.3 (t, CH_2CH_3), 31.9 (q, CH_2CH_3); Analysis: $C_8H_9AgO_3S•1/3H_2O$ (299.09) Calcd: C, 32.13; H, 3.26, Found: C, 32.21; H, 3.24

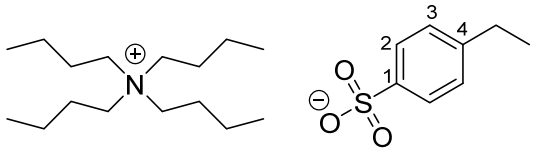
(12) 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium 4-ethylbenzenesulfonate



To a solution of 2-(2-iodophenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium iodide (0.0949 g, 0.199 mmol) in $CHCl_3$ (2 mL) was added silver 4-ethylbenzenesulfonate (0.0695 g, 0.0237 mmol) under N_2 atmosphere. The mixture was stirred over night at room temperature. The reaction mixture was filtrated off to remove AgI and the $CHCl_3$ solution was evaporated under reduced pressure. The product was washed with dried THF to give a white solid (0.0579 g, 54%).

mp: 163-165 ºC; IR: (KBr) 3518, 1219, 1194, 1035, 1012, 676 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2): 8.10 (m, 2H, 3-H and 6-H), 7.80 (dd, *J* = 6.3, 3.2 Hz, 2H, 9-H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.67 (dd, *J* = 6.3, 3.2 Hz, 2H, 10-H), 7.49 (td, *J* = 7.7, 1.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H, 12-H), 7.01 (d, *J* = 8.2 Hz, 2H, 13-H), 3.81 (s, 6H, Me x 2), 2.59 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 1.18 (t, *J* = 7.6 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, CD_2Cl_2): 151.3 (s, C-7), 145.3 (s), 140.1 (d), 135.0 (d), 134.0 (d), 132.1 (s, C-8), 130.2 (d), 127.7 (d), 127.5 (d), 127.4 (s, C-1), 126.0 (d, C-12), 113.6 (d, C-9), 97.2 (s, C-2), 33.2 (q, NMe x 2), 29.0 (t, *C*H$_2$CH$_3$), 15.8 (q, CH$_2$*C*H$_3$); ^1H NMR (400 MHz, CD_3CN): 8.20 (d, *J* = 7.7 Hz, 1H, 3-H), 7.97-7.95 (m, 2H, 9-H), 7.78-7.73 (m, 4H, 5-H, 6-H and 10-H), 7.59-7.53 (m, 3H, 4-H and 12-H), 7.13 (d, *J* = 7.7 Hz, 2H, 13-H), 3.80 (s, 6H, NMe x 2), 2.62 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 1.19 (t, *J* = 7.6 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, CD_3CN): 151.9 (s, C-7), 147.1 (s), 145.7 (s), 140.9 (d, C-3), 135.7 (d), 133.4 (d), 132.6 (s, C-8), 130.4 (d), 128.4 (d), 128.0 (d), 127.8 (s, C-1), 126.7 (d, C-12), 114.4 (d, C-9), 98.1 (s, C-2), 33.5 (q, NMe x 2), 29.1 (t, *C*H$_2$CH$_3$), 16.0 (q, CH$_2$*C*H$_3$); Analysis: $C_{23}H_{23}IN_2O_3S$ (534.41) Calcd: C, 51.69; H, 4.34; N, 5.24, Found: C, 51.36; H, 4.44; N, 5.24

(13) tetrabutylammonium 4-ethylbenzenesulfonate



To a solution of Bu_4NBr (0.0676 g, 0.210 mmol) in $CHCl_3$ (2 mL) was added silver 4-ethylbenzenesulfonate (0.0702 g, 0.240 mmol) under N_2 atmosphere. The mixture was stirred over night at room temperature. The reaction mixture was filtrated off to remove AgI and the $CHCl_3$ solution was evaporated under reduced pressure to give a white solid (0.0859 g, 96%).

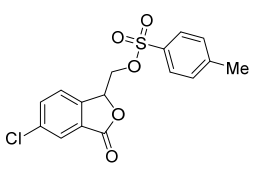
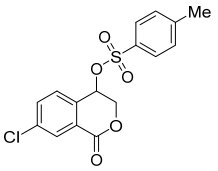
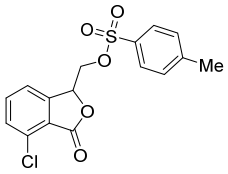
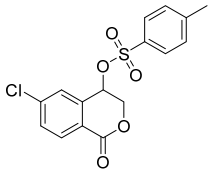
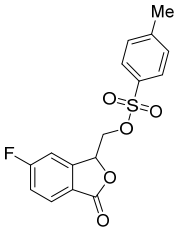
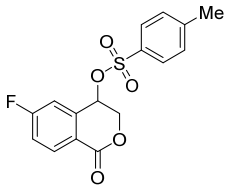
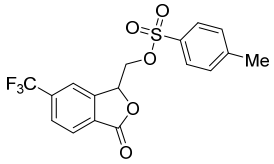
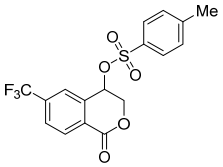
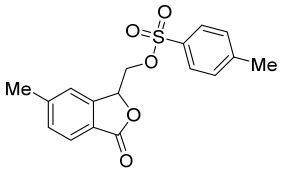
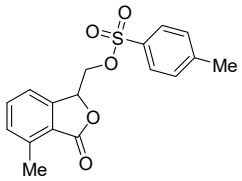
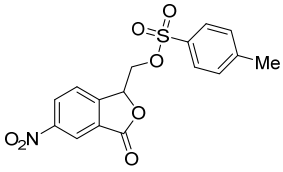
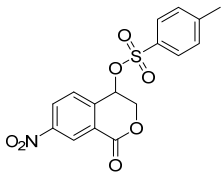
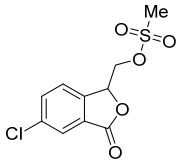
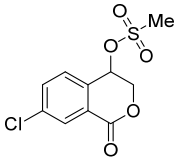
mp: 85-88 ºC; IR: (KBr) 2963, 2873, 1638, 1487, 1461, 1190 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.80 (d, *J* = 8.2 Hz, 2H, 2-H), 7.13 (d, *J* = 8.2 Hz, 2H, 3-H), 3.24-3.20 (m, 8H, C*H*$_2$CH$_2$CH$_2$CH$_3$ x 4), 2.62 (q, *J* = 7.6 Hz, 2H, 4-C*H*$_2$CH$_3$), 1.61-1.53 (m, 8H, CH$_2$C*H*$_2$CH$_2$CH$_3$ x 4), 1.42-1.32 (m, 8H, CH$_2$CH$_2$C*H*$_2$CH$_3$ x 4), 1.19 (t, *J* = 7.6 Hz, 3H, 4-CH$_2$C*H*$_3$), 0.95 (t, *J* = 7.5 Hz, 12H, CH$_2$CH$_2$CH$_2$C*H*$_3$ x 4); ^{13}C NMR (100 MHz, $CDCl_3$): 145.1 (s), 144.8 (s), 127.3 (d, C-3), 126.3 (d, C-2), 58.7 (t, *C*H$_2$CH$_2$CH$_2$CH$_3$), 28.8 (t, 4-*C*H$_2$CH$_3$), 24.0 (t, CH$_2$*C*H$_2$CH$_2$CH$_3$), 19.7 (t, CH$_2$CH$_2$*C*H$_2$CH$_3$), 15.7 (q, 4-CH$_2$*C*H$_3$), 13.7 (q, CH$_2$CH$_2$CH$_2$*C*H$_3$); Analysis: $C_{24}H_{45}NO_3S$ (427.69) Calcd: C, 67.40; H, 10.61; N, 3.28, Found: C, 67.17; H, 10.71; N, 3.33

Products

The preparation and characterization of new compounds were described below. Products **4ha** and **3ha** were reported compounds (The spectral data was agreement with the reference[15]). Compounds **3ia** and **3ab** could not be isolated because they were decomposed by a silica gel column chromatography.

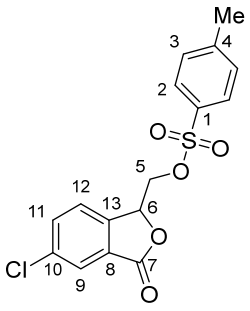
List of X-ray crystal structures

The structures of following products were determined by X-ray diffraction analysis.

4a (from 2a and 5a)  CCDC 2044374	**3a (from 2a and 5a)**  CCDC 2044375	**4ba (from 2b and 5a)**  CCDC 2044376
3ca (from 2c and 5a)  CCDC 2044377	**4da (from 2d and 5a)**  CCDC 2044378	**3da (from 2d and 5a)**  CCDC 2044379
4ea (from 2e and 5a)  CCDC 2044380	**4ea (from 2e and 5a)**  CCDC 2049845	**4fa (from 2f and 5a)**  CCDC 2044382
4ia (from 2i and 5a)  CCDC 2044390	**4ka (from 2k and 5a)**  CCDC 2044391	**3ka (from 2k and 5a)**  CCDC 2044392
4ag (from 2a and 5g)  CCDC 2049846	**3ag (from 2a and 5g)**  CCDC 2049847	

4a (from 2a and 5a)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

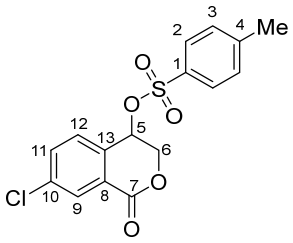


To a solution of **1a** (0.103 g, 0.87 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0290 g, 0.152 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0287 g, 0.157 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water phase was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4a** and **3a**; 64%, ratio **4a**/**3a** = 91:9). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0207 g, 37%).

The structure was determined by X-ray crystallography (Deposition number: CCDC 2044374); Rf (hexane/ethyl acetate = 50:50): 0.61; mp: 146-152 °C; IR: (KBr) 1755 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 7.84 (d, *J* = 1.7 Hz, 1H, 9-H), 7.71 (d, *J* = 8.2 Hz, 2H, 2-H), 7.64 (dd, *J* = 8.2, 1.7 Hz, 1H, 11-H), 7.45 (d, *J* = 8.2 Hz, 1H, 12-H), 7.35 (d, *J* = 8.2 Hz, 2H, 3-H), 5.60 (t, *J* = 4.7 Hz, 1H, 6-H), 4.41-4.33 (m, 2H, 5-H_2), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 168.0 (s, C-7), 145.7 (s, C-1), 143.4 (s, C-13), 136.7 (s, C-10), 134.8 (d, C-11), 132.2 (s, C-4), 130.2 (d, C-3), 128.2 (s, C-8), 128.0 (d, C-2), 126.1 (d, C-9), 123.9 (d, C-12), 77.4 (d, C-6), 68.4 (t, C-5), 21.8 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}ClO_5S$) 352.0172, Found: 352.0174

3a (from 2a and 5a)

7-chloro-1-oxoisochroman-4-yl 4-methylbenzenesulfonate

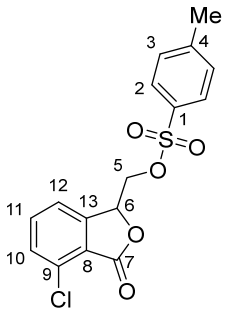


To a solution of PhI(OH)(OTs) (0.177 g, 0.300 mmol) in CH_2Cl_2 (5 mL) was added 5-chloro-2-vinylbenzoic acid (0.0554 g, 0.450 mmol). The reaction mixture was stirred for 3 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4a** and **3a**; 69%, ratio **4a**/**3a** = 4:96). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0332 g, 31%).

The structure was determined by X-ray crystallography (Deposition number: CCDC 2044375); Rf (hexane/ethyl acetate = 50:50): 0.78, mp: 107-109 °C; IR: (KBr) 1718 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.08 (d, *J* = 2.4 Hz, 1H, 9-H), 7.76 (d, *J* = 8.2 Hz, 2H, 2-H), 7.57 (dd, *J* = 8.2, 2.4 Hz, 1H, 11-H), 7.36 (d, *J* = 8.2 Hz, 2H, 3-H), 7.28 (d, *J* = 8.2 Hz, 1H, 12-H), 5.66 (t, *J* = 2.7 Hz, 1H, 5-H), 4.69 (dd, *J* = 12.7, 2.7 Hz, 1H, 6-H), 4.55 (dd, *J* = 12.7, 2.7 Hz, 1H, 6-H), 2.47 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9 (s, C-7), 145.8 (s, C-1), 137.5 (s, C-10), 134.6 (d, C-11), 133.4 (s, C-4), 132.4 (s, C-13), 130.5 (d), 130.2 (d, C-3), 129.7 (d), 127.9 (d, C-2), 126.5 (s, C-8), 70.8 (d, C-5), 69.6 (t, C-6), 21.8 (q, 4-Me); HRMS: (FAB, 70 eV) Calculated ($C_{16}H_{14}ClO_5S$) 353.0250 ($[M + H]^+$), Found: 353.0248

4ba (from 2b and 5a)

(4-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

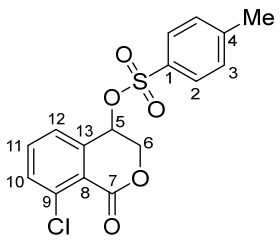


To a solution of **1a** (0.103 g, 0.185 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0295 g, 0.155 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The aforementioned procedure was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 6-chloro-2-vinylbenzoic acid (0.0277 g, 0.152 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ba** and **3ba**; 51%, ratio **4ba**/**3ba** = 88:12). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0221 g, 0.0626 mmol, 41%).

The structure was determined by X-ray crystallography (Deposition number: CCDC 2044376); Rf (hexane/ethyl acetate = 50:50): 0.55; mp: 128-130 °C; IR: (KBr) 1768 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.73 (d, *J* = 8.4 Hz, 2H, 2-H), 7.62 (t, *J* = 7.7 Hz, 1H, 11-H), 7.53 (d, *J* = 7.7 Hz, 1H, 12-H), 7.42 (d, *J* = 7.5 Hz, 1H, 10-H), 7.36 (d, *J* = 8.4 Hz, 2H, 3-H), 5.55 (t, *J* = 4.8 Hz, 1H, 6-H), 4.36 (d, *J* = 4.8 Hz, 2H, 5-H_2), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 166.2 (s, C-7), 147.4 (s, C-13), 145.6 (s, C-1), 135.3 (d, C-11), 133.8 (s, C-9), 132.0 (s, C-4), 131.5 (d, C-12), 130.1 (d, C-3), 127.9 (d, C-2), 122.9 (s, C-8), 120.9 (d, C-10), 76.0 (d, C-6), 68.3 (t, C-5), 21.7 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}ClO_5S$) 352.0172, Found: 352.0166

3ba (from 2b and 5a)

8-chloro-1-oxoisochroman-4-yl 4-methylbenzenesulfonate

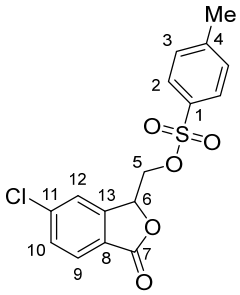


To a solution of $PhI(OAc)_2$ (0.0572 g, 0.177 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH·H_2O (0.0282 g, 0.148 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 6-chloro-2-vinylbenzoic acid (0.0273 g, 0.150 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a yellow solid (0.0280 g, 53%).

Rf (hexane/ethyl acetate = 50:50): 0.63; mp: 154-156 °C; IR (KBr): 1750 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (d, *J* = 8.4 Hz, 2H, 2-H), 7.59 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H, 11-H), 7.34 (d, *J* = 8.4 Hz, 2H, 3-H), 7.29 (d, *J* = 7.8 Hz, 1H), 5.66 (t, *J* = 2.9 Hz, 1H, 5-H), 4.60 (dd, *J* = 12.6, 2.9 Hz, 1H, 6-H), 4.48 (dd, *J* = 12.6, 2.9 Hz, 1H, 6-H), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 159.4 (s, C-7), 145.8 (s, C-1), 137.3 (s), 137.0 (s), 134.3 (d), 134.2 (d), 133.4 (s), 130.2 (d, C-3), 127.9 (d, C-2), 126.7 (d), 122.6 (s, C-13), 71.8 (d, C-5), 68.7 (t, C-6), 21.9 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}ClO_5S$): 352.0172, Found: 352.0168

4ca (from 2c and 5a)

(6-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

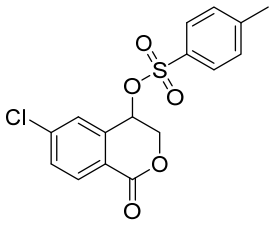


To a solution of **1a** (0.104 g, 0.188 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0283 g, 0.157 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, CH_2Cl_2 (0.3 mL) and 4-chrolo-2-vinylbenzoic acid (0.0279 g, 0.153 mmol) were added to the flask and stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted by CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ca** and **3ca**; 73%, ratio **4a**/**3a** = >99:<1). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0306 g, 0.0867 mmol, 60%).

Rf (hexane/ethyl acetate = 50:50): 0.72; mp: 170-173 °C; IR: (KBr) 1765 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.83 (d, *J* = 7.5 Hz, 1H, 9-H), 7.73 (d, *J* = 8.7 Hz, 2H, 2-H), 7.55 (d, *J* = 7.5 Hz, 1H, 10-H), 7.43 (s, 1H, 12-H), 7.36 (d, *J* = 8.2 Hz, 2H, 3-H), 5.57 (t, *J* = 4.8 Hz, 1H, 6-H), 4.36 (d, *J* = 4.8 Hz, 2H, 5-H_2), 2.47 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 168.3 (s, C-7), 146.9 (s, C-13), 145.7 (s, C-1), 141.4 (s, C-8), 132.0 (s, C-4), 131.0 (d, C-10), 130.2 (d, C-3), 128.1 (d, C-2), 127.3 (d, C-9), 124.9 (s, C-11), 123.0 (d, C-12), 76.8 (d, C-6), 68.3 (t, C-5), 21.9 (q, 4-Me); HRMS: (EI, 70 mV) Calculated ($C_{16}H_{13}ClO_5S$) 352.0172, Found: 352.0178

3ca (from 2c and 5a)

6-chloro-1-oxoisochroman-4-yl 4-methylbenzenesulfonate

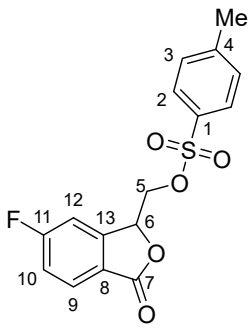


To a solution of PhI(OAc)$_2$ (0.0576 g, 0.179 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0300 g, 0.158 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The aforementioned procedure was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-chloro-2-vinylbenzoic acid (0.0267 g, 0.147 mmol) and stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ca** and **3ca**; 74%, ratio **4ca**/**3ca** = 37:63). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate = 50:50) to give the titled compound as a white solid (0.0031 g, 0.0093 mmol, 6%). The structure was determined by X-ray crystallography (Deposition number: CCDC 2044377)

Rf (hexane/ethyl acetate = 50:50): 0.67; mp: 149-150 °C; IR: (KBr) 1724 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.05 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.51 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 2H), 7.13 (d, *J* = 1.9 Hz, 1H), 5.60 (t, *J* = 2.9 Hz, 1H), 4.68 (dd, *J* = 12.6, 3.4 Hz, 1H), 4.55 (dd, *J* = 13.0, 2.9 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2 (s), 145.9 (s), 140.9 (s), 135.6 (s), 133.2 (s), 132.3 (d), 131.4 (d), 130.3 (d), 128.03 (d), 127.98 (d), 123.3 (s), 70.9 (d), 69.5 (t), 21.8 (q); HRMS: (ESI) Calculated ($C_{16}H_{13}O_5NaSCl$):375.0064 ([M + Na]$^+$), Found: 375.0058

4da (from 2d and 5a)

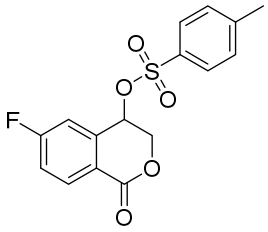
(6-fluoro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate



To a solution of **1a** (0.0994 g, 0.179 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0293 g, 0.154 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The aforementioned procedure was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-fluoro-2-vinylbenzoic acid (0.0266 g, 0.160 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4da** and **3da**; 67%, ratio **4da**/**3da** = 90:10). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0312 g, 0.0928 mmol, 58%). The structure was determined by X-ray crystallography (Deposition number: CCDC 2044378)

Rf (hexane/ethyl acetate = 50:50): 0.64; mp: 179-181 °C; IR: (KBr) 1763 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.90 (d, J = 8.6 Hz, d, $^4J_{HF}$ = 4.8 Hz, 1H, 9-H), 7.73 (d, J = 8.2 Hz, 2H, 2-H), 7.36 (d, J = 8.2 Hz, 2H, 3-H), 7.27 (dd, J = 8.6, 2.2 Hz, d, $^3J_{HF}$ = 8.6 Hz, 1H, 10-H), 7.13 (d, J = 2.2 Hz, d, $^3J_{HF}$ = 7.7 Hz, 1H, 12-H), 5.57 (t, J = 4.8 Hz, 1H, 6-H), 4.40-4.32 (m, 2H, 5-H_2) 2.47 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 168.0 (s, C-7), 166.8 (s, d, $^1J_{CF}$ = 284 Hz, C-11), 148.0 (s, d, $^3J_{CF}$ = 11 Hz, C-13), 145.8 (s, C-1), 132.0 (s, C-4), 130.2 (d, C-3), 128.6 (d, d, $^3J_{CF}$ = 11 Hz, C-9), 128.1 (d, C-2), 122.4 (s, d, $^4J_{CF}$ = 2 Hz, C-8), 118.5 (d, d, $^2J_{CF}$ = 25 Hz, C-10), 110.1 (d, d, $^2J_{CF}$ = 25 Hz, C-12), 76.7 (d, d, $^4J_{CF}$ = 3 Hz, C-6), 68.3 (t, C-5), 21.9 (q, 4-Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard:TFA in D_2O): -101.37; HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}FO_5S$) 336.0468, Found: 336.0466

3da (from 2d and 5a)



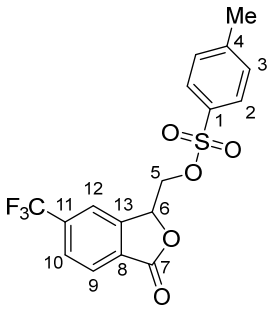
To a solution of PhI(OAc)$_2$ (0.0568 g, 0.176 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0295 g, 0.155 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-fluoro-2-vinylbenzoic acid (0.0259 g, 0.156 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4da** and **3da**; 47%, ratio **4da**/**3da** = 53:47). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0059 g, 0.0175 mmol, 11%). The structure was determined by X-ray crystallography (CCDC 2044379).

Rf (hexane/ethyl acetate = 50:50): 0.67; mp: 143-145 °C; IR: (KBr) 1714 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.15 (d, J = 8.7, d, J_{HF} = 5.8 Hz, 1H), 7.80 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.23 (dd, J = 8.7, 2.4 Hz, d, J_{HF} = 8.5 Hz, 1H), 6.96 (d, J = 2.4 Hz, d, J_{HF} = 8.2 Hz, 1H), 5.63 (t, J = 3.4 Hz, 1H), 4.65 (dd, J = 12.8, 3.4 Hz, 1H), 4.56 (dd, J = 12.8, 3.4 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.2 (s), 163.4 (s, d, $^1J_{CF}$ = 245.0 Hz), 146.0 (s), 137.2 (s, d, $^3J_{CF}$ = 9.0 Hz), 134.0 (d, d, $^3J_{CF}$ = 9.0 Hz), 133.2 (s),

130.3 (d), 128.0 (d), 121.2 (s, d, $^4J_{CF}$ = 3.3 Hz), 118.6 (d, d, $^2J_{CF}$ = 21.3 Hz), 115.0 (d, d, $^2J_{CF}$ = 22.9 Hz), 70.9 (d), 69.4 (t), 21.9 (q); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -101.0; HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}FO_5S$):336.0468, Found: 336.0469

4ea (from 2e and 5a)

(3-oxo-6-(trifluoromethyl)-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

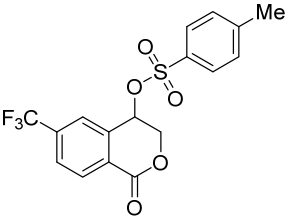


To a solution of **1a** (0.100 g, 0.181 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0288 g, 0.151 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-(trifluoromethyl)-2-vinylbenzoic acid (0.0334 g, 0.155 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ea** and **3ea**; 58%, ratio **4ea**/**3ea** = >99:<1). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0134 g, 22%). The structure was determined by X-ray crystallography (CCDC 2044380).

Rf (hexane/ethyl acetate = 50:50): 0.77; mp: 143-144 °C; IR: (KBr) 1775 (C=O) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): 8.03 (d, *J* = 8.1 Hz, 1H, 9-H), 7.85 (d, *J* = 8.1 Hz, 1H, 10-H), 7.73 (s, 1H, 12-H), 7.72 (d, *J* = 8.4 Hz, 2H, 2-H), 7.35 (d, *J* = 8.4 Hz, 2H, 3-H), 5.67 (t, *J* = 4.8 Hz, 1H, 6-H), 4.43 (dd, *J* = 11.2, 4.8 Hz, 1H, 5-H), 4.40 (dd, *J* = 11.2, 4.8 Hz, 1H, 5-H), 2.46 (s, 3H, 4-Me); ^{13}C NMR (150 MHz, $CDCl_3$): 167.7 (C, C-7), 145.7 (C), 145.6 (C), 136.3 (C, q, $^2J_{CF}$ = 32.9 Hz, C-11), 131.9 (C, C-4), 130.1 (CH, C-3), 129.5 (C, C-8), 127.9 (CH, C-2), 127.5 (CH, q, $^3J_{CF}$ = 3.3 Hz, C-10), 126.9 (CH, C-9), 123.1 (C, q, $^1J_{CF}$ = 273 Hz, CF_3), 119.9 (CH, q, $^3J_{CF}$ = 3.9 Hz, C-12), 77.3 (CH, C-6), 67.9 (CH_2, C-5), 21.7 (CH_3, 4-Me); ^{19}F NMR (372 MHz, $CDCl_3$, external standard:TFA in D_2O): -62.84; HRMS: (EI, 70 eV) Calculated ($C_{17}H_{13}F_3O_5S$) 386.0436, Found: 386.0433

3ea (from 2e and 5a)

1-oxo-6-(trifluoromethyl)isochroman-4-yl 4-methylbenzenesulfonate



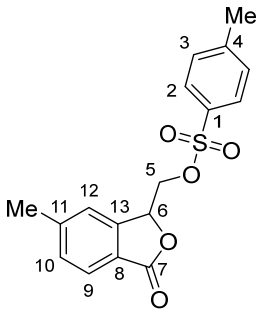
To a solution of PhI(OAc)$_2$ (0.0587 g, 0.182 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0297 g, 0.156 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-(trifluoromethyl)-2-vinylbenzoic acid (0.0332 g, 0.154 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0151 g, 25%). The structure was determined by X-ray crystallography (CCDC 2049845).

Rf (hexane/ethyl acetate = 50:50): 0.73; mp: 160-161 °C; IR: (KBr) 1716 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.24 (d, *J* = 8.2 Hz, 1H), 7.79-7.76 (m, 3H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.29 (s, 1H), 5.67 (t, *J* = 2.8

Hz, 1H), 4.77 (dd, J = 12.8, 2.8 Hz, 1H), 4.61 (dd, J = 12.8, 2.8 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.7 (s), 146.1 (s), 135.8 (s, q, $^2J_{CF}$ = 33.3 Hz), 134.9 (s), 133.3 (s), 131.6 (d), 130.3 (d), 128.04 (s), 128.00 (d), 127.8 (d, q, ^3J = 3.8 Hz), 125.1 (d, q, $^3J_{CF}$ = 3.8 Hz), 122.9 (s, q, $^1J_{CF}$ = 273 Hz), 70.8 (d), 69.7 (t), 21.8 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard:TFA in D_2O): -63.52; HRMS: (EI, 70 eV) Calculated ($C_{17}H_{13}F_3O_5S$) 386.0436, Found: 386.0436

4fa (from 2f and 5a)

(6-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

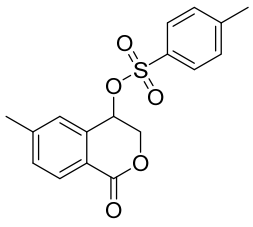


To a solution of **1a** (0.0996 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0301 g, 0.158 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-methyl-2-vinylbenzoic acid (0.0248 g, 0.153 mmol) and stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the solvent was evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4fa** and **3fa**; 58%, ratio **4fa**/**3fa** = 83:17). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0190 g, 0.0523 mmol, 37%). The structure was determined by X-ray crystallography (CCDC 2044382).

Rf (hexane/ethyl acetate = 50:50): 0.59; mp: 159-160 °C; IR: (KBr) 1757 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 7.78-7.74 (m, 3H, 2-H and 9-H), 7.38-7.34 (m, 3H, 3-H and 10-H), 7.27 (s, 1H, 12-H), 5.55 (t, J = 4.8 Hz, 1H, 6-H), 4.38 (dd, J = 10.9, 4.8 Hz, 1H, 5-H), 4.29 (dd, J = 10.9, 4.8 Hz, 1H, 5-H), 2.49 (s, 3H, CH_3, 11-Me), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 169.5 (s, C-7), 146.0 (s), 145.8 (s), 145.5 (s), 132.3 (s, C-4), 131.4 (d, C-10), 130.2 (d, C-3), 128.1 (d, C-2), 126.0 (d, C-9), 123.8 (s, C-11), 122.9 (d, C-12), 77.3 (d, C-6), 69.1 (t, C-5), 22.2 (q, Me), 21.8 (q, Me); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{16}O_5S$) 332.0718, Found: 332.0717

3fa (from 2f and 5a)

6-methyl-1-oxoisochroman-4-yl 4-methylbenzenesulfonate



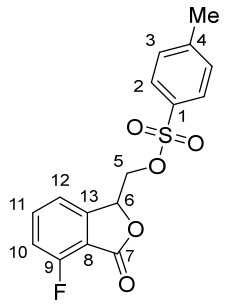
To a solution of PhI(OAc)$_2$ (0.0592 g, 0.184 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0300 g, 0.152 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 4-methyl-2-vinylbenzoic acid (0.0237 g, 0.146 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4fa** and **3fa**; 58%, ratio **4fa**/**3fa** = 29:71). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate) to give the titled compound as a white solid (0.0037 g, 0.0111 mmol, 8%).

Rf (hexane/ethyl acetate = 50:50): 0.67; mp: 86-89 °C; IR (KBr): 1714 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.00 (d, J = 7.7 Hz, 1H), 7.78 (d, J = 8.2 Hz, 2H), 7.35 (m, 3H), 7.03 (s, 1H), 5.62 (t, J = 2.5 Hz,

1H), 4.65 (dd, J = 12.9, 2.5 Hz, 1H), 4.52 (dd, J = 12.9, 2.5 Hz, 1H), 2.46 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.2 (C), 145.7 (C), 145.6 (C), 133.9 (C), 133.7 (C), 131.9 (CH), 130.8 (CH), 130.1 (CH), 128.6 (CH), 128.0 (CH), 122.3 (C), 72.0 (CH), 69.5 (CH_2), 21.91 (CH_3), 21.85 (CH_3); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{16}O_5S$): 332.0718, Found: 332.0713

4ga (from 2g and 5a)

(4-fluoro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

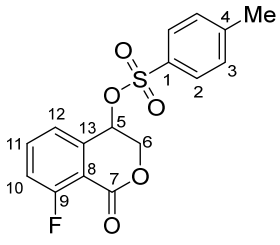


To a solution of **1a** (0.0997 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0292 g, 0.154 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 6-fluoro-2-vinylbenzoic acid (0.0255 g, 0.154 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ga** and **3ga**; 80%, ratio **4ga**/**3ga** = 90:10). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate) to give the titled compound as a white solid (0.0072 g, 14%).

Rf (hexane/ethyl acetate = 50:50): 0.44; mp: 145-147 °C; IR: (KBr) 1762 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.79-7.67 (m, 3H, 2-H and 11-H), 7.36 (d, J = 8.2 Hz, 2H, 3-H), 7.31 (d, J = 8.1 Hz, 1H, 12-H), 7.22 (d, J = 8.1 Hz, d, $^3J_{HF}$ = 8.1 Hz, 1H, 10-H), 5.60 (t, J = 4.7 Hz, 1H, 6-H), 4.37 (d, J = 4.7 Hz, 2H, 5-H), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 165.5 (s, C-7), 159.8 (s, d, $^1J_{CF}$ = 265.4 Hz, C-9), 147.7 (s, C-13), 145.7 (s, C-1), 137.2 (d, d, $^3J_{CF}$ = 6.6 Hz, C-11), 132.0 (s, C-4), 130.2 (d, C-3), 128.1 (d, C-2), 118.6 (d, d, $^4J_{CF}$ = 4.1 Hz, C-12), 117.3 (d, d, $^2J_{CF}$ = 18.8 Hz, C-10), 114.2 (s, d, $^2J_{CF}$ = 14.7 Hz, C-8), 77.2 (d, C-6), 68.4 (t, C-5), 21.9 (q, 4-Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -115.6; HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}FO_5S$) 336.0468, Found: 336.0463

3ga (from 2g and 5a)

8-fluoro-1-oxoisochroman-4-yl 4-methylbenzenesulfonate



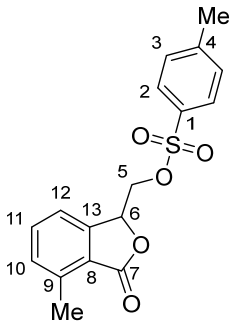
To a solution of PhI(OAc)$_2$ (0.0580 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0268 g, 0.141 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 6-fluoro-2-vinylbenzoic acid (0.0248 g, 0.149 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ga** and **3ga**; 83%, ratio **4ga**/**3ga** = 42:58). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate) to give the titled compound as a white solid (0.0071 g, 0.0211 mmol, 14%).

Rf (hexane/ethyl acetate = 50:50): 0.44; mp: 129-132 ºC; IR: (KBr) 1728 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 7.78 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 7.9 Hz, d, $^4J_{HF}$ = 4.8 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.27 (d,

J = 7.9 Hz, d, $^3J_{HF}$ = 9.4 Hz, 1H), 7.18 (d, J = 7.9 Hz, 1H), 5.68 (s, 1H), 4.63 (dd, J = 12.8, 2.9 Hz, 1H), 4.51 (dd, J = 12.8, 2.9 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.8 (s, d, $^1J_{CF}$ = 267.1 Hz), 158.6 (s, d, $^3J_{CF}$ = 4.9 Hz), 145.8 (s), 136.5 (s), 136.1 (d, d, $^3J_{CF}$ = 9.8 Hz), 133.3 (s), 130.2 (d), 127.9 (d), 123.9 (d, d, $^4J_{CF}$ = 4.1 Hz), 119.6 (d, d, $^2J_{CF}$ = 21.3 Hz), 113.4 (s), 71.2 (d), 69.2 (t), 21.9 (q); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -106.6; HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}FO_5S$) 336.0468, Found: 336.0469

4ia (from 2i and 5a)

(4-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate

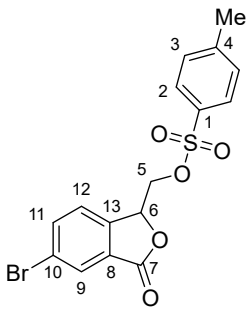


To a solution of **1a** (0.0993 g, 0.179 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0277 g, 0.146 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The aforementioned procedure was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 6-methyl-2-vinylbenzoic acid (0.0241 g, 0.149 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ia** and **3ia**; 55%, ratio **4ia**/**3ia** = 93:7). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0248 g, 0.0746 mmol, 50%). The structure was determined by X-ray crystallography (CCDC 2044390).

Rf (hexane/ethyl acetate = 50:50): 0.66; mp: 98-99 °C; IR: (KBr) 1750 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.74 (d, J = 8.7 Hz, 2H, 2-H), 7.54 (t, J = 7.5 Hz, 1H, 11-H), 7.38-7.21 (m, 4H, 3-H, 10-H and 12-H), 5.53 (t, J = 4.8 Hz, 1H, 6-H), 4.38 (dd, J = 11.0, 4.8 Hz, 1H, 5-H), 4.28 (dd, J = 11.0, 4.8 Hz, 1H, 5-H), 2.66 (s, 3H, 9-Me), 2.46 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 169.6 (s, C-7), 145.6 (s), 145.5 (s), 140.4 (s, C-9), 134.2 (d, C-11), 132.4 (s, C-1), 131.9 (d), 130.2 (d, C-3), 128.1 (d, C-2), 123.8 (s, C-8), 119.8 (d), 76.7 (d, C-6), 69.2 (t, C-5), 21.8 (q, 9-Me), 17.5 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{16}O_5S$) 332.0718; Found: 332.0716

4ja (from 2j and 5a)

(5-bromo-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate



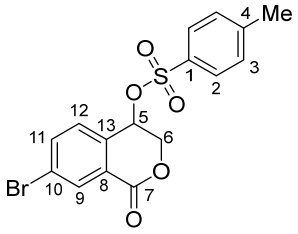
To a solution of **1a** (0.100 g, 0.181 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0295 g, 0.155 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-bromo-2-vinylbenzoic acid (0.0361 g, 0.159 mmol) and stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ja** and **3ja**; 62%, ratio **4ja**/**3ja** = >99:<1). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0296 g, 0.0745 mmol, 47%).

Rf (hexane/ethyl acetate = 50:50): 0.65; mp: 146-148 °C; IR: (KBr) 1755 cm^{-1} (C=O); ^{1}H NMR (400 MHz,

$CDCl_3$): 8.02 (s, 1H, 9-H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 2H, 2-H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H, 3-H), 5.57 (t, *J* = 4.8 Hz, 1H, 6-H), 4.40-4.32 (m, 2H, 5-H_2), 2.47 (s, 3H, 4-Me); ^{13}C NMR: (100 MHz, $CDCl_3$): 167.8 (s, C-7), 145.7 (s, C-1), 143.9 (s, C-13), 137.6 (d), 132.1 (s, C-4), 130.2 (d, C-3), 129.2 (d, C-9), 128.4 (s, C-8), 128.1 (d, C-2), 124.4 (s, C-10), 124.2 (d), 77.4 (d, C-6), 68.3 (d, C-5), 21.9 (d, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}BrO_5S$) 395.9667, Found: 395.9670

3ja (from 2j and 5a)

7-bromo-1-oxoisochroman-4-yl 4-methylbenzenesulfonate

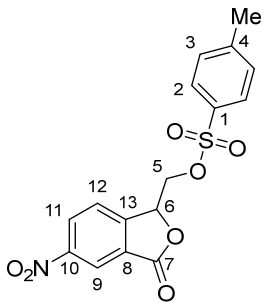


To a solution of $PhI(OAc)_2$ (0.0579 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0300 g, 0.158 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-bromo-2-vinylbenzoic acid (0.0348 g, 0.153 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ja** and **3ja**; 62%, ratio **4ja**/**3ja** = 6:94). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0221 g, 36%).

Rf (hexane/ethyl acetate = 50:50): 0.48; mp: 102-103 °C; IR: (KBr) 1718 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): 8.25 (d, *J* = 2.1 Hz, 1H, 9-H), 7.77 (d, *J* = 8.2 Hz, 2H, 2-H), 7.73 (dd, *J* = 8.1, 2.1 Hz, 1H, 11-H), 7.36 (d, *J* = 8.2 Hz, 2H, 3-H), 7.21 (d, *J* = 8.1 Hz, 1H, 12-H), 5.64 (t, *J* = 2.9 Hz, 1H, 5-H), 4.69 (dd, *J* = 13.0, 2.9 Hz, 1H, 6-H), 4.55 (dd, *J* = 13.0, 2.9 Hz, 1H, 6-H), 2.47 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 161.7 (s, C-7), 145.8 (s, C-1), 137.5 (d, C-11), 133.6 (d, C-9), 133.3 (s), 132.9 (s), 130.2 (d, C-3), 129.8 (d, C-12), 127.9 (d, C-2), 126.6 (s), 125.4 (s), 70.8 (d, C-5), 69.6 (t, C-6), 21.9 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}BrO_5S$) 395.9667, Found: 395.9660

4ka (from 2k and 5a)

(5-nitro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-methylbenzenesulfonate



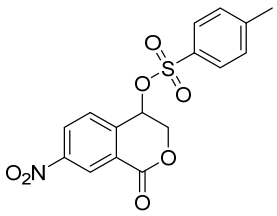
To a solution of **1a** (0.0997 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0316 g, 0.166 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-nitro-2-vinylbenzoic acid (0.0302 g, 0.156 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water phase was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ka** and **3ka**; 59%, ratio **4ka**/**3ka** = >99:<1). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel)) to give the titled compound as a white solid (0.0303 g, 53%). The structure was determined by X-ray crystallography (CCDC 2044391).

Rf (hexane/ethyl acetate = 50:50): 0.40; mp: 152-155 °C; IR: (KBr) 1769 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): 8.73 (d, *J* = 2.1 Hz, 1H, 9-H), 8.57 (dd, *J* = 8.5, 2.1 Hz, 1H, 11-H), 7.76-7.69 (m, 3H, 2-H and 12-

H), 7.36 (d, J = 8.2 Hz, 2H, 3-H), 5.73 (t, J = 4.5 Hz, 1H, 6-H), 4.52 (dd, J = 11.1, 4.5 Hz, 1H, 5-H), 4.39 (dd, J = 11.1, 4.5 Hz, 1H, 5-H), 2.47 (s, 3H, 4-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 166.9 (s, C-7), 150.6 (s, C-10), 149.7 (s, C-8), 146.0 (s, C-1), 131.9 (s, C-4), 130.3 (d, C-3), 129.4 (d, C-11), 128.3 (s, C-13), 128.1 (d, C-2), 124.2 (d, C-12), 121.7 (d, C-9), 77.4 (d, C-6), 67.7 (t, C-5), 21.9 (q, C-4-Me); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}NO_7S$) 363.0413, Found: 363.0419

3ka (from 2k and 5a)

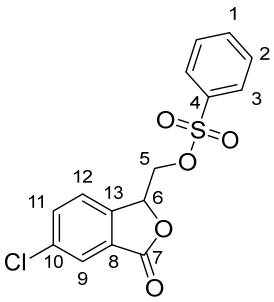
7-nitro-1-oxoisochroman-4-yl 4-methylbenzenesulfonate



To a solution of $PhI(OAc)_2$ (0.0583 g, 0.181 mmol) in CH_2Cl_2 (0.3 mL) was added *p*-TsOH•H_2O (0.0307 g, 0.161 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-nitro-2-vinylbenzoic acid (0.0299 g, 0.155 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ka** and **3ka**; 46%, ratio **4ka**/**3ka** = 54:46). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10 to 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate) to give the titled compound as a white solid (0.0069 g, 0.0190 mmol, 12%). The structure was determined by X-ray crystallography (CCDC 2044392).
Rf (hexane/ethyl acetate = 50:50): 0.50; mp: 161-165 °C; IR: (KBr) 1742 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.95 (d, J = 2.2 Hz, 1H), 8.46 (dd, J = 8.4, 2.2 Hz, 1H), 7.81 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 5.78 (t, J = 3.3 Hz, 1H), 4.69 (dd, J = 12.8, 3.9 Hz, 1H), 4.60 (dd, J = 12.8, 2.9 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.0 (s), 149.4 (s), 146.3 (s), 140.2 (s), 132.8 (s), 130.4 (d), 129.6 (d), 128.7 (d), 128.0 (d), 126.5 (s), 125.9 (d), 69.8 (d), 69.2 (t), 21.9 (q); HRMS: (EI, 70 eV) Calculated ($C_{16}H_{13}NO_7S$): 363.0413, Found: 363.0407

4ab (from 2a and 5b)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl benzenesulfonate

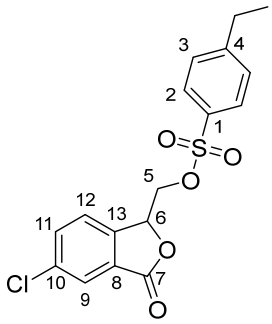


To a solution of **1a** (0.102 g, 0.183 mmol) in CH_2Cl_2 (0.3 mL) was added $PhSO_3H$ (0.0247 g, 0.156 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0282 g, 0.154 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ab** and **3ab**; 80%, ratio **4ab**/**3ab** = 80:20). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10 to 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a viscous colorless liquid (0.0171 g, 33%).
Rf (hexane/ethyl acetate = 50:50): 0.55; IR: (neat) 1773 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 7.85-7.83 (m, 3H, 3-H and 9-H), 7.69 (t, J = 7.7 Hz, 1H, 1-H), 7.65 (dd, J = 8.0, 1.9 Hz, 1H, 11-H), 7.57 (t, J = 7.7 Hz, 2H, 2-H), 7.45 (d, J = 8.0 Hz, 1H, 12-H), 5.61 (t, J = 4.6 Hz, 1H, 6-H), 4.40 (d, J = 4.6 Hz, 2H, 5-H_2); ^{13}C

NMR (100 MHz, $CDCl_3$): 167.9 (s, C-7), 143.3 (s, C-13), 136.7 (s, C-10), 135.2 (s, C-4), 134.9 (d), 134.5 (d), 129.6 (d, C-2), 128.2 (s, C-8), 128.0 (d), 126.2 (d), 123.9 (d, C-12), 77.3 (d, C-6), 68.5 (t, C-5); HRMS: (ESI) Calculated ($C_{15}H_{11}O_5NaSCl$):360.99079 ($[M + Na]^+$), Found: 360.99042

4ac (from 2a and 5c)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-ethylbenzenesulfonate

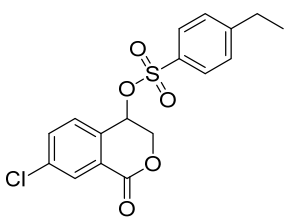


To a solution of **1a** (0.102 g, 0.185 mmol) in CH_2Cl_2 (0.3 mL) was added 4-ethylbenzenesulfonic acid (0.0290 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The aforementioned procedure was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0283 g, 0.155 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ac** and **3ac**; 63%, ratio **4ac**/**3ac** = 86:14). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC to give the titled compound as a white solid (0.0217 g, 38%).

Rf (hexane/ethyl acetate = 50:50): 0.66; mp: 115-116 °C; IR: (KBr) 1754 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.85 (d, *J* = 1.9 Hz, 1H, 9-H), 7.74 (d, *J* = 8.5 Hz, 2H, 2-H), 7.65 (dd, *J* = 8.2, 1.9 Hz, 1H, 11-H), 7.46 (d, *J* = 8.2 Hz, 1H, 12-H), 7.37 (d, *J* = 8.5 Hz, 2H, 3-H), 5.60 (t, *J* = 4.8 Hz, 1H, 6-H), 4.41-4.33 (m, 2H, 5-H_2), 2.75 (q, *J* = 7.7 Hz, 2H, CH_2CH$_3$), 1.28 (t, *J* = 7.7 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): 168.0 (s, C-7), 151.8 (s, C-1), 143.5 (s, C-13), 136.7 (s, C-10), 134.8 (d, C-11), 132.4 (s, C-4), 129.1 (d, C-3), 128.21 (s, C-8), 128.16 (d, C-2), 126.1 (d, C-9), 124.0 (d, C-12), 77.3 (d, C-6), 68.4 (t, C-5), 29.1 (t, CH_2CH_3), 15.1 (q, CH_2CH_3); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{15}ClO_5S$) 366.0329, Found: 366.0324

3ac (from 2a and 5c)

7-chloro-1-oxoisochroman-4-yl 4-ethylbenzenesulfonate



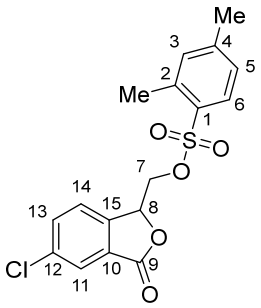
To a solution of $PhI(OAc)_2$ (0.0562 g, 0.174 mmol) in CH_2Cl_2 (0.3 mL) was added 4-ethylbenzenesulfonic acid (0.0256 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0291 g, 0.159 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with $CHCl_3$. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ac** and **3ac**; 62%, ratio **4ac**/**3ac** = 29:71). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0187 g, 32%).

Rf (hexane/ethyl acetate = 50:50): 0.71; mp: 110-112 °C; IR: (KBr) 1715 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.09 (d, *J* = 2.1 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.56 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 1H), 5.66 (s, 1H), 4.70 (dd, *J* = 12.8, 2.7 Hz, 1H), 4.55 (dd, *J* = 12.8, 2.7 Hz, 1H), 2.75 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9 (s), 151.9 (s),

137.5 (s), 134.5 (d), 133.5 (s), 132.4 (s), 130.6 (d), 129.8 (d), 129.1 (d), 128.0 (d), 126.5 (s), 70.8 (d), 69.7 (t), 29.1 (t), 15.3 (q); HRMS: (FAB+, 70 eV) Calculated ($C_{17}H_{15}ClO_5SNa$) 389.0226 ([M + Na]$^+$), Found: 389.0233

4ad (from 2a and 5d)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 2,4-dimethylbenzenesulfonate

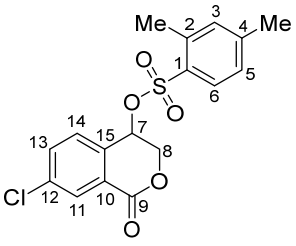


To a solution of **1a** (0.100 g, 0.181 mmol) in CH_2Cl_2 (0.3 mL) was added 2,4-$Me_2C_6H_3SO_3H$•nH_2O (0.0347 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0283 g, 0.155 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ad** and **3ad**; 79%, ratio **4ad**/**3ad** = 87:13). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0300 g, 53%).

Rf (hexane/ethyl acetate = 50:50): 0.67; mp: 124-126 °C; IR: (KBr) 1767 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.84 (d, *J* = 1.8 Hz, 1H, 11-H), 7.79 (d, *J* = 8.2 Hz, 1H, 6-H), 7.63 (dd, *J* = 8.2, 1.8 Hz, 1H, 13-H), 7.42 (d, *J* = 8.2 Hz, 1H, 14-H), 7.14-7.12 (m, 2H, 3-H and 5-H), 5.61 (t, *J* = 4.4 Hz, 1H, 8-H), 4.39 (dd, *J* = 11.2, 4.4 Hz, 1H, 7-H), 4.31 (dd, *J* = 11.2, 4.4 Hz, 1H, 7-H), 2.45 (s, 3H, 4-Me), 2.40 (s, 3H, 2-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 167.9 (s, C-9), 145.5 (s, C-1), 143.3 (s, C-15), 138.6 (s, C-4), 136.7 (s, C-12), 134.8 (d, C-13), 133.7 (d, C-3), 130.5 (s, C-2), 130.2 (d, C-6), 128.3 (s, C-10), 126.9 (d, C-5), 126.0 (d, C-11), 123.8 (d, C-14), 77.5 (d, C-8), 68.2 (t, C-7), 21.6 (q, 2-Me), 20.1 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{15}ClO_5S$) 366.0329, Found: 366.0325

3ad (from 2a and 5d)

7-chloro-1-oxoisochroman-4-yl 2,4-dimethylbenzenesulfonate



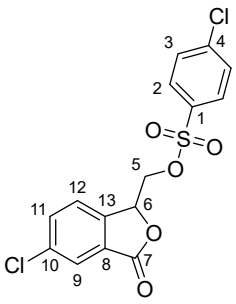
To a solution of PhI(OAc)$_2$ (0.0597 g, 0.185 mmol) in CH_2Cl_2 (0.3 mL) was added 2,4-dimethylbenzenesulfonic acid hydrate (0.0362 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0282 g, 0.154 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ad** and **3ad**; 91%, ratio **4ad**/**3ad** = 11:89). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a yellow oil (0.0223 g, 39%).

Rf (hexane/ethyl acetate = 50:50): 0.71; IR: (neat) 1725 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.08 (d, *J* = 2.3 Hz, 1H, 11-H), 7.84 (d, *J* = 8.7 Hz, 1H, 6-H), 7.54 (dd, *J* = 8.1, 2.3 Hz, 1H, 13-H), 7.22 (d, *J* = 8.1 Hz, 1H, 14-H), 7.15-7.14 (m, 2H, 3-H and 5-H), 5.61 (t, *J* = 2.4 Hz, 1H, 7-H), 4.70 (dd, *J* = 13.0, 2.4 Hz,

1H, 8-H), 4.53 (dd, *J* = 13.0, 2.4 Hz, 1H, 8-H), 2.48 (s, 3H, 4-Me), 2.40 (s, 3H, 2-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9 (s, C-9), 145.6 (s, C-1), 138.5 (s, C-4), 137.5 (s, C-10), 134.5 (d, C-13), 133.7 (d), 132.1 (s), 132.0 (s), 130.5 (d, C-11), 129.9 (d, C-6), 129.9 (d, C-14), 127.0 (d), 126.6 (s, C-2), 70.8 (d, C-7), 69.7 (t, C-8), 21.6 (q, 2-Me), 20.1 (q, 4-Me); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{15}ClO_5S$) 366.0329, Found: 366.0323

4ae (from 2a and 5e)

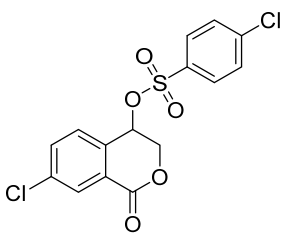
(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl 4-chlorobenzenesulfonate



To a solution of **1a** (0.100 g, 0.181 mmol) in CH_2Cl_2 (0.3 mL) was added 4-chlorobenzenesulfonic acid (0.0321 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0282 g, 0.154 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ae** and **3ae**; 59%, ratio **4ae**/**3ae** = 32:68). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate = 50:50) to give the titled compound as a white solid (0.0213 g, 37%).

Rf (hexane/ethyl acetate = 50:50): 0.64; mp: 147-148 °C; IR: (KBr) 1762 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.86 (d, *J* = 1.7 Hz, 1H, 9-H), 7.77 (d, *J* = 8.7 Hz, 2H, 2-H), 7.67 (dd, *J* = 8.2, 1.7 Hz, 1H, 11-H), 7.54 (d, *J* = 8.7 Hz, 2H, 3-H), 7.45 (d, *J* = 8.2 Hz, 1H, 12-H), 5.61 (dd, *J* = 4.8, 4.3 Hz, 1H, 6-H), 4.44 (dd, *J* = 11.1, 4.3 Hz, 1H, 5-H), 4.40 (dd, *J* = 11.1, 4.8 Hz, 1H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.8 (s, C-7), 143.1 (s, C-13), 141.3 (s, C-1), 136.9 (s, C-10), 134.9 (d, C-11), 133.7 (s, C-4), 130.0 (d, C-3), 129.4 (d, C-2), 128.3 (s, C-8), 126.2 (d, C-9), 123.8 (d, C-12), 77.3 (d, C-6), 68.7 (t, C-5); HRMS: (CI, 70 eV) Calculated ($C_{15}H_{11}Cl_2O_5S$) 372.9704 ($[M + H]^+$), Found: 372.9708

3ae (from 2a and 5e) 7-chloro-1-oxoisochroman-4-yl 4-chlorobenzenesulfonate



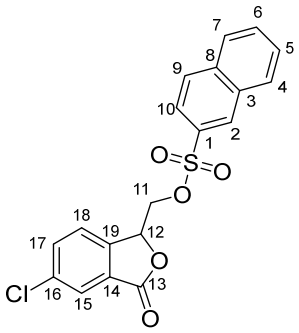
To a solution of $PhI(OAc)_2$ (0.0564 g, 0.175 mmol) in CH_2Cl_2 (0.3 mL) was added 4-chlorobenzenesulfonic acid (0.0305 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0730 g, 0.400 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with $CHCl_3$. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ae** and **3ae**; 32%, ratio **4ae**/**3ae** = 19:81). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0137 g, 23%).

Rf (hexane/ethyl acetate = 50:50): 0.78; mp: 80-82 °C; IR: (KBr) 1719 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.10 (s, 1H), 7.81 (d, *J* = 8.7 Hz, 2H), 7.60 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 1H), 5.72 (t, *J* = 2.4 Hz, 1H), 4.74 (dd, *J* = 13.0, 2.4 Hz, 1H), 4.59 (dd, *J* = 13.0, 2.4 Hz, 1H);

^{13}C NMR (100 MHz, $CDCl_3$): 161.7 (s), 141.3 (s), 137.8 (s), 134.8 (s), 134.7 (d), 131.9 (s), 130.7 (d), 130.0 (d), 129.8 (d), 129.3 (d), 126.6 (s), 71.3 (d), 69.7 (t); HRMS: (FAB+, 70 eV) Calculated ($C_{15}H_{10}Cl_2O_5SNa$): 394.9524 ([M + Na]$^+$), Found: 394.9524.

4af (from 2a and 5f)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl naphthalene-2-sulfonate

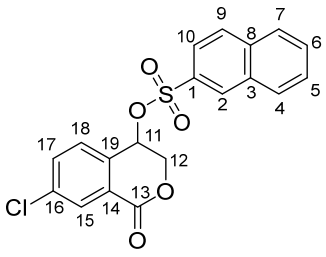


To a solution of **1a** (0.101 g, 0.182 mmol) in CH_2Cl_2 (0.3 mL) was added 2-naphtylSO_3H•nH_2O (0.0362 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0281 g, 0.154 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4af** and **3af**; 60%, ratio **4af**/**3af** = 85:15). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a pale yellow solid (0.0305 g, 51%).

Rf (hexane/ethyl acetate = 50:50): 0.63; mp: 111-112 °C; IR: (KBr) 1763 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.42 (s, 1H, 2-H), 8.00-7.94 (m, 3H), 7.81 (d, *J* = 1.9 Hz, 1H, 15-H), 7.76-7.65 (m, 3H), 7.55 (dd, *J* = 8.2, 1.9 Hz, 1H, 10-H), 7.40 (d, *J* = 8.2 Hz, 1H, 9-H), 5.60 (t, *J* = 4.5 Hz, 1H, 12-H), 4.43 (d, *J* = 4.5 Hz, 2H, 11-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 167.9 (s, C-13), 143.3 (s, C-1), 136.7 (s), 135.6 (s), 134.8 (d, C-10), 132.0 (s), 131.9 (s), 130.1 (d), 130.0 (d), 129.9 (d), 129.5 (d), 128.2 (d), 128.2 (s), 126.1 (d, C-15), 123.8 (d, C-9), 122.3 (d), 77.3 (d, C-12), 68.6 (t, C-11); HRMS: (EI, 70 eV) Calculated ($C_{19}H_{13}ClO_5S$) 388.0172, Found: 388.0166

3af (from 2a and 5f)

7-chloro-1-oxoisochroman-4-yl naphthalene-2-sulfonate



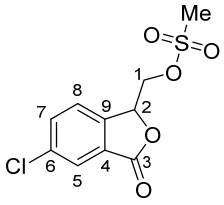
To a solution of $PhI(OAc)_2$ (0.0589 g, 0.183 mmol) in CH_2Cl_2 (0.3 mL) was added 2-naphtalenesulfonic acid hydrate (0.0358 g) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0280 g, 0.153 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4af** and **3af**; 67%, ratio **4af**/**3af** = 28:72). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle GPC ($CHCl_3$) to give the titled compound as a yellow sluggish liquid (0.0072 g, 12%).

Rf (hexane/ethyl acetate = 50:50): 0.70; IR: (neat) 1746 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (s, 1H, 2-H), 8.06 (d, *J* = 2.2 Hz, 1H, 15-H), 8.02-7.94 (m, 3H), 7.80 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.75-7.66 (m, 2H), 7.51 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.30-7.23 (m, 1H), 5.72 (t, *J* = 2.7 Hz, 1H, 11-H), 4.72 (dd, *J* = 12.9, 2.7

Hz, 1H, 12-H), 4.56 (dd, *J* = 12.9, 2.7 Hz, 1H, 12-H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.8 (s, C-13), 137.6 (s), 135.5 (s), 134.5 (d), 133.1 (s), 132.2 (s), 131.9 (s), 130.6 (d), 130.2 (d), 130.0 (d), 129.9 (d), 129.8 (d), 129.5 (d), 128.33 (d), 128.25 (d), 126.6 (s), 122.2 (d), 71.1 (d, C-11), 69.7 (t, C-12); HRMS: (EI, 70 eV) Calculated ($C_{19}H_{13}ClO_5S$): 388.0172, Found: 388.0169.

4ag (from 2a and 5g)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl methanesulfonate

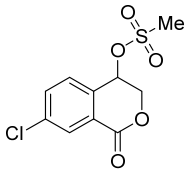


To a solution of **1a** (0.204 g, 0.368 mmol) in CH_2Cl_2 (0.6 mL) was added CH_3SO_3H (0.0273 g, 0.284 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.6 mL) and 5-chloro-2-vinylbenzoic acid (0.0558 g, 0.306 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by and the aqueous layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ag** and **3ag**; 62%, ratio **4ag**/**3ag** = 82:18). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a yellow solid (0.0408 g, 0.147 mmol, 48%). The structure was determined by X-ray crystallography (CCDC 2049846)

Rf (hexane/ethyl acetate = 50:50): 0.37; mp: 81-83 °C; IR: (KBr) 1759 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.91 (d, *J* = 1.7 Hz, 1H, 5-H), 7.72 (dd, *J* = 8.2, 1.7 Hz, 1H, 7-H), 7.53 (d, *J* = 8.2 Hz, 1H, 8-H), 5.71 (t, *J* = 4.3 Hz, 1H, 2-H), 4.67 (dd, *J* = 11.6, 4.3 Hz, 1H, 1-H), 4.52 (dd, *J* = 11.6, 4.3 Hz, 1H, 1-H), 3.05 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): 168.0 (s, C-3), 143.0 (s, C-9), 136.8 (s, C-6), 135.0 (d, C-7), 128.2 (s, C-4), 126.2 (d, C-5), 123.9 (d, C-8), 77.7 (d, C-2), 68.2 (t, C-1), 38.0 (q, Me); HRMS: (CI, 70 eV) Calculated ($C_{10}H_{10}ClO_5S$) 276.9937 ($[M + H]^+$), Found: 276.9937

3ag (from 2a and 5g)

7-chloro-1-oxoisochroman-4-yl methanesulfonate

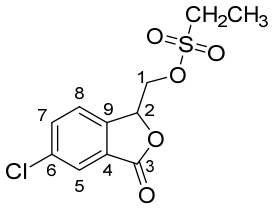


To a solution of $PhI(OAc)_2$ (0.0566 g, 0.176 mmol) in CH_2Cl_2 (0.3 mL) was added CH_3SO_3H (0.0197 g, 0.205 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0263 g, 0.144 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the aqueous layer was extracted with $CHCl_3$. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ag** and **3ag**; 67%, ratio **4ag**/**3ag** = 4:96). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) to give the titled compound as a white solid (0.0235 g, 59%). The structure was determined by X-ray crystallography (CCDC 2049847).

Rf (hexane/ethyl acetate = 50:50): 0.70; mp: 79-81 °C; IR: (KBr) 1736 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.17 (s, 1H), 7.69 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 5.83 (t, *J* = 2.3 Hz, 1H), 4.89 (dd, *J* = 13.2, 2.3 Hz, 1H), 4.68 (dd, *J* = 13.2, 2.3 Hz, 1H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.9 (s), 137.8 (s), 134.8 (d), 132.2 (s), 130.7 (d), 130.2 (d), 126.7 (s), 70.0 (t), 69.8 (d), 39.4 (q); HRMS: (EI, 70 eV) Calculated ($C_{10}H_9ClO_5S$) 275.9859, Found: 275.9863

4ah (from 2a and 5h)

(5-chloro-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl ethanesulfonate

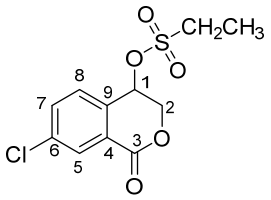


To a solution of **1a** (0.0997 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added $EtSO_3H$ (0.0178 g, 0.162 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0278 g, 0.152 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ah** and **3ah**; 56%, ratio **4ah**/**3ah** = 89:11). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel) and recycle HPLC (hexane/ethyl acetate = 50:50) to give the titled compound as a colorless oil (0.0067 g, 15%).

Rf (hexane/ethyl acetate = 50:50): 0.43; IR: (neat) 1773 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.92 (d, *J* = 1.9 Hz, 1H, 5-H), 7.71 (dd, *J* = 8.2, 1.9 Hz, 1H, 7-H), 7.53 (d, *J* = 8.2 Hz, 1H, 8-H), 5.70 (dd, *J* = 5.2, 4.0 Hz, 1H, 2-H), 4.64 (dd, *J* = 11.6, 4.0 Hz, 1H, 1-H), 4.50 (dd, *J* = 11.6, 5.2 Hz, 1H, 1-H), 3.15 (q, *J* = 7.4 Hz, 2H, C*H*$_2$CH$_3$), 1.37 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 168.1 (s, C-3), 143.1 (s, C-9), 136.9 (s, C-6), 135.0 (d, C-7), 128.3 (s, C-4), 126.2 (d, C-5), 123.9 (d, C-8), 77.9 (d, C-2), 67.7 (t, C-1), 45.7 (t, *C*H$_2$CH$_3$), 8.2 (q, CH$_2$*C*H$_3$); HRMS: (CI, 70 eV) Calculated ($C_{11}H_{12}ClO_5S$) 291.0094 ([M + H]$^+$), Found: 291.0090.

3ah (from 2a and 5h)

7-chloro-1-oxoisochroman-4-yl ethanesulfonate



To a solution of $PhI(OAc)_2$ (0.0579 g, 0.180 mmol) in CH_2Cl_2 (0.3 mL) was added $EtSO_3H$ (0.0159 g, 0.144 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0284 g, 0.156 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard (total yield of **4ah** and **3ah**; 58%, ratio **4ah**/**3ah** = 22:78). The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 50:50, column length 10 cm, diameter 26 mm silica gel and recycle HPLC (hexane/ethyl acetate = 50:50) to give the titled compound as a colorless liquid (0.0145 g, 0.0175 mmol, 32%).

Rf (hexane/ethyl acetate = 50:50): 0.51; IR: (neat) 1764 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.18 (d, *J* = 2.4 Hz, 1H, 5-H), 7.68 (dd, *J* = 8.2, 2.4 Hz, 1H, 7-H), 7.58 (d, *J* = 8.2 Hz, 1H, 8-H), 5.82 (t, *J* = 2.3 Hz, 1H, 1-H), 4.88 (dd, *J* = 13.2, 2.3 Hz, 1H, 2-H), 4.67 (dd, *J* = 13.2, 2.3 Hz, 1H, 2-H), 3.14 (q, *J* = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 1.38 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 162.0 (s, C-3), 137.8 (s, C-4), 134.8 (d, C-7), 132.4 (s, C-6), 130.8 (d, C-5), 130.2 (d, C-8), 126.7 (s, C-9), 70.1 (t, C-2), 69.2 (d, C-1), 46.7 (t, *C*H$_2$CH$_3$), 8.2 (q, CH$_2$*C*H$_3$); HRMS: (CI, 70 eV) Calculated ($C_{11}H_{12}ClO_5S$): 291.0094 ([M + H]$^+$), Found: 291.0098

General Procedures

Method A: Tosyloxylactonization of 2-vinyl benzoic acid 2a using $PhI(OAc)_2$ (Table 1.1, Entry 1)

To a solution of $PhI(OAc)_2$ (0.18 mmol) in CH_2Cl_2 (0.3 mL) was added $TsOH·H_2O$ (*p*-toluenesulfonic acid monohydrate) (0.15 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation were repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid **2a** (0.15 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* product **4a** and 6-*endo* product **3a** were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard.

Tosyloxy lactonization of 2-vinyl benzoic acid 2a using PhI(OH)OTs (Table 1.1, Entry 2)

To a solution of PhI(OH)OTs (0.18 mmol) in CH_2Cl_2 (0.3 mL) was added 5-chloro-2-vinylbenzoic acid **2a** (0.15 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* product **4a** and 6-*endo* product **3a** were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard.

Method B: Tosyloxylactonization of 2-vinyl benzoic acid 2a using $ArI(OAc)_2$ 1a and $TsOH·H_2O$ (Table 1.1, Entry 3)

To a solution of **1a** (0.18 mmol) in CH_2Cl_2 (0.3 mL) was added $TsOH·H_2O$ (*p*-toluenesulfonic acid monohydrate) (0.15 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid **2a** (0.15 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* product **4a** and 6-*endo* product **3a** were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard.

Tosyloxylactonization of 2-vinyl benzoic acid 2a using $ArI(OAc)_2$ 1a and $TsOH·H_2O$ in the presence of 1-butyl-3-methylimidazolium tetrafluoroborate (Table 1.1, Entry 4)

To a solution of PhI(OH)OTs (0.18 mmol) in CH_2Cl_2 (0.3 mL) was added 1-butyl-3-methylimidazolium tetrafluoroborate (0.65 mmol) and 5-chloro-2-vinylbenzoic acid **2a** (0.15 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* product **4a** and 6-*endo* product **3a** were determined by ^1H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard.

Tosyloxylactonization of 2-vinyl benzoic acid 2 using $ArI(OAc)_2$ 1a and $TsOH·H_2O$ (Table 1.2, Scope of 2)

All experiments were carried out according to Method B.

Tosyloxylactonization of 2-vinyl benzoic acid 2 using $PhI(OAc)_2$ and $TsOH \cdot H_2O$ (Table 1.2, Scope of 2)

All experiments were carried out according to Method A.

Sulfonyloxylactonization of 2-vinyl benzoic acid (2a) using $ArI(OAc)_2$ (1a) and RSO_3H (5) (Table 1.3, Scope of 5)

All experiments were carried out according to Method B.

Sulfonyloxylactonization of 2-vinyl benzoic acid (2a) using $PhI(OAc)_2$ and RSO_3H (5) (Table 1.3, Scope of 5)

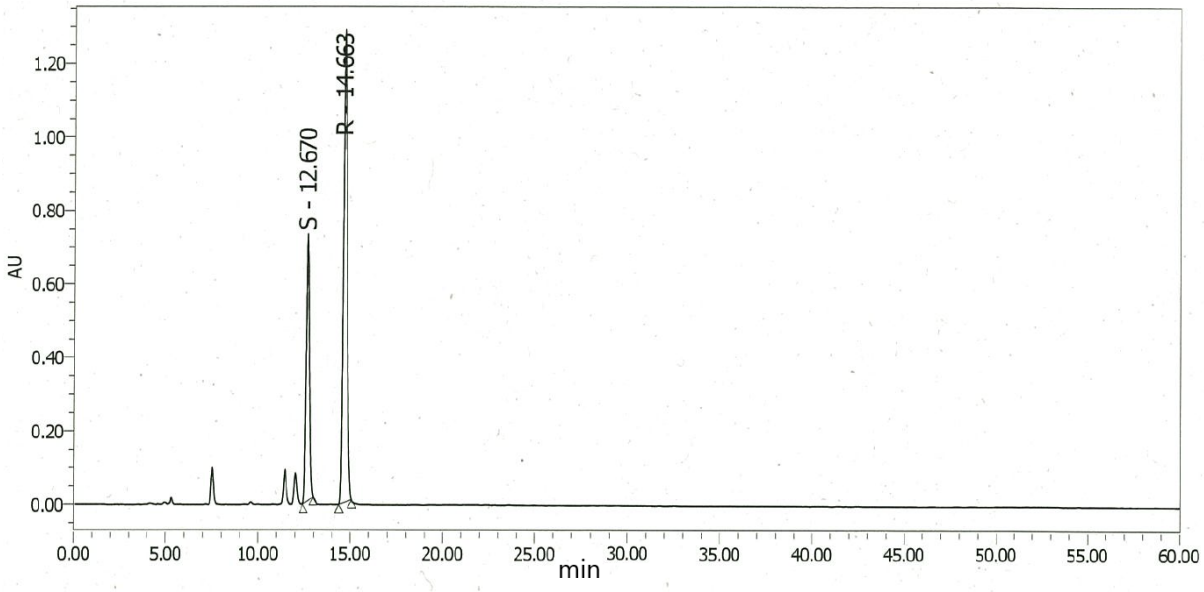
All experiments were carried out according to Method A.

Tosyloxylactonization of 2-vinyl benzoic acid (2a) using $ArI(OAc)_2$ (1) and $TsOH \cdot H_2O$ (Table 1.4)

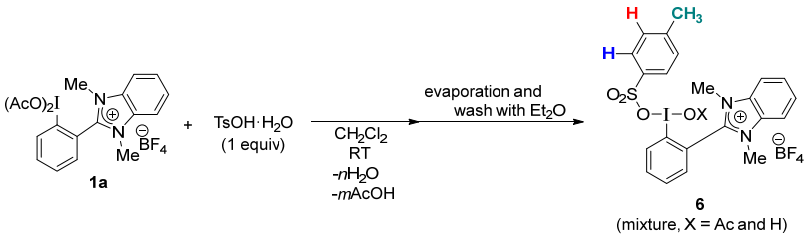
All experiments were carried out according to Method B.

Enantioselective tosyloxylactonization using optically active hypervalent iodine ((*R*,*R*)-1d) (Scheme 1.2)

The experiment was carried out according to Method B. Retention times of (*S*)-**9a** and (*R*)-**9a** were 12.7 and 14.7 min, respectively, for HLPC analyses using a chiral column Chiralpak IA (0.46 cm φ × 25 cm) (eluent: CH_2Cl_2/hexane = 40:60, the flow rate = 0.7 mL/min). The retention time was referred to reported values (M. Fujita, Y. Yoshida, K. Miyata, A. Wakisaka, T. Sugimura, *Angew. Chem. Int. Ed.* **2010**, *49*, 7068.).



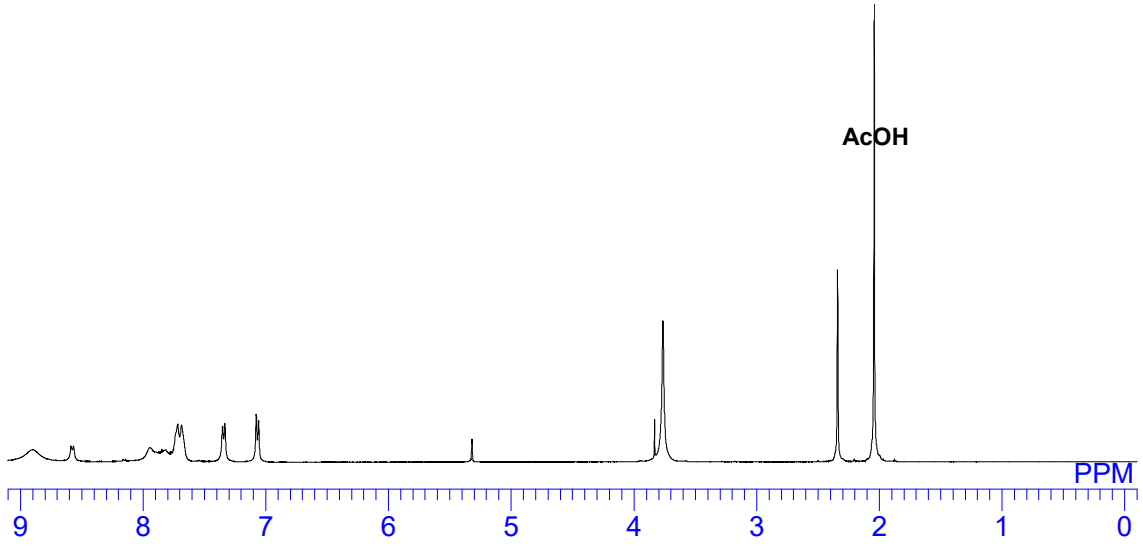
Isolation and identification of intermediate 6 (Figure 1.4A)



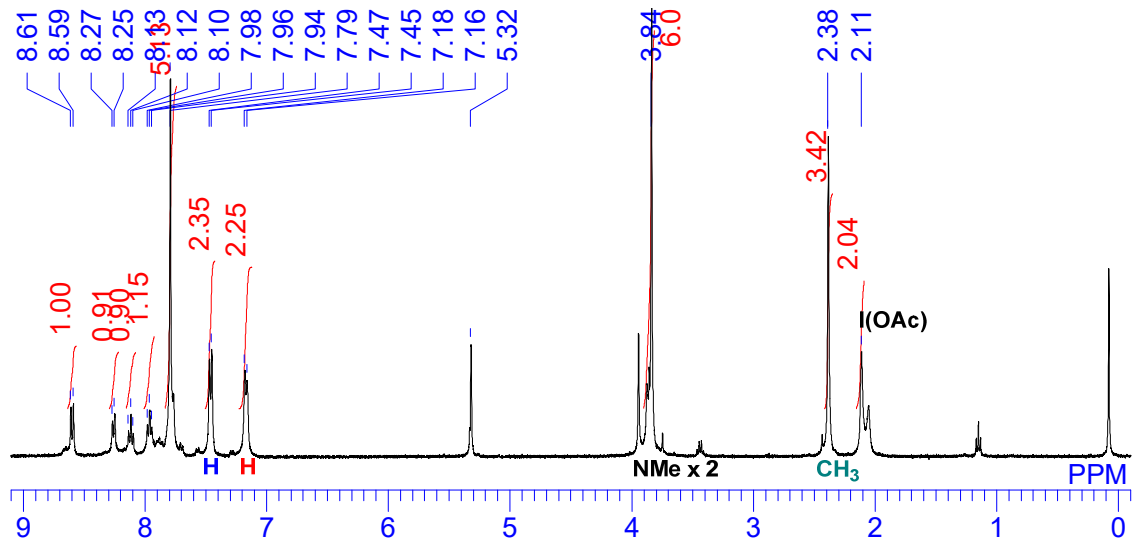
All manipulations were carried out in glove box filled with dry nitrogen gas. To the solution of **1a** (0.05 mmol) in CH_2Cl_2 (0.5 mL) was added TsOH·H_2O (0.06 mmol) at room temperature, and the reaction mixture was stirred for 30 min. Then, the volatiles were evaporated in vacuo, the residue was washed with Et_2O to remove AcOH and H_2O. The volatiles were evaporated again to obtain compound **6**.

^{1}H NMR (400 MHz, CD_2Cl_2)

Before evaporation and washing with Et_2O



After evaporation and washing with Et_2O

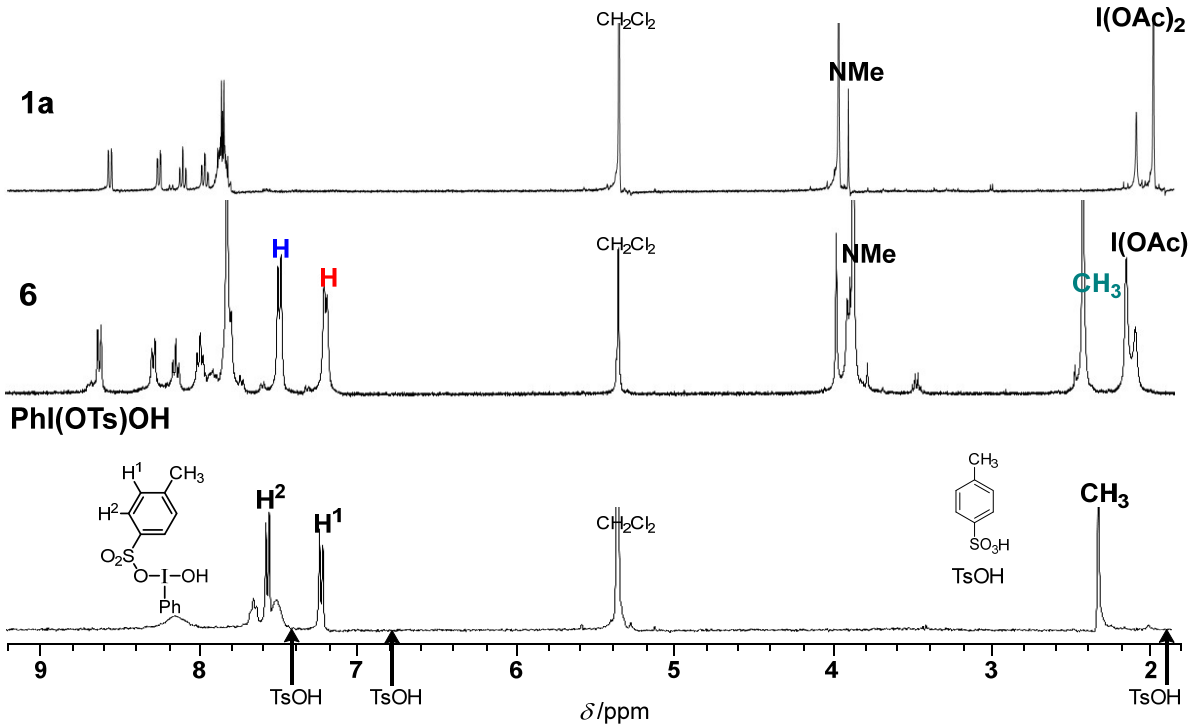


Scheme 1.S1

Comparison among ^{1}H NMR spectra of 1a, intermediate 6, Ph(OH)OTs, and TsOH·H_2O (Figure 1.4B)

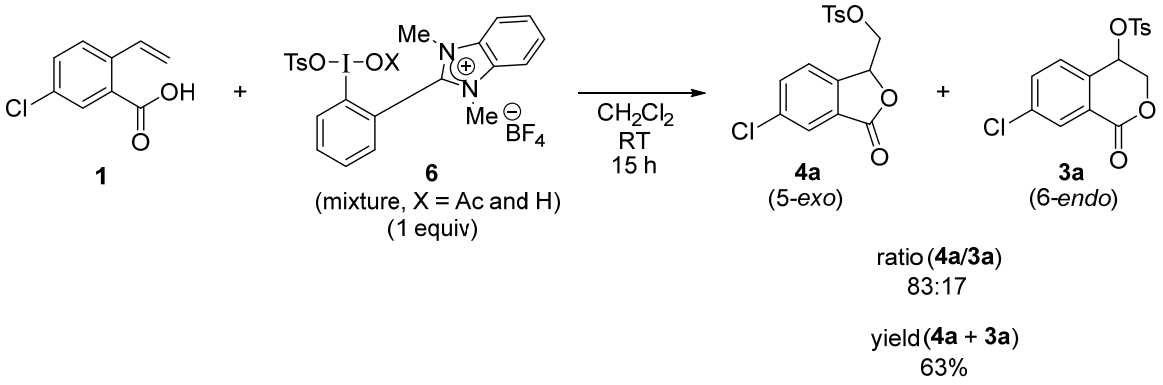
The comparison among ^{1}H NMR of spectra of **1a**, intermediate **6**, Ph(OH)OTs, and TsOH·H_2O is shown below.

^{1}H NMR (400 MHz, CD_2Cl_2)



Scheme 1.S2

Tosyloxylation using intermediate 6 (Figure 1.4C)



Scheme 1.S3

To the solution of compound **6** (0.1121 g, ca. 0.15 mmol), which was prepared and isolated by the procedure described above, in CH_2Cl_2 (0.5 mL) was added carboxylic acid (**1a)** (0.0279 g, 0.168 mmol) at room temperature, and then the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched with water (5 mL), and the mixture was extracted by CH_2Cl_2 (10 mL x 3). The corrected organic

layers were dried over $MgSO_4$. The solvent was evaporated, and the NMR yield and the ratio in the crude product was determined by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Observation of 4-EtPhSO$_3$ anion in the presence of pyrone (Figure 1.6)

Preparation of compound 9 (Chart D, Figure 1.6)

All manipulations were carried out in glove box filled with dry nitrogen gas. To the solution of **1a** (0.05 mmol) in CH_2Cl_2 (0.5 mL) was added 4-EtSO$_3$H (0.06 mmol) at room temperature, and the reaction mixture was stirred for 30 min. Then, the volatiles were evaporated in vacuo, the residue was washed with Et_2O to remove AcOH. The volatiles were evaporated again to obtain compound **9**.

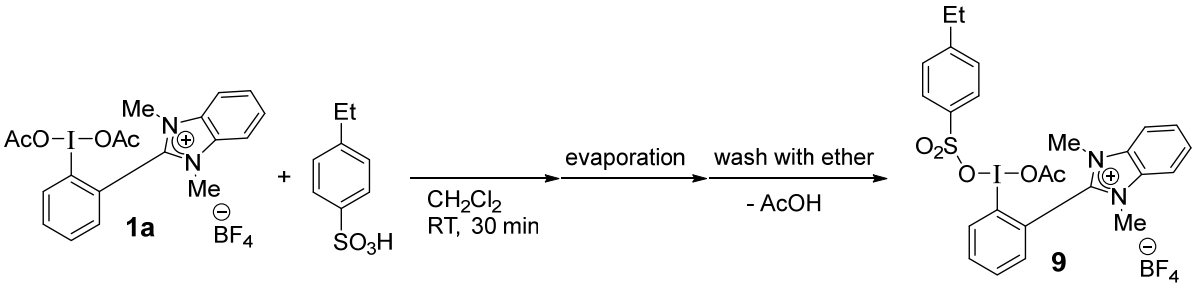
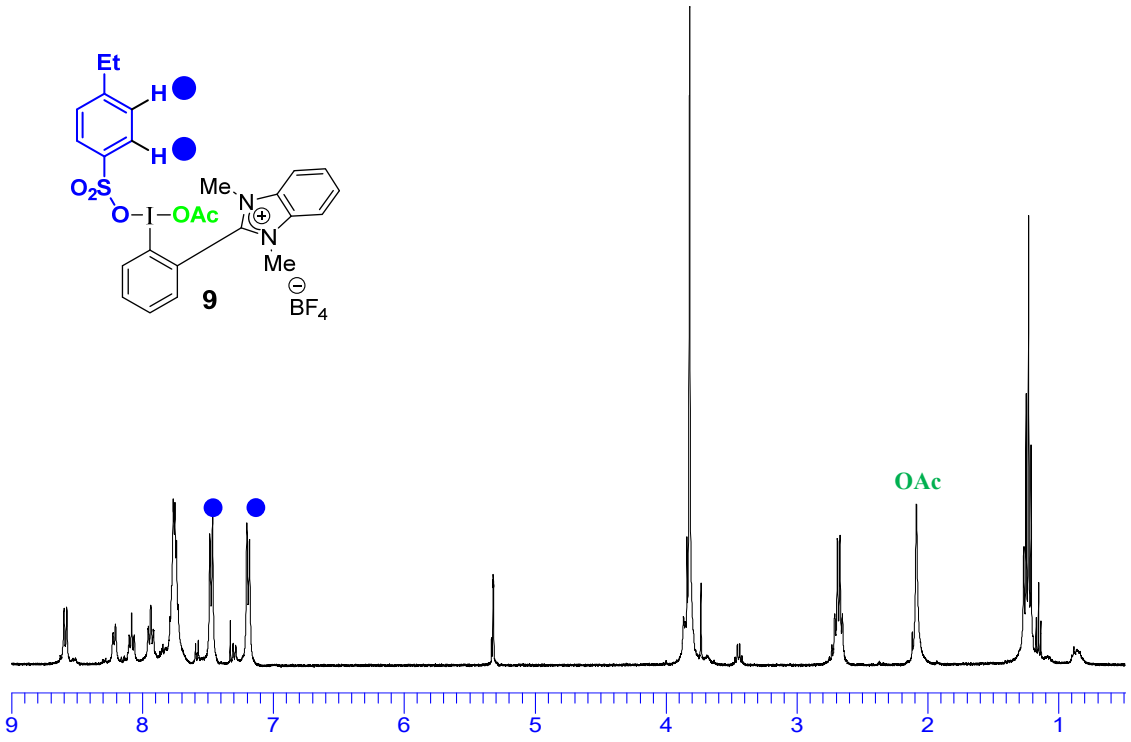


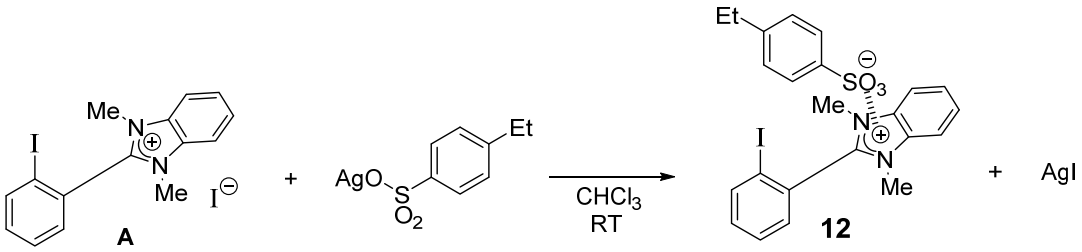
Chart D in full scale

^1H NMR (400 MHz, CD_2Cl_2) at 20 °C



Scheme 1.S4

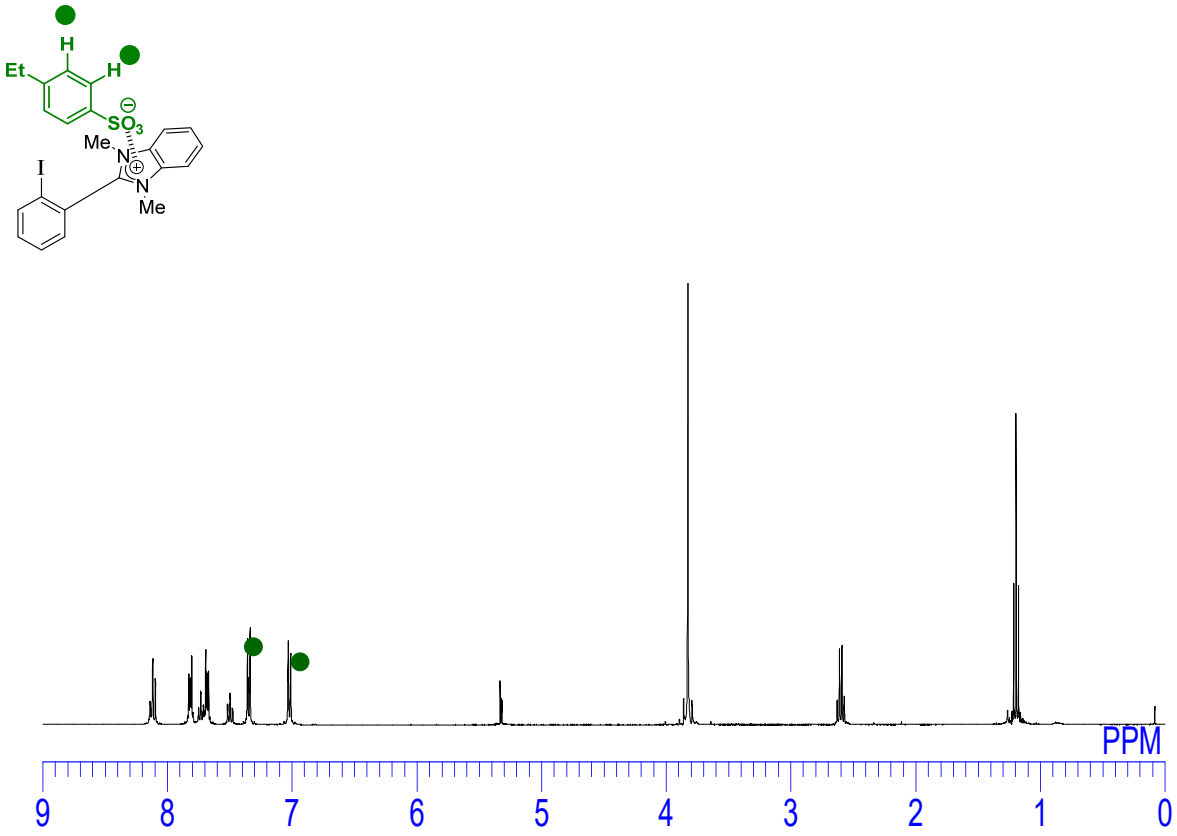
Preparation of imidazolium 4-ethylbenzene sulfonate 12 (Chart B, Figure 1.6)



To the solution of imidazolium iodide (**A)** (0.2 mmol) in $CHCl_3$ was added silver 4-ethylbenzenesulfonate (0.22 mmol), and the reaction mixture was stirred at room temperature for overnight. Then, precipitating AgI was removed by filtration and the filtrate was concentrated to obtain compound **12**.

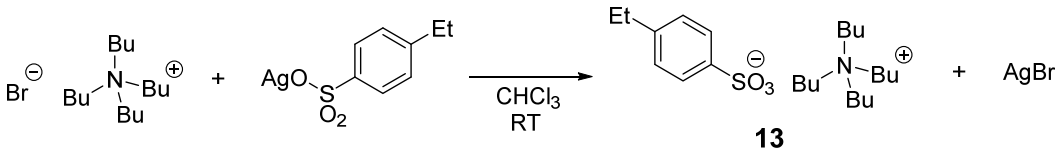
Chart B in full scale

^1H NMR (400 MHz, CD_2Cl_2) at 20 °C



Scheme 1.S5

Preparation of tetrabutylammonium 4-ethylbenzene sulfonate 13 (Chart A, Figure 1.6)

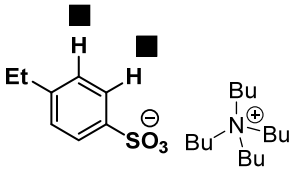


13

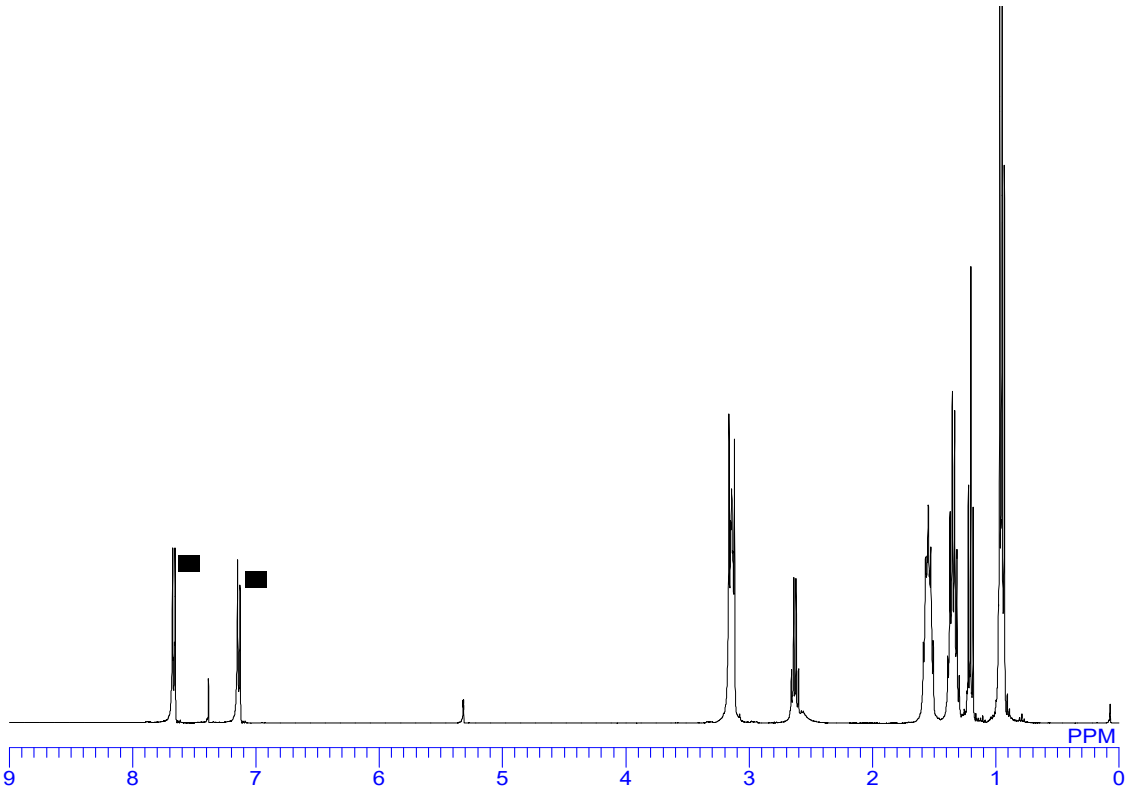
To the solution of tetrabutylammonium bromide (0.2 mmol) in $CHCl_3$ was added silver 4-ethylbenzenesulfonate (0.22 mmol), and the reaction mixture was stirred at room temperature for overnight. Then, precipitating AgI was removed by filtration and the filtrate was concentrated to obtain compound **13**.

Chart A in full scale

^1H NMR (400 MHz, CD_2Cl_2) at 20 °C



13



Scheme 1.S6

Reaction of 9 with γ-pyrone (10) (Chart C, Figure 1.6)

To the solution of **9** (0.05 mmol) in CD_2Cl_2 (0.5 mL) was γ-pyrone (**10**) (0.125 mmol) at room temperature, and the reaction mixture was stirred for 30 min. The ^1H NMR spectrum is shown below at room temperature.

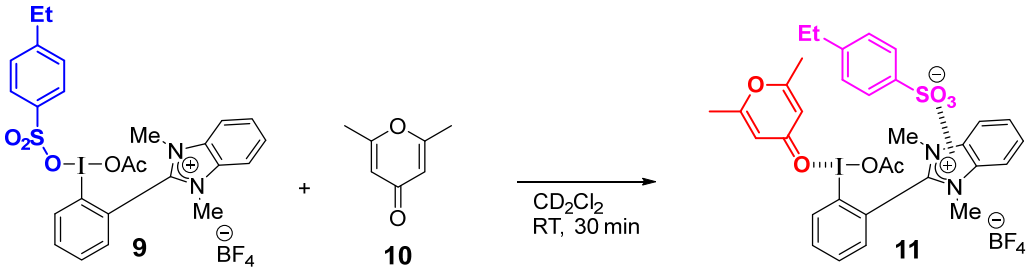
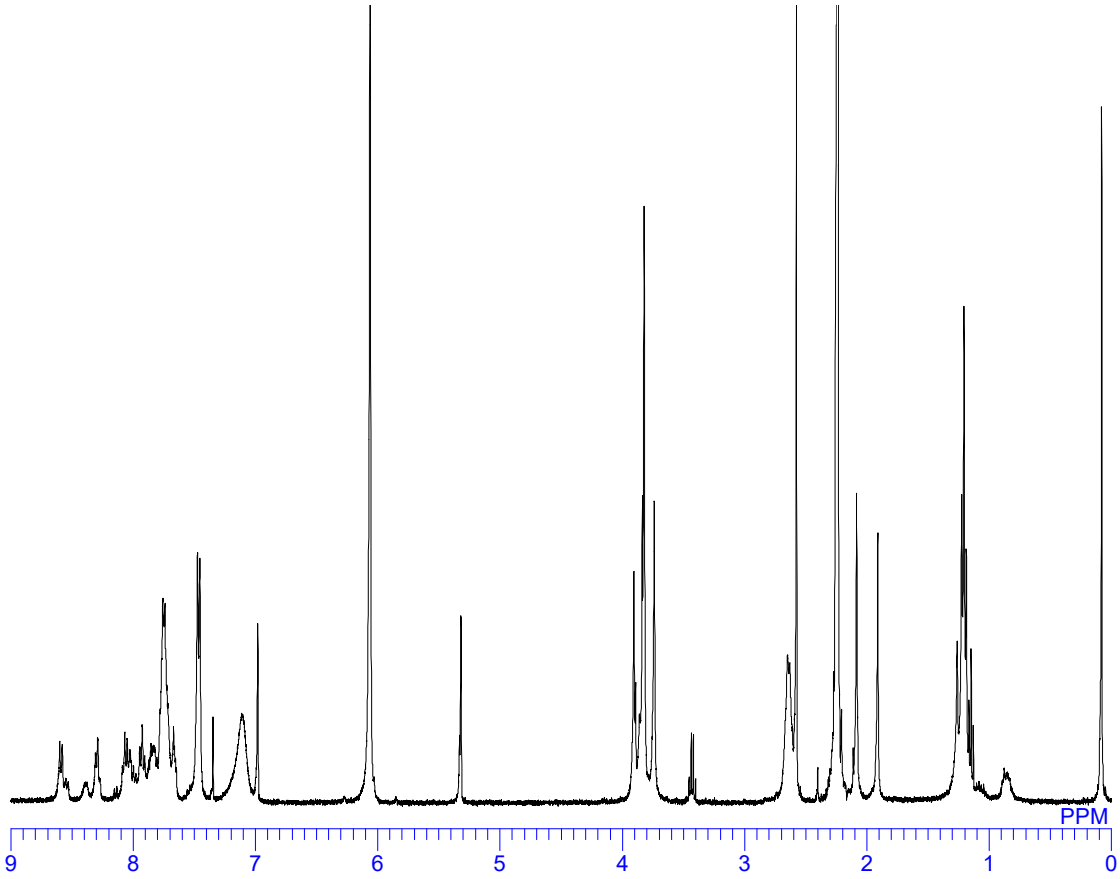


Chart C in full scale

^1H NMR (400 MHz, CD_2Cl_2) at 20 °C

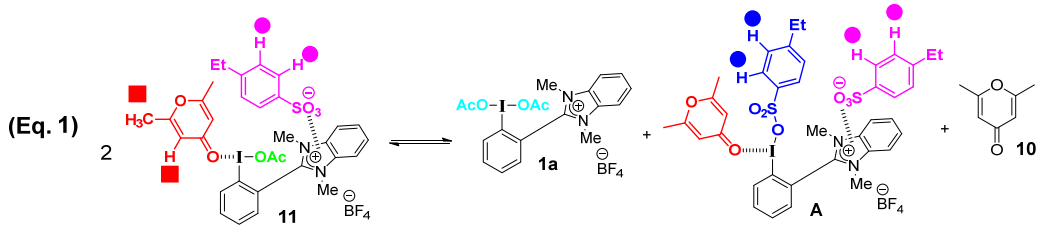


Scheme 1.S7

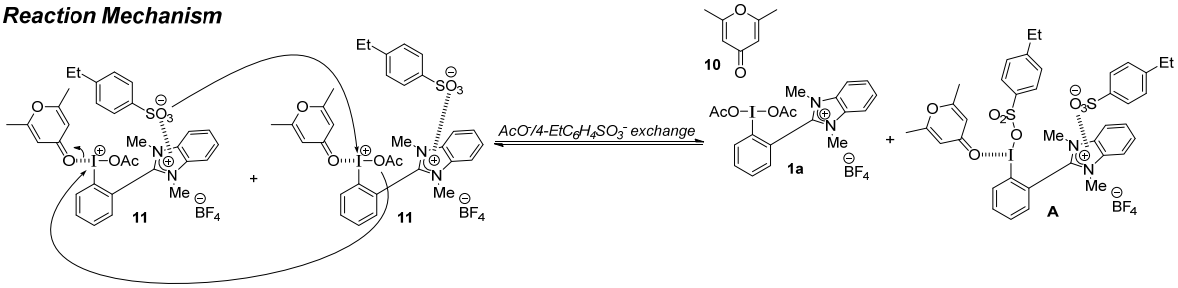
VT NMR study on reaction of 9 with γ-pyrone (10) (VT NMR of Chart C)

The broadening of aromatic proton signals of 4-$EtC_6H_4SO_3$ group in Chart C (Figure 5) indicates fast equilibrium among a few kinds of 4-ethylbenzenesulfonate. Therefore, we carried out the VT NMR study (20, -10, -30, and -50 °C) as shown below, and then discovered that disproportionation between two molecules of **11** via AcO^-/4-$EtC_6H_4SO_3^-$ exchange occurred to give the mixture of **11**, **1a**, **A**, and **10** (Eq. 1 and Reaction Mechanism in Scheme 8). There are two types of 4-$EtC_6H_4SO_3^-$ in this equilibrium: one

(colored by blue) is on the iodine atom, and another (colored by pink) is trapped by the imidazolium moiety. Focusing on aromatic proton signals in ^{1}H NMR spectra (7.0-7.5 ppm), the equilibrium at 20 °C is fast so the signals of 4-Et$C_6H_4SO_3$ groups of **11** and **A** coalesce. At low temperature (-10, -30, and -50 °C), the aromatic proton signals of 4-Et$C_6H_4SO_3$ group trapped by the imidazolium moiety (colored by pink) and the signals of 4-Et$C_6H_4SO_3$ group on the iodine atom (colored by blue) appear independently. Thus, it is important that the coalesce signals of 4-Et$C_6H_4SO_3$ group at 20 °C reflects the property of 4-Et$C_6H_4SO_3$ group trapped by the imidazolium moiety in **11**.

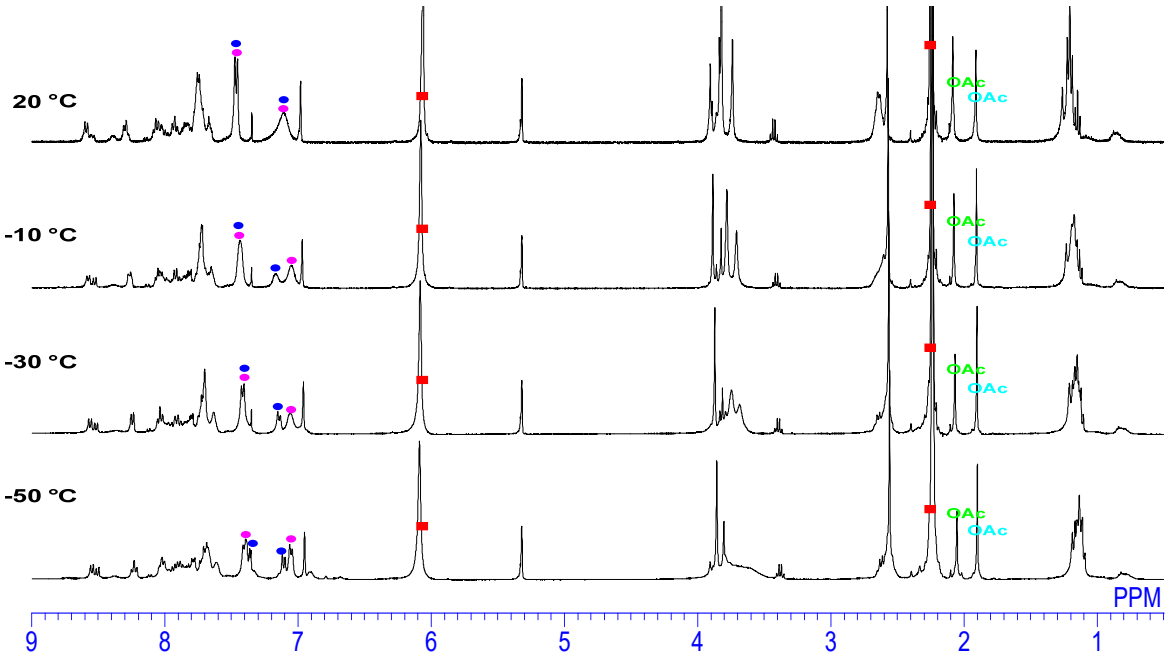


Reaction Mechanism



VT NMR spectra of Chart C on Figure 1.6

^{1}H NMR (400 MHz, CD_2Cl_2)

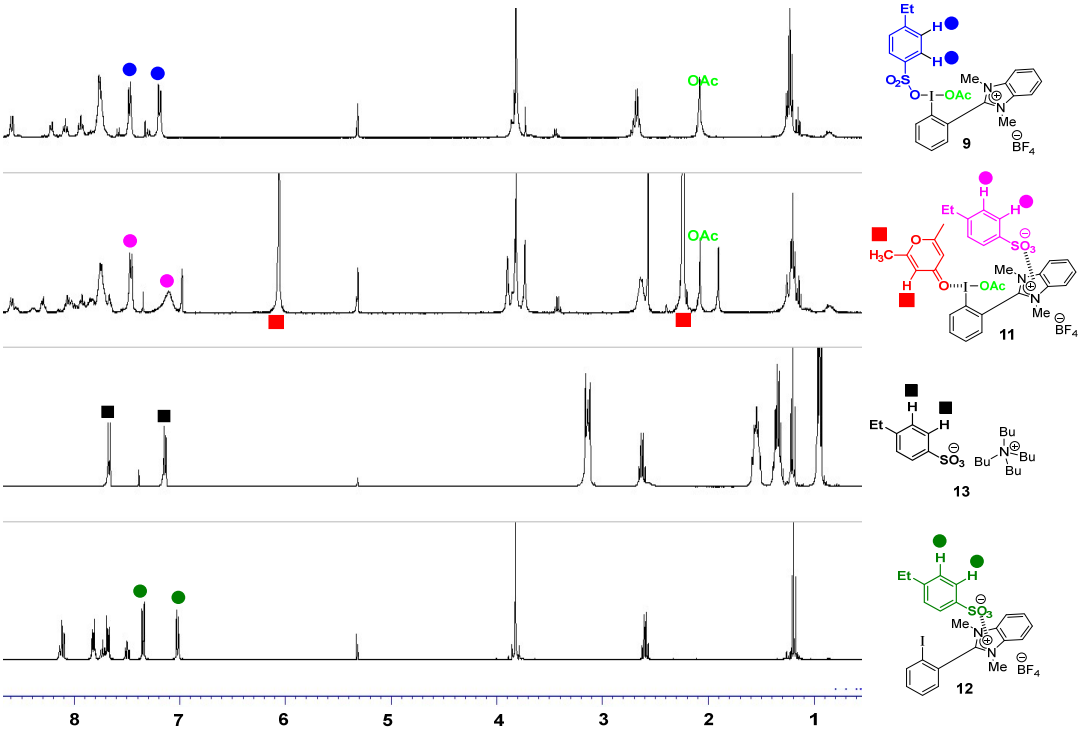


Scheme 1.S8

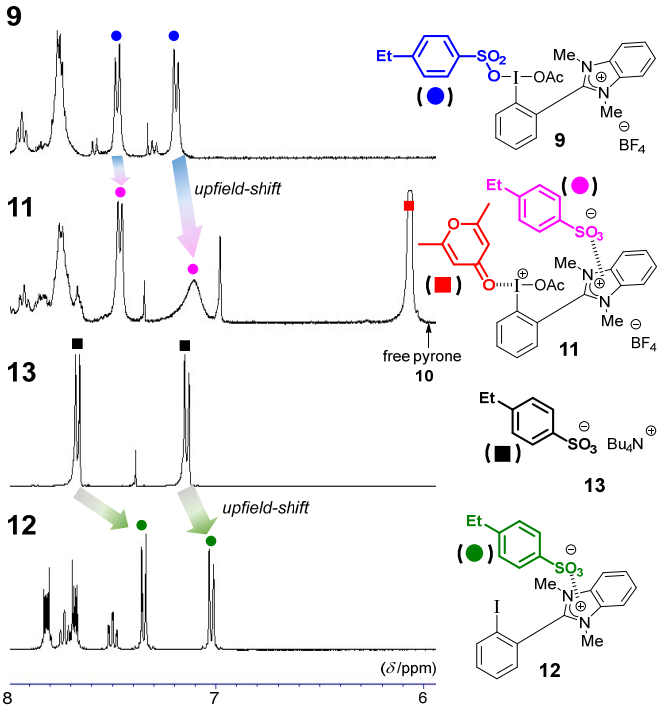
Comparison among compounds 9, 11, 12, and 13 of ^{1}H NMR (Figure 1.6)

We show the comparison among ^{1}H NMR spectra (5.8-8.0 ppm) at 20 °C of compounds **9**, **11**, **12**, and **13** in Figure 5 of the main text. ^{1}H NMR spectra at 20 °C in full scale (0.4-8.8 ppm) are shown below.

Full scale at 20 °C (^{1}H NMR in CD_2Cl_2)



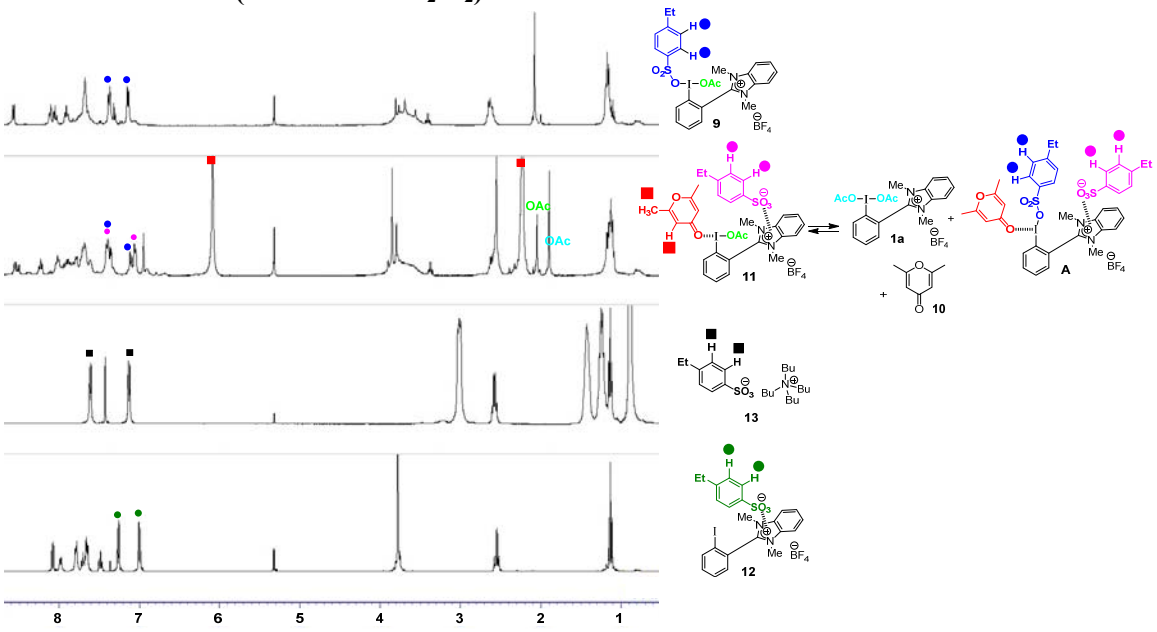
Enlarged view at 20 °C (^{1}H NMR in CD_2Cl_2)



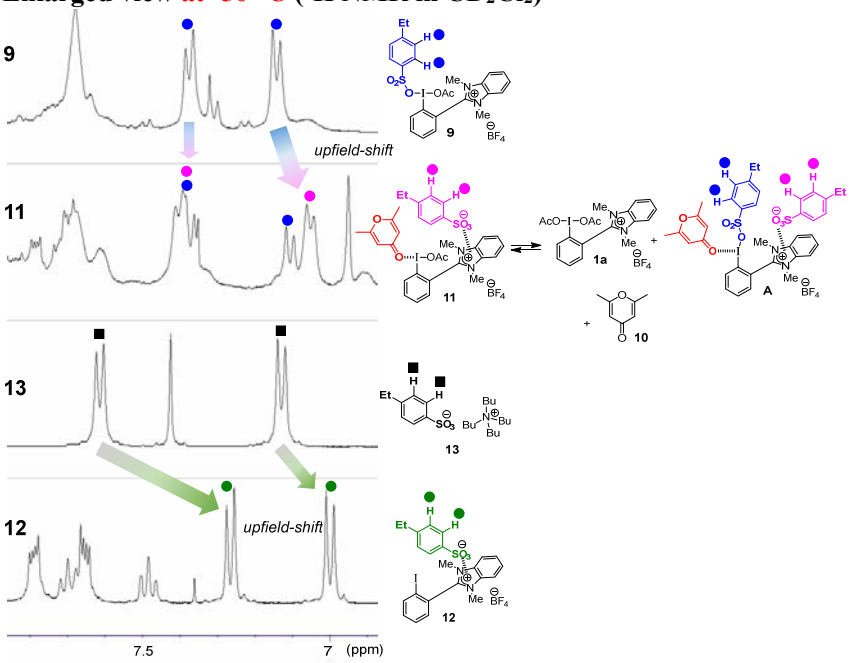
Scheme 1.S9

Considering the result of the VT NMR study on compound **11** described above, we investigated the comparison among ^{1}H NMR spectra at -50 °C, too. In Scheme 1.S10, the ^{1}H NMR spectra at -50 °C are shown. In the chart of 11, signals of two types of 4-Et$C_6H_4SO_3$ groups appeared (pointed by blue or pink circles). The signals (pointed by blue circles) correspond to 4-Et$C_6H_4SO_3^-$ on the iodide atom in species **A** because their chemical shift values are similar to that of **9**. Another signals (pointed by pink circles), which appear at more upfield than that of **A**, correspond to 4-Et$C_6H_4SO_3^-$ trapped by the imidazolium moiety in **11** and **A**, which are overlapped due to the same environment in the interaction with the imidazolium moiety. In fact, the chemical shift values of these signals (pointed by pink circles) are close to those of imidazolium sulfonate **12** (pointed by green circles) as a reference compound rather than Bu_4N salt **13** (pointed by black squares) Therefore, the ^{1}H NMR spectra at -50 °C supports that 4-Et$C_6H_4SO_3$ anion is kicked out and trapped by the imidazolium moiety and complex **11** is generated.

Full scale at -50 °C (^{1}H NMR in CD_2Cl_2)



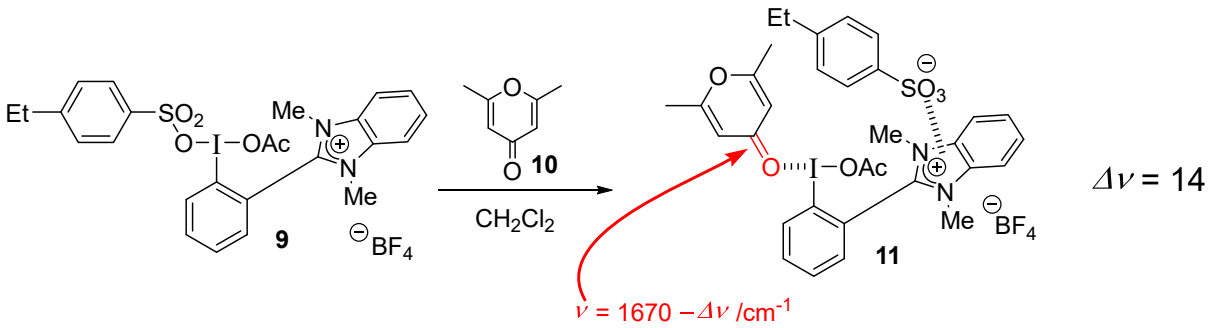
Enlarged view at -50 °C (^{1}H NMR in CD_2Cl_2)

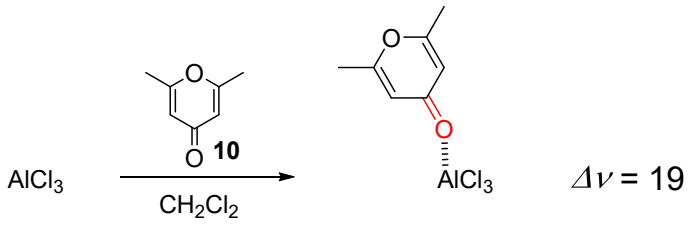


Scheme 1.S10

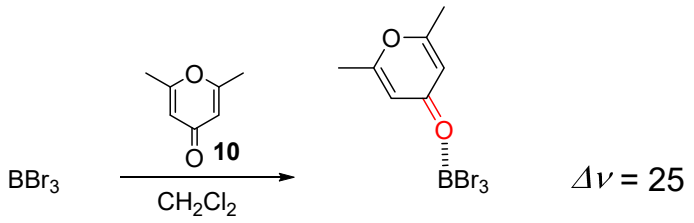
Confirmation of coordination of γ-pyrone (10) to the iodine canter by IR stretching frequency of the C=O bond

We established the evaluation of the Lewis acidity by IR stretching frequency of the C=O bond of γ-pyrone (**10**) in the complexation between a Lewis acid and **10**. Therefore, the coordination of the carbonyl oxygen atom of **10** to the iodine center in **9** was observed by this method. In the solution of **9** and **10** in CH_2Cl_2, $\Delta\nu$ is 14 cm^{-1}. Considering the values of $\Delta\nu$ exhibited by $AlCl_3$ and BBr_3, this value clearly suggests the the coordination of the carbonyl oxygen atom of **10** to the iodine center in **9**.





Y. Nishimoto, S. Nakao, S. Machinaka, F. Hidaka, M. Yasuda, *Chem. Eur. J.* **2019**, *25*, 10792



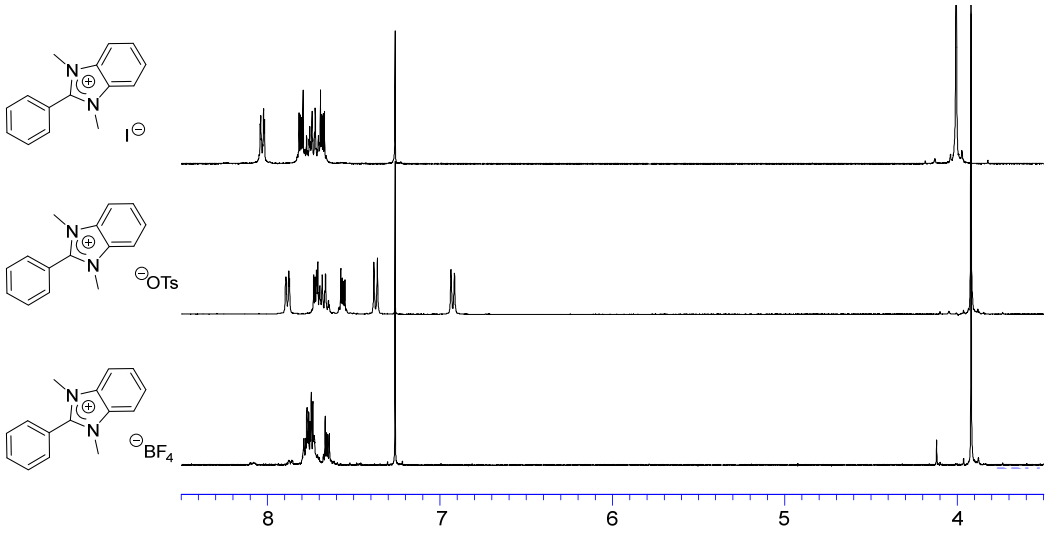
A. Konishi, R. Yasunaga, K. Chiba, M. Yasuda, *Chem. Commun.* **2016**, *52*, 3348.

Scheme 1.S11

Effects of counter anions on ^{1}H NMR spectra of imidazolium salts

Effects of counter anions on imidazolium salts were investigated by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of imidazolium iodide, tosylate, and tetrafluoroborate in $CDCl_3$ are shown below. Chemical shifts of each imidazolium salts are considerably different, which suggests that imidazolium cation interacts with each anion to form contact ion pairs.

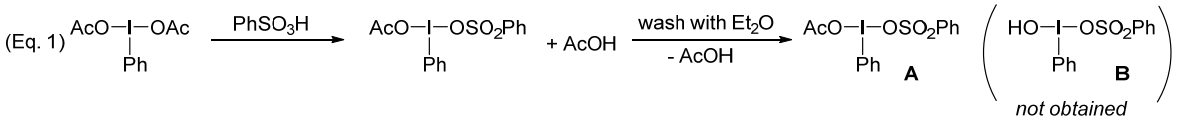
^{1}H NMR (400 MHz, $CDCl_3$)



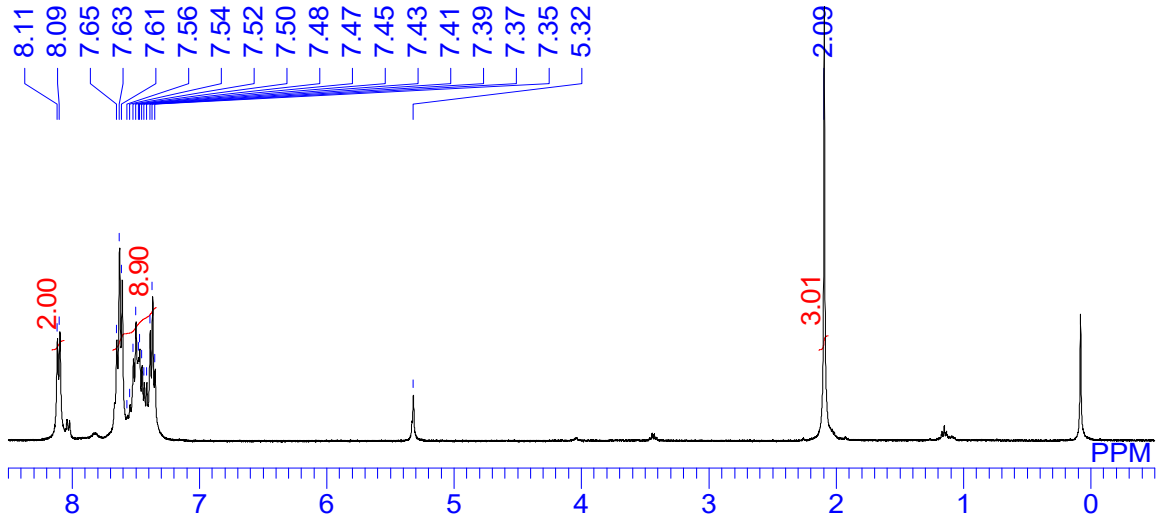
Scheme 1.S12

Effects of OH and OAc groups on I atom of hypervalent iodines on the regioselectivity

To the solution of $PhI(OAc)_2$ in CH_2Cl_2 was added $PhSO_3H$, and the reaction mixture was stirred at room temperature for 30 min. Then, the volatiles were evaporated in vacuo and the residual oil was lightly washed Et_2O to give $PhI(OAc)OSO_2Ph$ (**A**) as a colorless oil (Eq. 1). ^{1}H NMR spectra of $PhI(OAc)OSO_2Ph$ (**A**) is shown below. This result is contrast to the reaction of $PhI(OAc)_2$ with $TsOH{\cdot}H_2O$ giving PhI(OH)OTs. This experiment suggests that not $PhI(OH)OSO_2Ph$ (**B**) but $PhI(OAc)OSO_2Ph$ (**A**) is generated without H_2O.

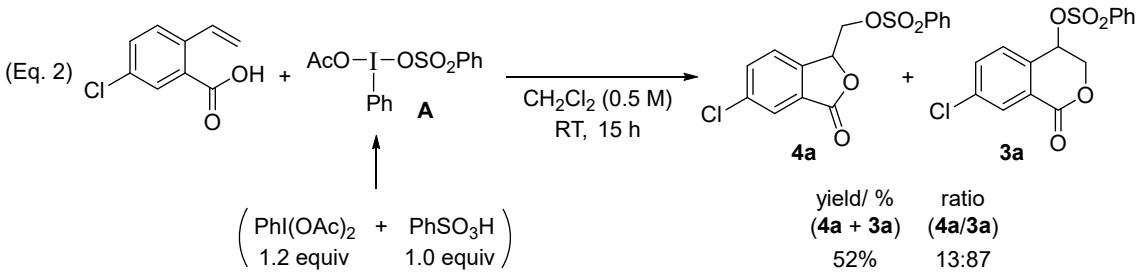


^{1}H NMR of $PhI(OAc)OSO_2Ph$ (400 MHz, CD_2Cl_2)



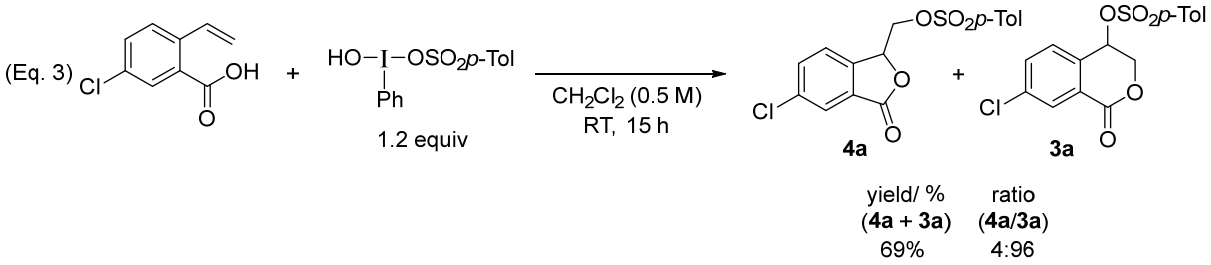
Scheme 1.S13

Therefore, we used PhI(OAc)OSO_2Ph (**A**) to investigate the effect of OH and OAc groups on I atom of hypervalent iodines on the regioselectivity, as shown below (Eq. 2). To a solution of $PhI(OAc)_2$ (0.0577 g, 0.179 mmol) in CH_2Cl_2 (0.3 mL) was added $PhSO_3H$ (0.0241 g, 0.152 mmol) under N_2 atmosphere. The mixture was stirred for 30 min at room temperature. Then, CH_2Cl_2 and AcOH were evaporated under reduced pressure (1.0 Torr) for 5 min at 30 °C and filled with N_2. The evaporation and N_2-filling manipulation was repeated twice. After evaporation, to the mixture was added CH_2Cl_2 (0.3 mL) and 5-chloro-2-vinylbenzoic acid (0.0289 g, 0.158 mmol). The reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by water and the water layer was extracted with CH_2Cl_2. The collected organic layer was dried over $MgSO_4$ and the volatiles were evaporated. The yields of 5-*exo* and 6-*endo* product were determined by ^{1}H NMR spectroscopy with 1,1,2,2-tetrachloroethane as an internal standard.



Scheme 1.S14

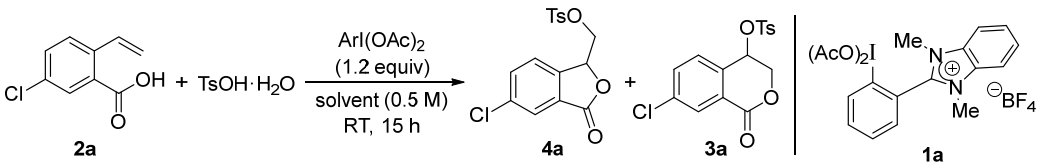
The result of Eq. 2 revealed that PhI(OAc)OSO_2Ph **A** exhibited the 6-*endo* selectivity, and the level of selectivity is almost same as that exhibited by PhI(OH)OSO_2*p*-Tol (Koser's reagent) (Eq. 3). Therefore, OH and OAc groups on I atom of hypervalent iodines do not influence on the regioselectivity of the present tosyloxylactonization.

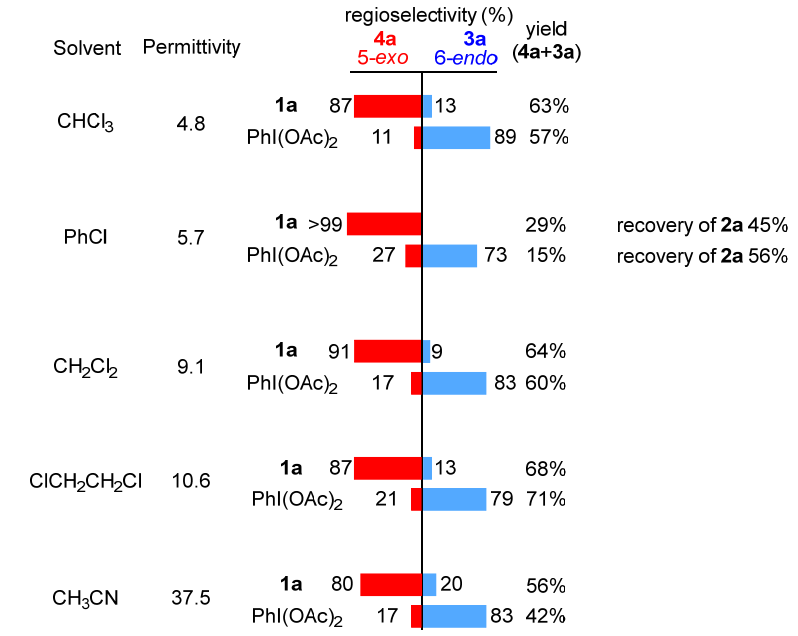


Scheme 1.S15

Effect of solvents on the regioselectivity of 1a and $PhI(OAc)_2$

Solvent effects on the regioselectivity in the tosyloxylactonization of **2a** with $TsOH\cdot H_2O$ using **1a** or $PhI(OAc)_2$ as shown below. In the use of $CHCl_3$, PhCl, CH_2Cl_2, $ClCH_2CH_2Cl$, and CH_3CN as solvents, **1a** and $PhI(OAc)_2$ exhibited the high level of 5-*exo* selectivity and 6-endo selectivity, respectively, regardless of the permittivity. Theexaminations in hexane, toluene, Et_2O, and THF resulted in no reaction because **1a** and $PhI(OAc)_2$ are insoluble in these solvents.



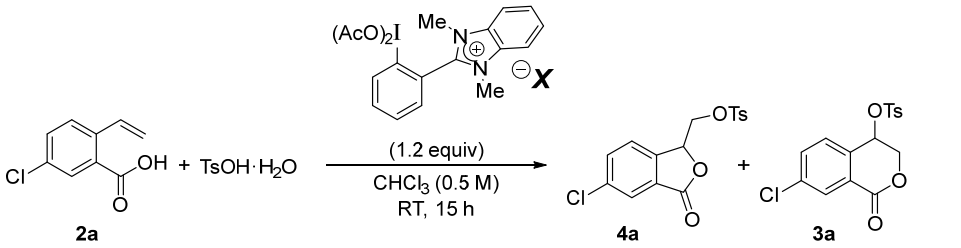


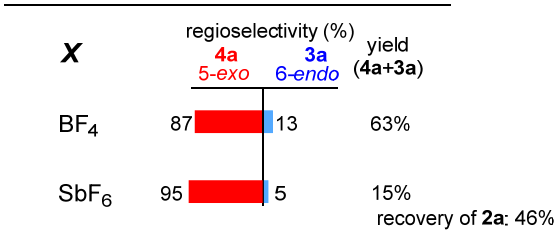
The use of other solvents such as hexane, toluene, Et_2O, and THF resulted in no reaction because **1a** and $PhI(OAc)_2$ are insoluble in these solvents.

Scheme 1.S16

Effect of couteranions of imidazolium moiety on the regioselectivity

The use of SbF_6^- instead of BF_4^- in $ArI(OAc)_2$ (**1a**) also gave 5-*exo* product (**4a**). The selectiveity of the SbF_6 salt was the same level as that of the BF_4 salt. The low yield was due to the low solubility of the SbF_6 salt. Other hypervalent iodines (***X*** = Br, I, OTs, PF_6) could not been synthesized.



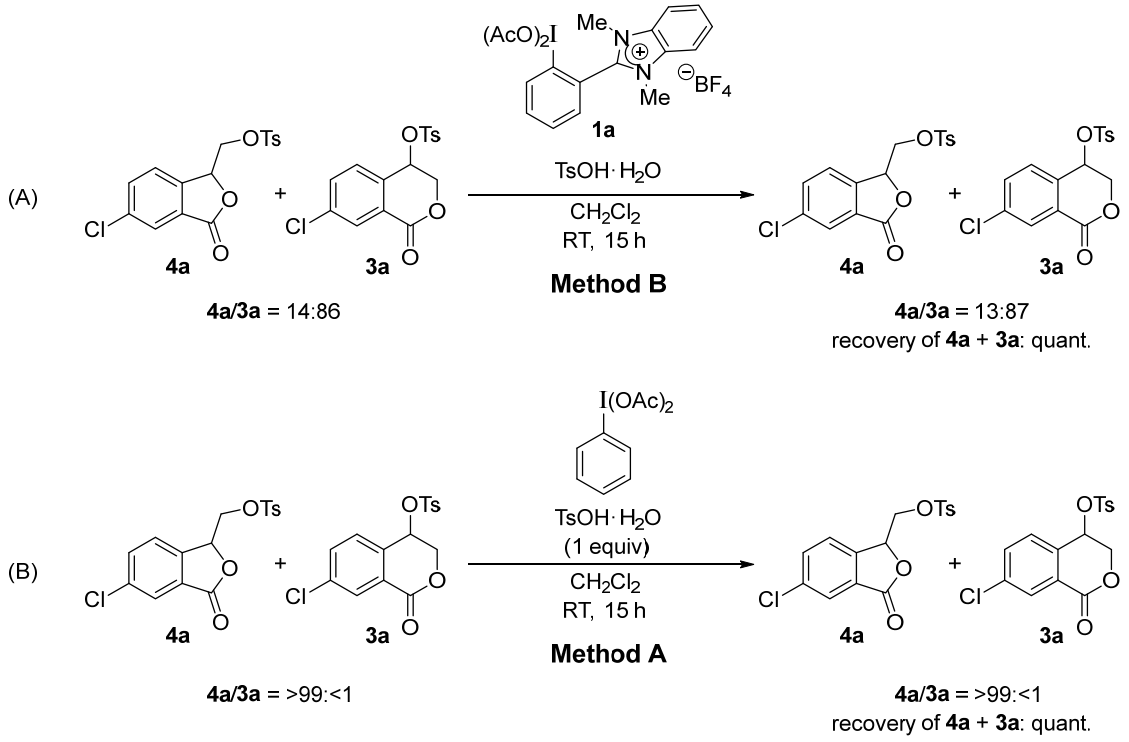


Other hypervalent iodines (***X***= Br, I, OTs, PF_6) could not been synthesized.

Scheme 1.S17

Investigation of isomerization between 5-*exo* and 6-*endo* products

The results shown in Scheme 1.S18 suggested the isomerization between 5-*exo* and 6-*endo* products did not occur. Method A and Method B are the reaction conditions giving preferentially 5-*exo* (**4a**) and 6-*endo* (**3a**), respectively (see General Procedures). After the mixture of 5-*exo* (**4a**) and 6-*endo* (**3a**) (**4a**/**3a** = 14:86) was underwent the reaction conditions using **1a** (Method B), the ratio of **4a** to **3a** was not changed, and **4a** and **3a** was recovered quantitatively. When the 5-*exo* **4a** was treated with the reaction conditions using $PhI(OAc)_2$ (Method A), 6-*endo* (**3a**) was not obtained and 5-*exo* (**4a**) was recovered quantitatively.



Scheme 1.S18

Computational Studies

Calculation Method Details

All geometry optimizations and thermal energy correction calculations (frequency analyses) using density functional theory (DFT) were performed with the Gaussian 16 (revision C.01). Quantum chemical calculations were performed under vacuum at 298 K and 1 bar. The geometry optimizations were carried out at ωB97X-D level of theory in gas phase with a mixed basis set; 6-311+G(d,p) for C, H, O, N, S, B, F and Lanl2DZ for I.

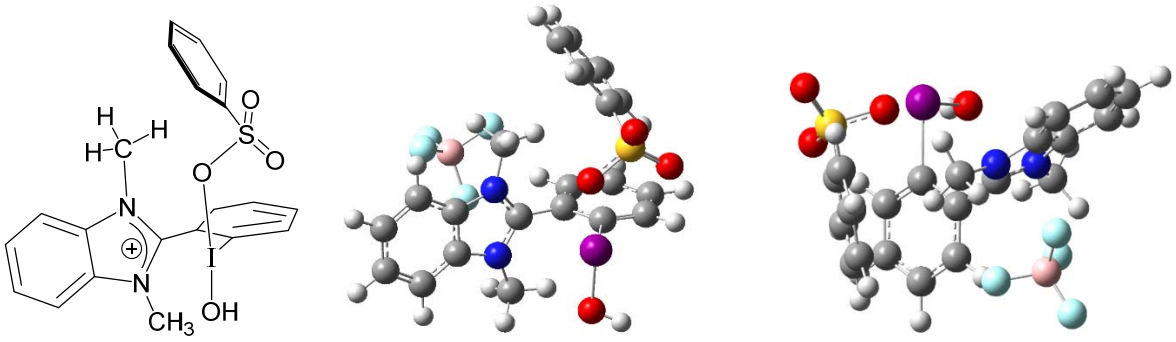
M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, S112 J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, Gaussian 16, Revision C.01, Gaussian, Inc., Wallingford CT, 2016.

Summary of calculated energies and thermochemical parameters of the optimized structures

	electronic and zero-point Energies [hartree]	electronic and thermal Energies [hartree]	electronic and thermal Enthalpies [hartree]	electronic and thermal Free Energies [hartree]	imaginary frequency
***o*-7-A**	-2056.124012	-2056.090567	-2056.089623	-2056.191884	0
***o*-7-B**	-2056.120972	-2056.087956	-2056.087012	-2056.186394	0
8-B	-1522.773154	-1522.746052	-1522.745108	-1522.831828	0
PhI(OH)OSO2Ph	-1173.957596	-1173.940561	-1173.939617	-1174.004019	0
ArI(OH)OSO2Ph bearing an imidazolidinium moiety					
conformer A	-1903.730259	-1903.699333	-1903.698388	-1903.793765	0
conformer B	-1903.729659	-1903.698608	-1903.697664	-1903.793549	0
***m*-7**	-2056.129737	-2056.096809	-2056.095865	-2056.196892	0
***p*-7**	-2056.120003	-2056.087134	-2056.08619	-2056.186741	0
ArI(OH)OMs bearing an imidazolium moiety	-1864.465139	-1864.434952	-1864.434007	-1864.528787	0

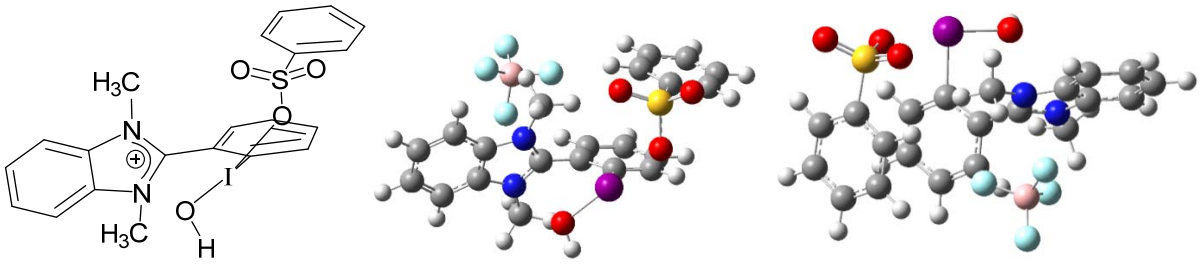
Optimized Structures

o-7-A



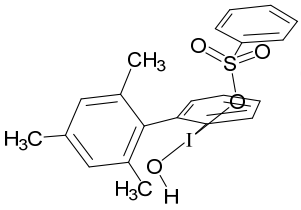
Another view

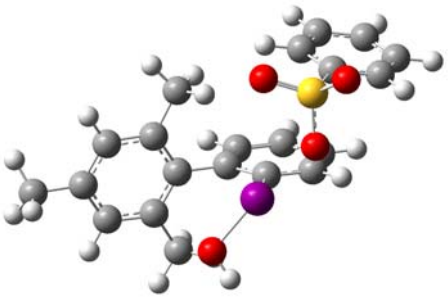
o-7-B

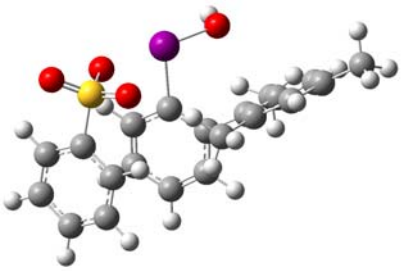


Another view

8-B

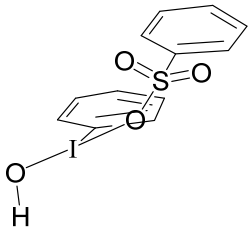


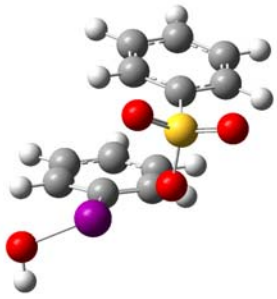


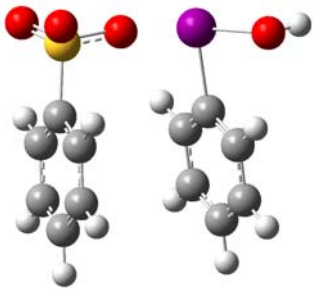


Another view

PhI(OH)OSO$_2$Ph



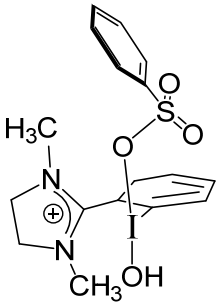


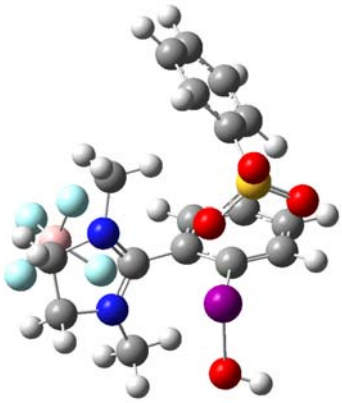


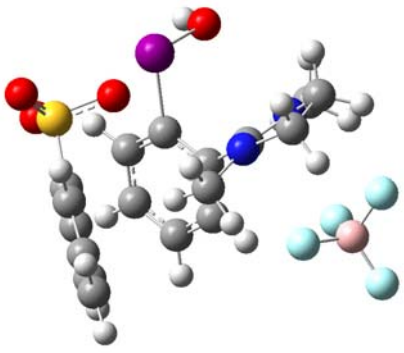
Another view

ArI(OH)OSO$_2$Ph bearing an imidazolidinium moiety

Conformer A



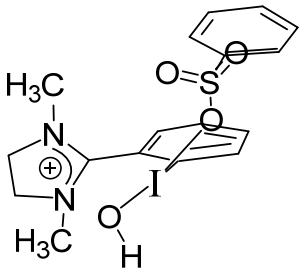


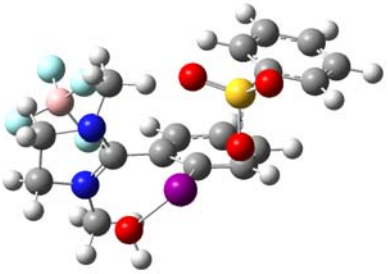


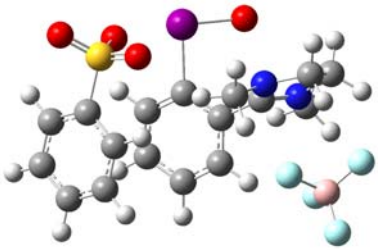
Another view

ArI(OH)OSO$_2$Ph bearing an imidazolidinium moiety

Conformer B

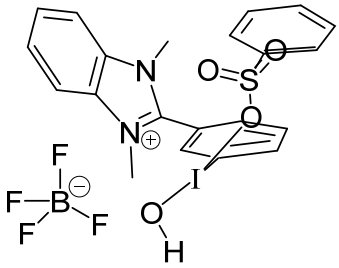


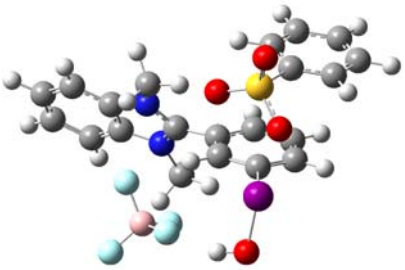


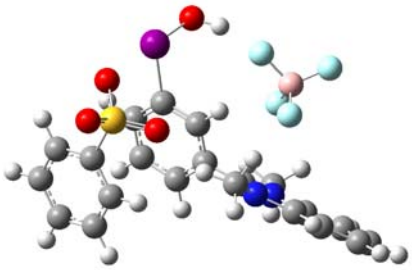


Another view

***m*-7**

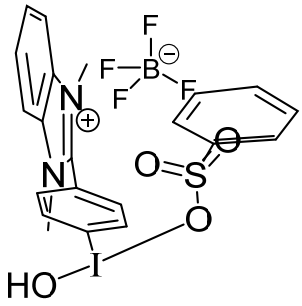


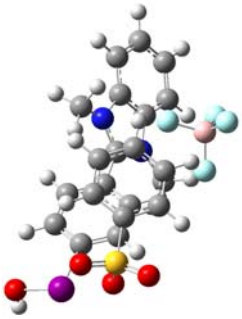


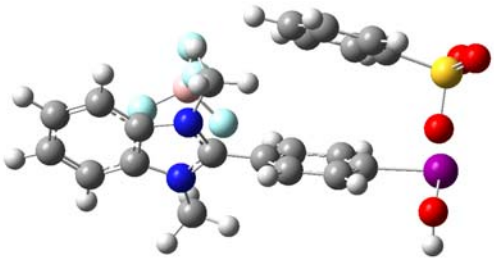


Another view

***p*-7**

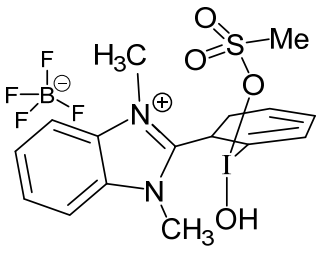


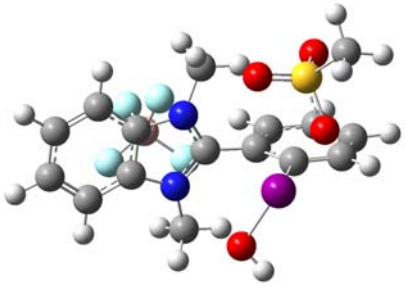


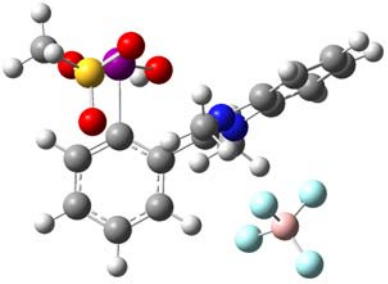


Another view

ArI(OH)OMs bearing an imidazolium moiety







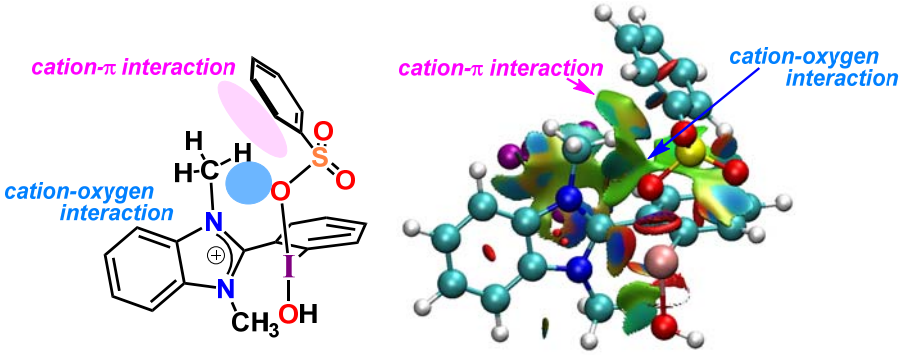
Another view

Non-Covalent Interaction (NCI)-Plot

Non-covalent interactions (NCI) were computed using the non-covalent interaction index from the optimized electron density at ωB97X-D level of theory in gas phase with a mixed basis set; cc-pVTZ for C, H, O, N, S, B, F and cc-pVTZ-DK3 for I. The wave function files (.wfn) were obtained from single point energy calculation using the optimized structures as above at ωB97X-D level of theory in gas phase with a mixed basis set; cc-pVTZ for C, H, O, N, S, B, F and cc-pVTZ-DK3 for I.

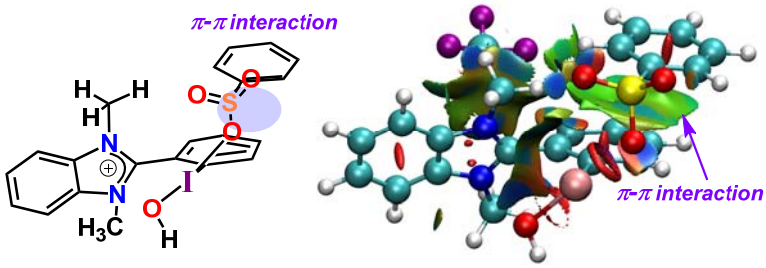
The generation of the NCI plot surfaces were obtained by NCIPLOT program.[38,39] The surfaces were colored on a blue-green-red (BGR) scale using VMD program[40] with a reduced density gradient (RDG) surfaces = 0.65 a.u. and the color range blue(attractive)-green-red(repulsive) for $-0.015 < \rho < +0.015$ a.u.. The blue region indicates strong attractive interactions and the red region indicates strong repulsive interactions.

***o*-7-A**



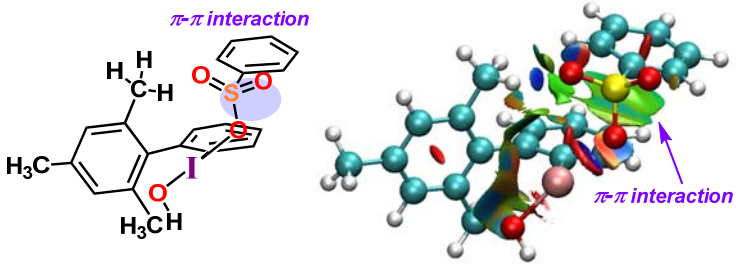
Scheme 1.S19

***o*-7-B**



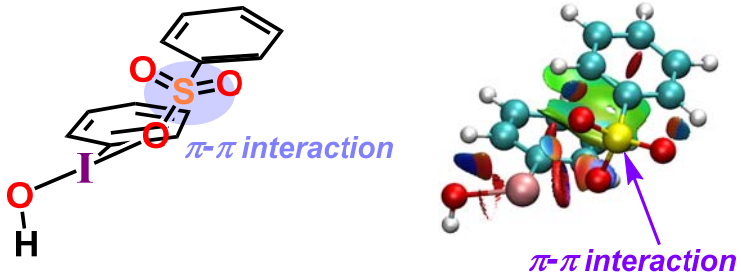
Scheme 1.S20

8-B



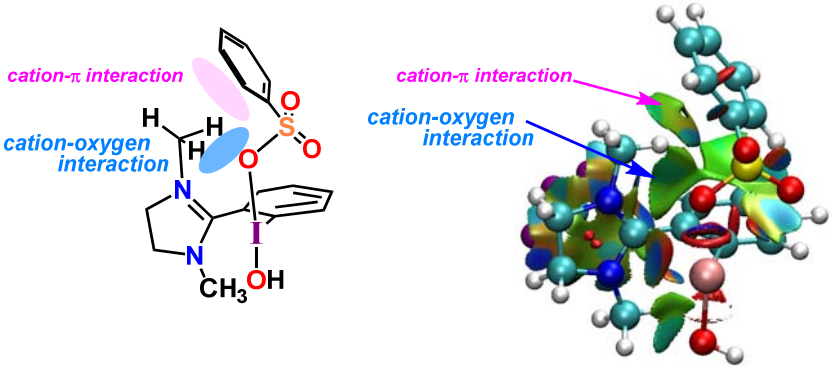
Scheme 1.S21

PhI(OH)OSO$_2$Ph



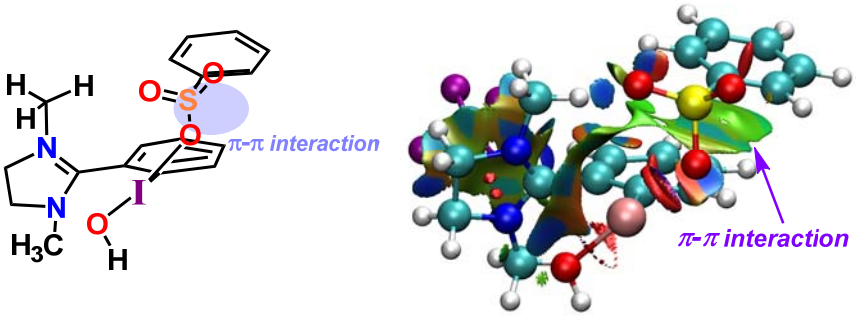
Scheme 1.S22

ArI(OH)OSO$_2$Ph bearing an imidazolidinium moiety Conformer A



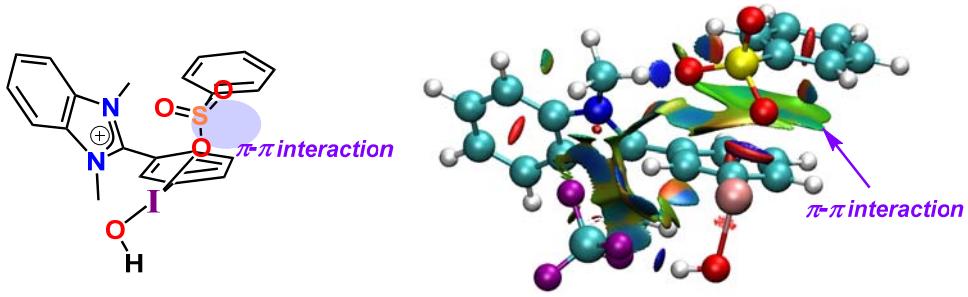
Scheme 1.S23

ArI(OH)OSO$_2$Ph bearing an imidazolidinium moiety Conformer B



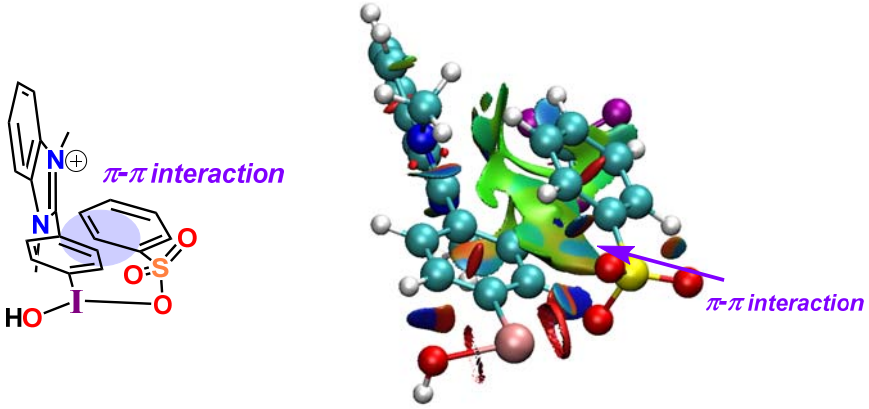
Scheme 1.S24

***m*-7**



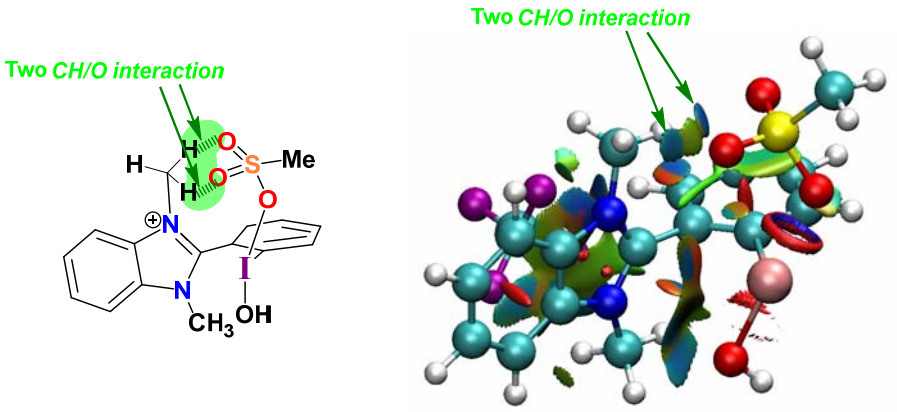
Scheme 1.S25

***p*-7**



Scheme 1.S26

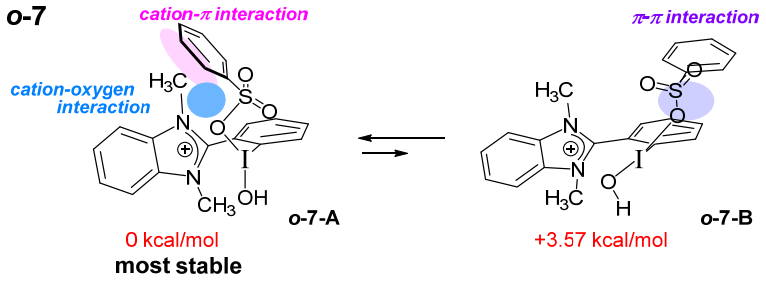
ArI(OH)OMs bearing an imidazolium moiety



Scheme 1.S27

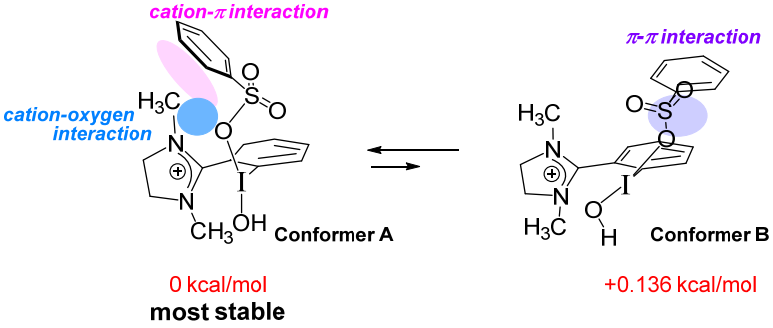
Summary of NCI analysis and thermochemical parameters

ArI(OH)OSO_2Ph ***o*-7** has two enegetic local minimums, and major conformer ***o*-7-A** is more stable than minor one ***o*-7-B** by 3.57 kcal/mol. Noncovalent interaction analysis shows that in ***o*-7-A** the Me group of the imidazolium moiety and the phenyl ring of the $PhSO_3$ group generates a cation–π interaction surface. In addition, the same Me group forms an effective cation-oxygen interaction with the oxygen atom of the $PhSO_3$ group, as evident from the large isosurface. In the minor conformer ***o*-7-B**, a π–π interaction of the $PhSO_3$ group with the iodobenzene framework contributes to the stabilization of the conformation. Therefore, the noncovalent interactions between the anionic $PhSO_3$ group and the imidazolium moiety is stronger than the π–π interaction of the $PhSO_3$ group with the iodobenzene framework. In ArI(OH)OSO_2Ph bearing an imidazolidinium moiety like **1d**, most stable **conformer A** (0.136 kcal/mol) has cation–π and cation-oxygen interactions between the imidazolidinium moiety and the $PhSO_3$ group like ***o*-7-A**. Minor **conformer B** has a π–π interaction of the $PhSO_3$ group with the iodobenzene framework. Thus, imidazolium and imidazolidinium moieties attracts the $PhSO_3$ group via the noncovalent forces in Koser-type intermediates.



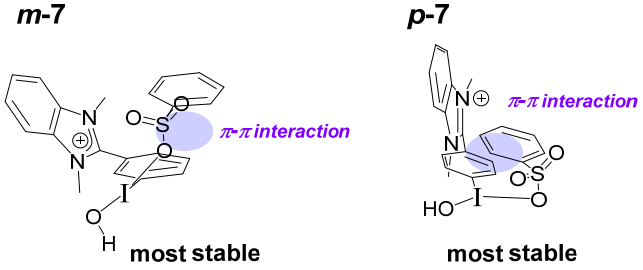
Scheme 1.S28

ArI(OH)OSO_2Ph bearing an imidazolidinium moiety



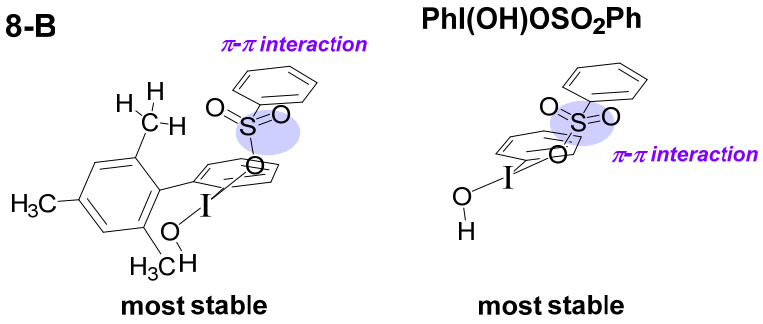
Scheme 1.S29

In contrast to ***o*-7**, the most stable conformers of *meta*-substituted ***m*-7** and *para*-substituted ***p*-7**, are the structures involving a π–π interaction like ***o*-7-B**. Therefore, effective noncovalent interactions work only between the anionic $PhSO_3$ group and the imidazolium moiety at the *ortho* position of the iodine atom.



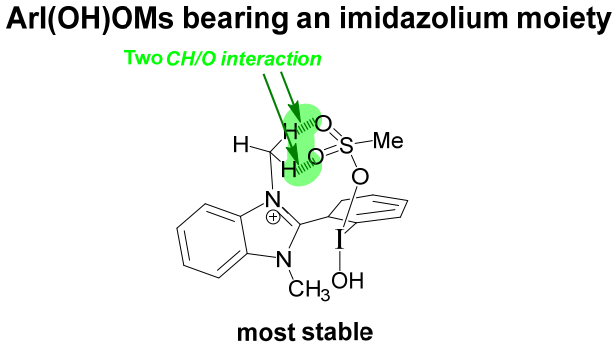
Scheme 1.S30

The most stable conformers of **8** and PhI(OH)OSO$_2$Ph include the π–π interaction of the PhSO$_3$ group with the iodobenzene framework. So, this type of π–π interaction is a main factor to stabilize the conformation of Koser-type reagents.



Scheme 1.S31

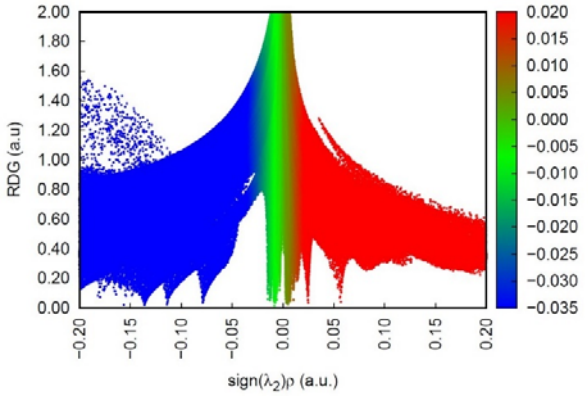
The combination of ArI(OAc)$_2$ (**1a**) with MsOH also exhibits the 5-*exo* selectivity. In this case, ArI(OX)OMs (X = H or OAc) would be an intermediate. The NCI analysis shows two CH/O interaction between the Me group of the imidazolium moiety and the MsO group. Thus, the imidazolium moiety effectively attracts the MsO group via the noncovalent forces.



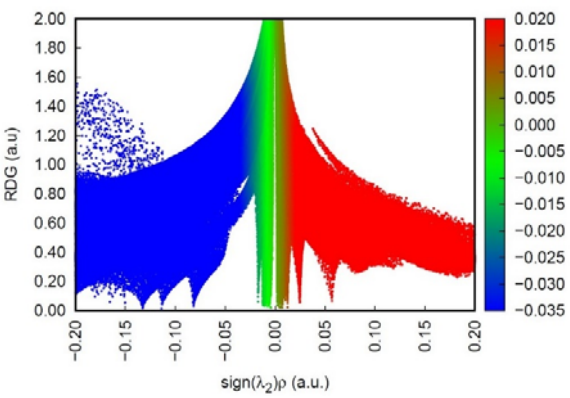
Scheme 1.S32

Scatter plots of the non-covalent interaction index

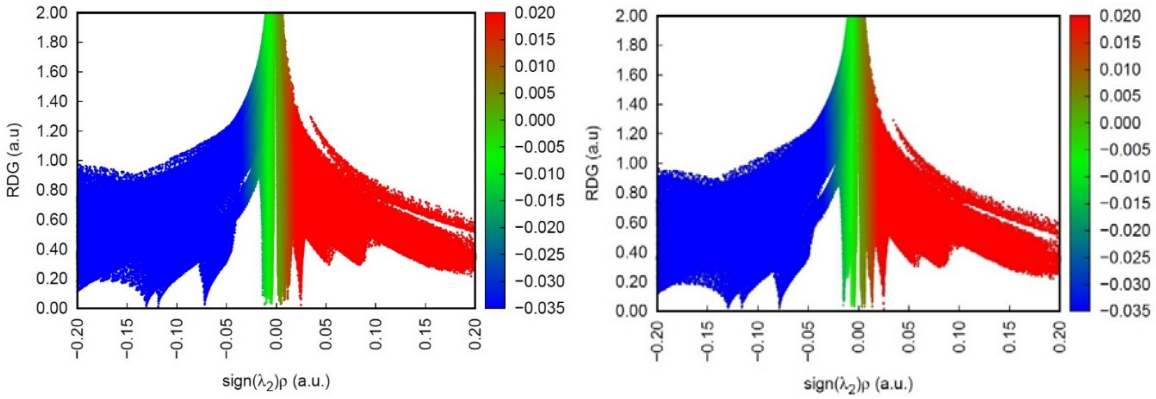
o-7-A



o-7-B

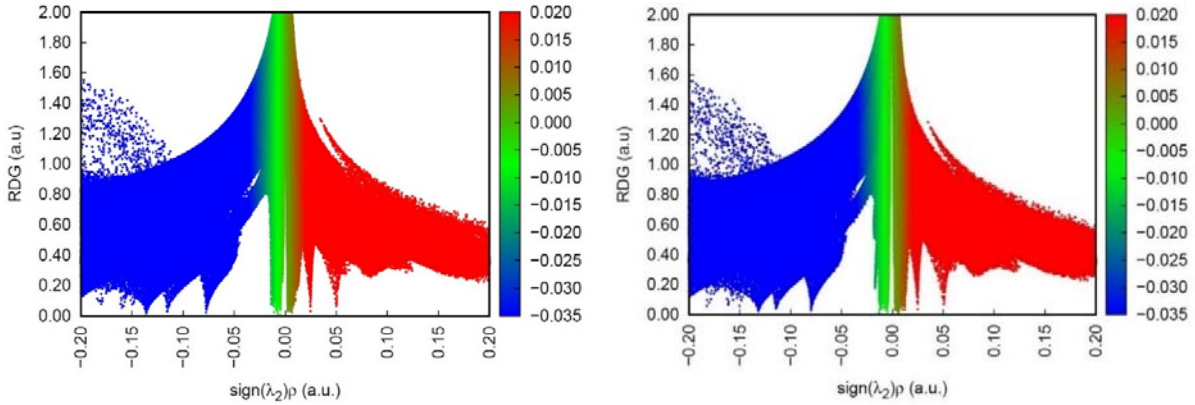


8-B **PhI(OH)OSO$_2$Ph**

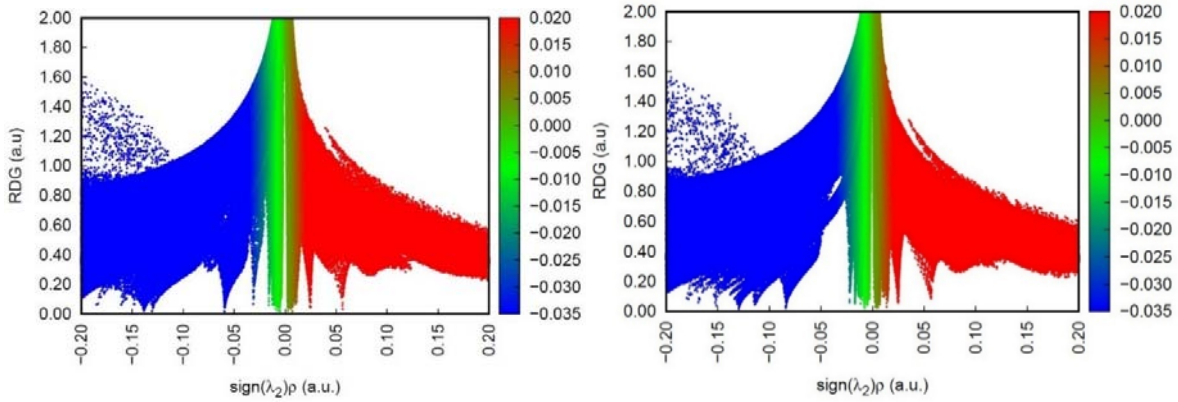


ArI(OH)OSO$_2$Ph bearing an imidazolidinium moiety

Conformer A **Conformer B**



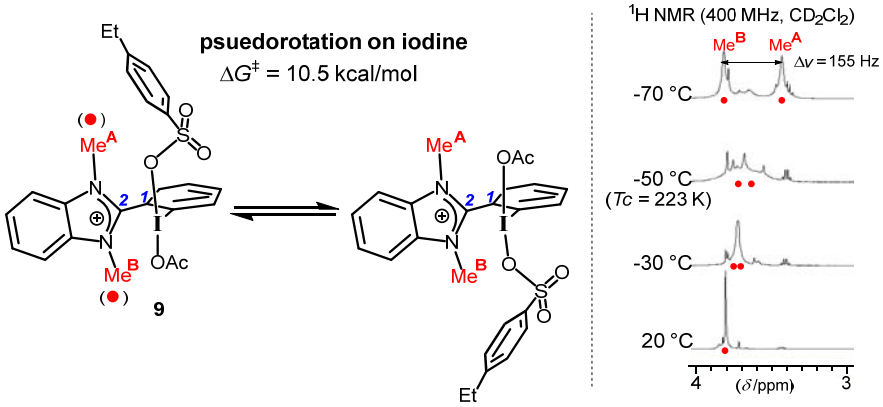
***m*-7** ***p*-7**



VT NMR Study on ArI(OAc)(*p*-EtC$_6$H$_4$SO$_3$) (9)

When ArI(OAc)(*p*-EtC$_6$H$_4$SO$_3$) (**9**), which was generated from the reaction of **1a** with 4-EtC$_6$H$_4$SO$_3$H, was observed by ^{1}H NMR spectroscopy, at 20 °C and -30 °C the two Me groups on nitrogen atoms are isochronous, but at -70 °C they are anisochronous and each of singlet signals appear at 3.44 and 3.83 ppm (Schemes 1.S33 and 1.S34). A coalescence point is -50 °C. The signal of Me^A group interacting with *p*-EtC$_6$H$_4$SO$_3$ group would shift upfield compared with that of Me^B group due to cation-π interactions. A value

of activation energy is estimated at 10.5 kcal/mol by equation (a). This activation energy would be small for C^1-C^2 bond rotation considering an activation energy of C-C bond rotation in 2,2'-disubstituted biphenyl skeleton (ref. G. Bott, L. D. Field, S. Sternhell, *J. Am. Chem. Soc.* **1980**, *102*, 5618.). Actually, activation energies of C^1-C^2 bond rotation in compound (*R*,*R*)-**1d** and its precursors **S10** and **S11** are much more larger than that in **9** because the two Me groups on nitrogen atoms in (*R*,*R*)-**1d**, its precursors **S10**, or **S11** are anisochronous even at 20 °C (Scheme S35), despite the fact that steric hindrance around the corresponding C^1-C^2 bond is almost same among **9**, (*R*,*R*)-**1d**, **S10**, and **S11**. Therefore, the coalescence of two Me groups in **9** would be due to psuedorotation on an iodine atom. The value of activation energy of psuedorotation on an iodine atom in λ^3-iodanes was reported to be about 15 kcal/mol by Ochiai (M. Ochiai, Y. Takaoka, Y. Masaki, *J. Am. Chem. Soc.* **1990**, *112*, 5677.) and Reich (F. J. Reich, C. S. Cooperman, *J. Am. Chem. Soc.* **1973**, *95*, 5077.).

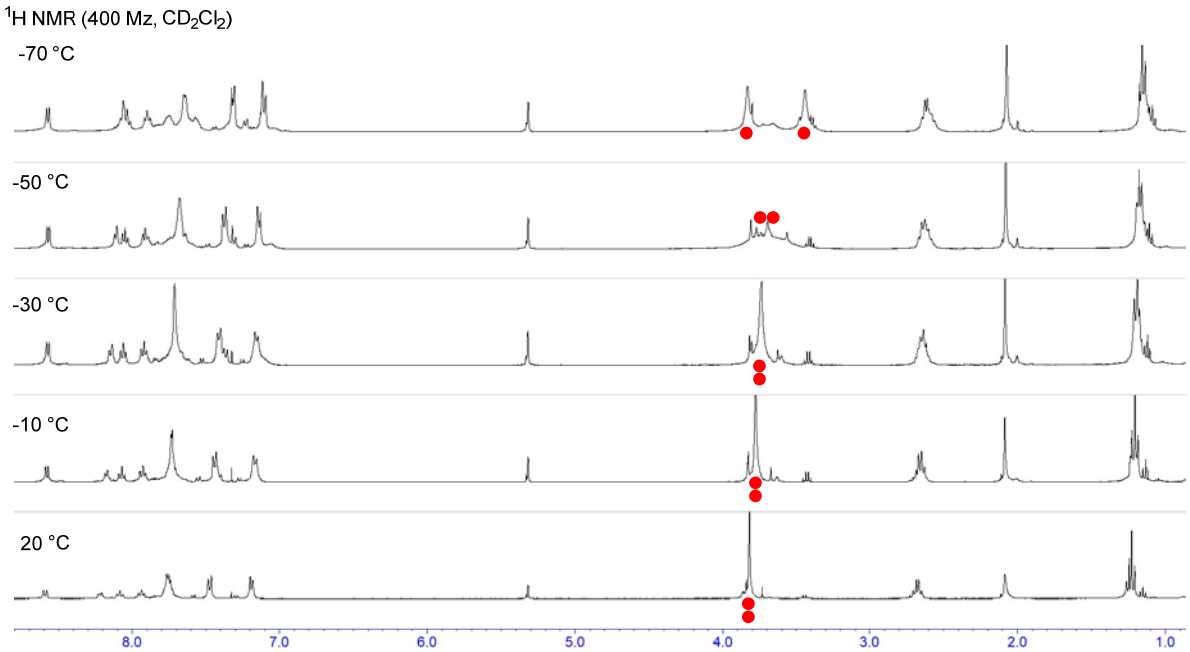


(a) $\Delta G^{\ddagger} = 19.1 \times 10^{-3} \times Tc \times (9.97 + \log Tc - \log\Delta\nu) = 44.0$ kJ/mol = 10.5 kcal/mol

Tc = 223 K (-50 °C)

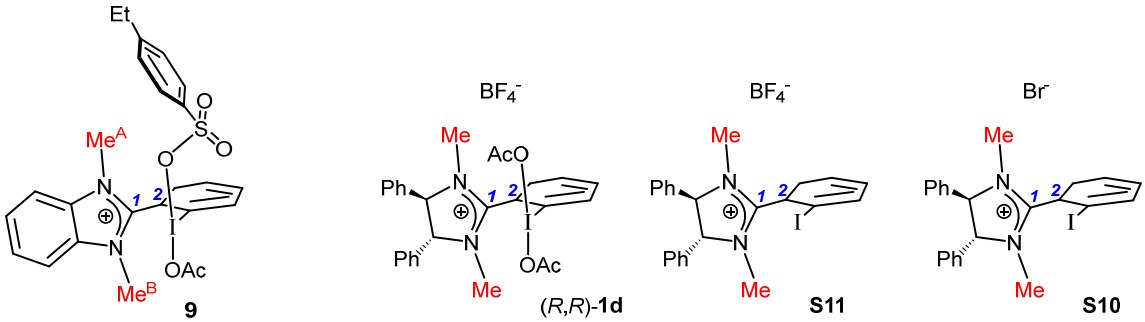
$\Delta\nu$ = 155 Hz

Scheme 1.S33



Scheme 1.S34. VT ^{1}H NMR spectra of ArI(OAc)(*p*-Et$C_6H_4SO_3$) (9)

^{1}H NMR ***at 20 °C***



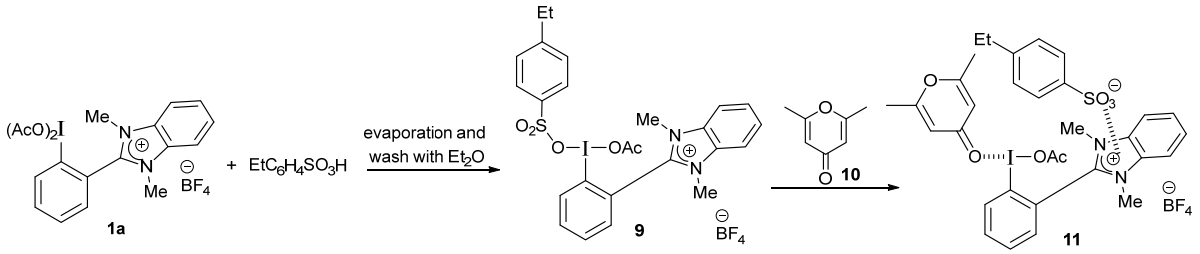
Me^A: 3.81 ppm Me^B: 3.81 ppm	Me: 2.91 ppm Me: 2.77 ppm	Me: 2.85 ppm Me: 2.76 ppm	Me: 2.99 ppm Me: 2.78 ppm
isochronous	*anisochronous*	*anisochronous*	*anisochronous*

Scheme 1.S35

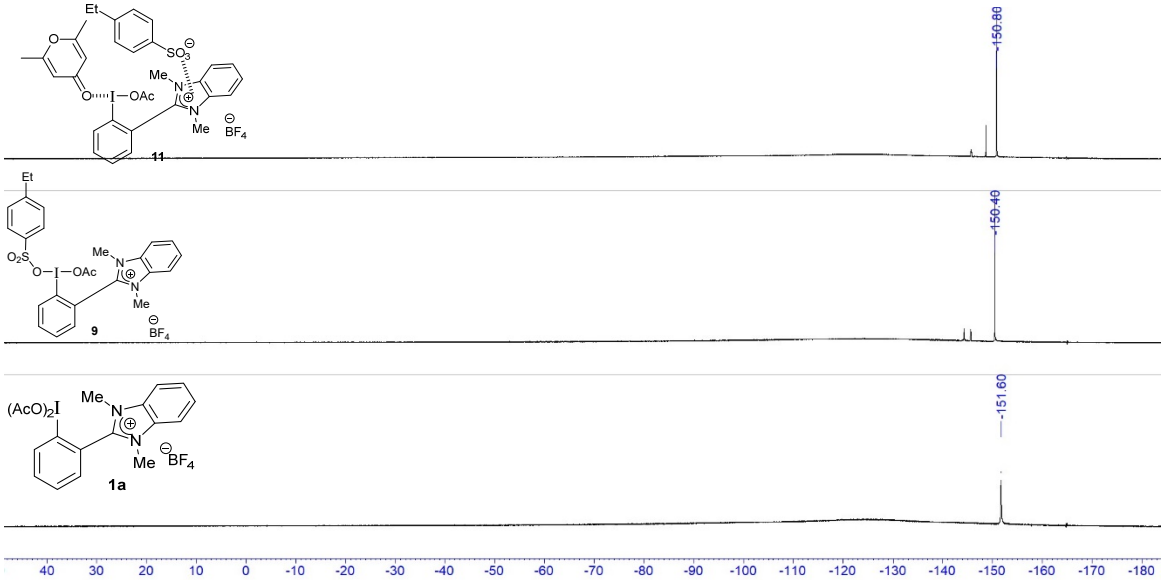
^{1}H NMR signals of two Me groups on nitrogen atoms in (*R*,*R*)-**1d**, **S10**, or **S11** are anisochronous even at 20 °C, which suggests that C^1-C^2 bond rotation in (*R*,*R*)-**1d**, **S11**, **S10** are slow at 20 °C. Therefore, C^1-C^2 bond rotation in **9** should be slow at 20 °C because steric hindrance around C^1-C^2 bonds is almost same amoung **9**, (*R*,*R*)-**1d**, **S10**, and **S11**. But actually signals of two Me groups on nitrogen atoms in **9** are isochronous. Therefore, not C^1-C^2 bond rotation but rapid psuedorotation on an iodine atom makes signals of two Me groups on nitrogen atoms in **9** isochronous at 20 °C.

Comparison of 1a with 9 and 11 in ^{19}F NMR to Investigate Effect of BF_4^- on Regioselectiviety

^{19}F NMR spectra of hypervalent iodine species **1a**, **9**, and **11** are shown in Scheme 1.S36. The chemical shift of BF_4^- in ^{19}F NMR hardly changed among **1a**, **9**, and **11**. Therefore, noncoordinating BF_4^- is a spectator and does not affect the regioselectivity in the present sulfonyloxylactonization. In fact, we carried out calculations without BF_4^-, and the results led to the same conclusion as the results derived by calculation with BF_4^-.



^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O)



Scheme 1.S36

1-5. Reference

[1] For recent reviews on hypervalent iodine chemistry, see: (a) *PATAI's Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds*, Edited by B. Olofsson, I. Marek, Z. Rappoport, Wiley-Blackwell, **2019**; (b) A. Yoshimura and V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328; (c) T. Wirth, *Hypervalent Iodine Chemistry (Topics in Current Chemistry, 373)*, Springer, **2016** (c) V. V. Zhdankin in *Hypervalent Iodine Chemistry: Preparation, Structure and Synthetic Applications of Polyvalent Iodine Compounds*, Wiley-VCH, Weinheim, **2013**.

[2] V. V. Zhdankin and J. D. Protasiewicz, *Coord. Chem. Rev.* **2014**, *275*, 54.

[3] In hypervalent iodine(V) like IBX and Dess-Martin reagent, a hypervalent twisting is important in the oxidation mechanism. (a) J. T. Su and W. A. Goddard, III. *J. Am. Chem. Soc.* **2005**, *127*, 14146; (b) M. Uyanik, M. Akakura and K. Ishihara, *J. Am. Chem. Soc.* **2009**, *131*, 251.

[4] For recent reviews, see; (a) M. Fujita, *Heterocycles*, **2018**, *96*, 563; (b) S. Ghosh, S. Pradhan and I. Chatterjee, *Beilstein J. Org. Chem.*, **2018**, *14*, 1244; (c) F. Berthiol, *Synthesis*, **2015**, *47*, 587; (d) A. Parra, *Chem. Rev.* **2019**, *119*, 12033. For selected hypervalent iodines realizing enantioselective oxidations, see; e) T. Hashimoto, Y. Shimazaki, Y. Omatsu, K. Maruoka, *Angew. Chem. Int. Ed.* **2018**, *57*, 7200; f) T. Dohi, A. Maruyama, N. Takenaga, K. Senami, Y. Minamitsuji, H. Fujioka, S. B. Caemmerer, Y. Kita, *Angew. Chem. Int. Ed.* **2008**, *47*, 3787; (g) U. H. Hirt, B. Spingler and Wirth, T. *J. Org. Chem.*, **1998**, *63*, 7674; (h) A.-A. Guilbault, B. Basdevant, V. Wanie and C. Y. Legault, *J. Org. Chem.* **2012**, *77*, 11283.

[5] (a) M. Uyanik, T. Yasui and K. Ishihara, *Angew. Chem. Int. Ed.*, **2013**, *52*, 9215; (b) M. Uyanik, N. Sasakura, M. Mizuno and K. Ishihara, *ACS Catal.*, **2017**, *7*, 872; (c) S. Haubenreisser, T. H. Wöste, C. Martínez, K. Ishihara and K. Muñiz, *Angew. Chem. Int. Ed.* **2016**, *55*, 413; (d) M. Uyanik, T. Yasui and K. Ishihara, *J. Org. Chem.*, **2017**, *82*, 11946.

[6] (a) B. Zhou, M. K. Haj, E. N. Jacobsen, K. N. Houk and X. S. Xue, *J. Am. Chem. Soc.* **2018**, *140*, 15206; (b) M. D. Levin, J. M. Ovian, J. A. Read, M. S. Sigman and E. N. Jacobsen, *J. Am. Chem. Soc.* **2020**, *142*, 14831.

[7] (a) J. R. M. Bastidas, T. J. Oleskey, S. L. Miller, M. R. Smith III and R. E. Maleczka, Jr. *J. Am. Chem. Soc.* **2019**, *141*, 15483; (b) M. T. Mihai, B. D. Williams and R. J. Phipps, *J. Am. Chem. Soc.* **2019**, *141*, 15477; c) Z. Kang, Y. Wang, D. Zhang, R. Wu, X. Xu and W. Hu, *J. Am. Chem. Soc.* **2019**, *141*, 1473; (d) H. J. Davis, M. T. Mihai and R. J. Phipps, *J. Am. Chem. Soc.* **2016**, *138*, 12759; (e) V. M. Lau, C. F. Gorina and M. W. Kanan, *Chem. Sci.* **2014**, *5*, 4975.

[8] For recent reviews on asymmetric phase-transfer catalysis, see: (a) J. Schörgenhumer, M, Tiffner and M. Waser, *Beilstein J. Org. Chem.* **2017**, *13*, 1753; (b) Kaneko, Y. Kumatabara and S. Shirakawa, *Org. Biomol. Chem.* **2016**, *14*, 5367; c) J. Tan, N. Yasuda, *Org. Process Res. Dev.* **2015**, *19*, 1731.

[9] For reviews on asymmetric counteranion-directed catalysis, see: (a) M. Mahlau and B. List, A*ngew. Chem. Int. Ed.* **2013**, *52*, 518; (b) R. J. Phipps, G. L. Hamilton and F. D. Toste, *Nat. Chem.* **2012**, *4*, 603.
[10] For a review on asymmetric ion-pairing catalysis, see: K. Brak and E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2013**, *52*, 534.
[11] Recent computational studies on noncovalent interaction in ion pairs, see: (a) S. Tsuzuki, W. Shinoda, M. S. Miran, H. Kinoshita, T. Yasuda and M. Watanabe, *J. Chem. Phys.* **2013**, *139*, 174504; (b) S. Tsuzuki, H. Tokuda, K. Hayamizu and M. Watanabe, *J. Phys. Chem. B* **2005**, *109*, 16474.
[12] R. Breslow and D. Heyer, *Tetrahedron Lett.* **1983**, *24*, 5039.
[13] M. Fujita, *Tetrahedron Lett.* **2017**, *58*, 4409.
[14] (a) M. K. Muthyala, S. Choudhary, K. Pandey, G. M. Shelke, M. Jha and A. Kumar, *Eur. J. Org. Chem.* **2014**, *2014*, 2365; (b) J. Zhang, D. Zhao, Y. Wang, H. Kuang and H. Jia, *J. Chem. Res.* **2011**, *35*, 333; (c) F. Su, J. Zhang, G. Jin, T. Qiu, D. Zhao and H. Jia, *J. Chem. Res.* **2009**, *2009*, 741; (d) W. Qian, E. Jin, W. Bao and Y. Zhang, *Angew. Chem. Int. Ed.* **2005**, *44*, 952; (e) S. T. Handy and M. Okello, *J. Org. Chem.* **2005**, *70*, 2874.
[15] M. Fujita, Y. Yoshida, K. Miyata, A. Wakisaka and T. Sugimura, *Angew. Chem. Int. Ed.* **2010**, *49*, 7068.
[16] Tosyloxylation using $PhI(OAc)_2$ and *p*-TsOH: (a) J. Yan, H. Wang, Z. Yang and Y. He, *Synlett*, **2009**, 2669. Selected reports for preparation of $ArI(OH)OTs$ from $ArI(OAc)_2$ and *p*-TsOH: (b) R. Edwards, W. de Vries, A. D. Westwell, S. Daniels and T. Wirth, *Eur. J. Org. Chem.*, **2015**, *2015*, 6909; (c) J.-H. Chun and V. W. Pike, *J. Org. Chem.* **2012**, *77*, 1931.
[17] G. F. Koser and R. H. Wettach, *J. Org. Chem.* **1976**, *41*, 3609.
[18] $ArI(OAc)_2$ bearing SbF_6^- instead of BF_4^- was also synthesized. In the tosyloxylactonization of **2a** with **5a**, $ArI(OAc)_2$ bearing SbF_6^- gave 5-*exo* product **4a**, and the selectiveity of the SbF_6 salt was the same level as that of the BF_4 salt. See Scheme 1.S17 in ESI.
[19] The effect of OH and OAc groups on an I(III) atom on the regioselectivity was investigated. The difference between OH and OAc groups did not influence on the regioselectivity. The details were described in Schemes 1.S13-1.S15 of ESI.
[20] J. Contreras-García, E. R. Johnson, S. Keinan, R. Chaudret, J.-P. Piquemal, D. N. Beratan and W. Yang, *J. Chem. Theory Comput.* **2011**, *7*, 625.
[21] (a) D. A. Dougherty, *Science* **1996**, *271*, 163; For reviews, see: (b) J. C. Ma and D. A. Dougherty, *Chem. Rev.* **1997**, *97*, 1303; c) D. A. Dougherty, *Acc. Chem. Res.* **2013**, *46*, 885.
[22] Recent Computational studies on cation-π interactions, see: (a) J. P. Gallivan and D. A. Dougherty, *J. Am. Chem. Soc.* **2000**, *122*, 870; (b) S. Tsuzuki, M. Mikami and S. Yamada, *J. Am. Chem. Soc.* **2007**, *129*, 8656; for a review, (c) S. Tsuzuki and A. Fujii, *Phys. Chem. Chem. Phys.* **2008**, *10*, 2584.
[23] For a review on the cation–π interaction in catalysis: C. R. Kennedy, S. Lin and E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2016**, *55*, 12596.
[24] (a) M. Elsherbini, B. Winterson, H. Alharbi, A. A. Folgueiras-Amador, C. Génot and T. Wirth, *Angew. Chem. Int. Ed.* **2019**, *58*, 9811; (b) G. F. Koser and R. H. Wettach, *J. Org. Chem.* **1976**, *41*, 3609.
[25] The calculated stable-conformer of $PhI(OH)OSO_2Ph$ also involves a π–π interaction of the $PhSO_3$ group with the iodobenzene framework. See Schemes 1.S22 and 1.S31 in ESI.
[26] In noncovalent interaction analysis of $ArI(OH)OSO_2Ph$ with an imidazolidinium moiety like **1d**, cation–π and cation-oxygen interactions are found between the imidazolidinium moiety and the $PhSO_3$ group (Schemes 1.S23, 1.S24, and 1.S29). In addition, the noncovalent interaction analysis of ArI(OH)OMs revealed the attractive interaction between the imidazolidinium moiety and the MsO group (Schemes 1.S27 and 1.S32).
[27] To avoid the influence of H_2O, 4-$EtPhSO_3H$ unhydrate was used. The treatment of $ArI(OAc)_2$ **1a** with 4-$EtPhSO_3H$ gave the mixture of $ArI(OAc)OSO_2$(4-EtPh) **9**. See Scheme 1.S4 in ESI.
[28] For details of NMR study of $ArI(OAc)OSO_2$(4-EtPh) **9**, see Schemes 1.S33-1.S35 in ESI.
[29] For upfield shift in ^1H NMR via cation-pi interactions, see selected papers; (a) T. J. Shepodd, M. A. Petti, D. A. Dougherty, *J. Am. Chem. Soc.* **1986**, *108*, 6085; (b) M. A. Petti, T. J. Shepodd, R. E. Barrans, Jr., D. A. Dougherty, *J. Am. Chem. Soc.* **1988**, *110*, 6825; (c) D. A. Stauffer, D. A. Dougherty, *Tetrahedron Lett.* **1988**, *29*, 6039.
[30] Selected reports: (a) H. W. Richter, B. R. Cherry, T. D. Zook and G. F. Koser, *J. Am. Chem. Soc.* **1997**, *119*, 9614; (b) T. Wirth and U. H. Hirt, *Tetrahedron Asymmetry* **1997**, *8*, 23; (c) U. H. Hirt, M. F. H. Schuster, A. N. French, O. G. Wiest and T. Wirth, *Eur. J. Org. Chem.* **2001**, *2001*, 1569; (d) M. Ochiai, K. Miyamoto, Y. Yokota, T. Suefuji, M. Shiro, *Angew. Chem. Int. Ed.* **2005**, *44*, 75.

[31] The details of Figure 1.6B were described in Scheme 1.S5-1.S7 of ESI.
[32] In a less polar solvent like CH_2Cl_2, an imidazolium ion and a couteranion generate the corresponding contact ion pair, which is supported by the difference of chemical shift values in ^1H NMR spectroscopy in imidazolium salts. See Scheme 1.S12 in ESI.
[33] The coordination of γ-pyrone **10** to the iodine canter was also confirmed by IR stretching frequency of the C=O bond of **10** (See Scheme 1.S11 in ESI). We established the evaluation of the Lewis acidity using the complexation between a Lewis acid and γ-pyrone **10**. (a) Y. Nishimoto, S. Nakao, S. Machinaka, F. Hidaka, M. Yasuda, *Chem. Eur. J.* **2019**, *25*, 10792; (b) M. Yasuda, H. Nakajima, R. Takeda, S. Yoshioka, S. Yamasaki, K. Chiba, A. Baba, *Chem. Eur. J.* **2011**, *17*, 3856.
[34] The detailed investigation for broadening signals of protons of the benzene ring in 4-$EtC_6H_4SO_3$ group were described in Schemes 1.S8-1.S10 in ESI.
[35] Isolation and characterization of iodonium ions; (a) M. Ochiai, *Coord. Chem. Rev.* **2006**, *250*, 2771; (b) M. Ochiai, K. Miyamoto, M. Shiro, T. Ozawa and K. Yamaguchi, *J. Am. Chem. Soc.* **2003**, *125*, 13006; (c) M. Ochiai, K. Miyamoto, T. Suefuji, S. Sakamoto, K. Yamaguchi and M. Shiro, *Angew. Chem. Int. Ed.* **2003**, *42*, 2191.
[36] The chemical shift of BF_4^- in ^{19}F NMR hardly changed among hypervalent iodine species **1a**, **9**, and **11** (Scheme 1.S36). Noncoordinating BF_4^- is a spectator and does not affect the regioselectivity in the present sulfonyloxylactonization.
[37] Y.-B. Kang, L. H. Gade, *J. Am. Chem. Soc.* **2011**, *133*, 3658.
[38] E. R. Johnson, S. Keinan, P. Mori-Sánchez, J. Contreras-García, A. J. Cohen, W. Yang, *J. Am. Chem. Soc.* **2010**, *132*, 6498.
[39] J. Contreras-García, E. R. Johnson, S. Keinan, R. Chaudret, J.-P. Piquemal, D. N. Beratan, W. Yang, *J. Chem. Theory Comput.* **2011**, *7*, 625.
[40] W. Humphrey, A. Dalke, K. Schulten, *J. Mol. Graph.* **1996**, *14*, 33.

Chapter 2: 1-Fluoro-1-sulfonyloxylation of Alkenes by Sterically and Electronically Tuned Hypervalent Iodine: Regression Analysis toward 1,1-Heterodifunctionalization

2-1. Introduction

Heterodifunctionalization of alkenes via the addition of different heteroatoms to a carbon–carbon double bond is one of the most efficient methods for constructing highly functionalized compounds (Figure 2.1A).[1] To achieve 1,2-regioselectivity, various methods such as classical halohydrin synthesis and transition-metal-catalyzed reactions have been developed.[2] By contrast, 1,1-heterodifunctionalization has rarely been achieved because the reaction must proceed with the desired 1,1-heteroselectivity while suppressing 1,1-/1,2-homo- and 1,2-heteroselectivities (Figure 2.1B).[3] Two-component oxyaminations using a Pd catalyst/oxidant,[4] a Ag salt/oxidant,[5] an I(III) reagent,[6] or *m*-chloroperoxybenzoic acid (*m*-CPBA)[6a] are the only reactions reported thus far. In these processes, 2-amino alcohols have been used exclusively for the 1-amino-1-alkoxylation of alkenes by suppressing the undesired selectivities (Figure 2.1C). Three-component 1,1-heterodifunctionalization among an alkene and two different heteroatom source reagents has not yet been established.

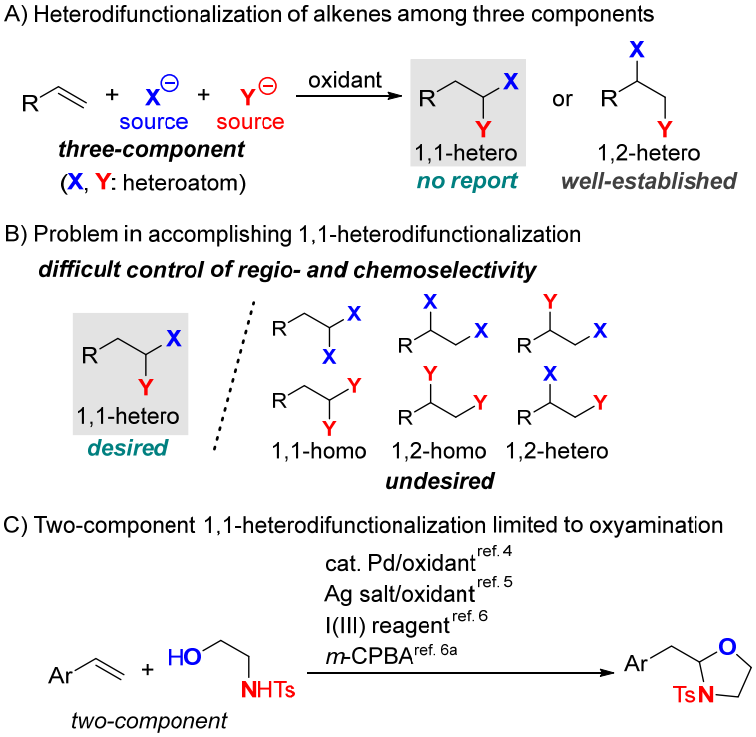


Figure 2.1. (A) Heterodifunctionalization of alkenes. (B) Problems in accomplishing 1,1-heterodifunctionalization. (C) Examples of 1,1-heterodifunctionalization in two-component.

Hypervalent iodine reagents are versatile metal-free-oxidants that enable various distinctive oxidative difunctionalization of alkenes.[7-11] Even in this field, 1,1-heterodifunctionalization remains elusive. During our study of the tosyloxylactonization of alkenes mediated by hypervalent iodine,[12] we obtained unexpected

results for a 1,1-heterodifunctionalization (Figure 2.2A). The reaction of alkene (**1a**), TfOH, and Bu_4NBF_4 in the presence of $PhI(OAc)_2$ (**A**) gave 1-fluoro-1-trifluoromethanesulfonyloxy product (**2a**) in 10% yield; however, 1,2-homodifunctionalization dominantly proceeded to give ordinarily expected 1,2-diacetoxy product (**3a**) (36%).[13,14] More interestingly, *p*-Me-substituted $ArI(OAc)_2$ (**B**) resulted in a lower yield of **2a**, whereas the use of *p*-NO_2-substituted $ArI(OAc)_2$ (**C**) resulted in a greater yield.[15] These results prompted us to develop a 1,1-heterodifunctionalization reaction.

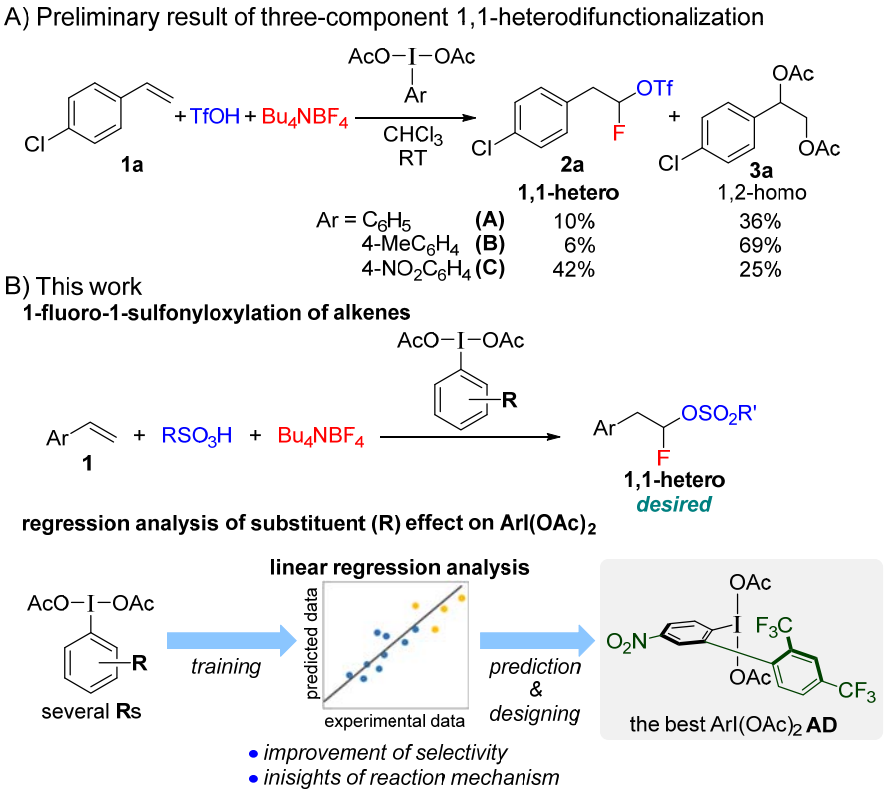


Figure 2.2. (A) Preliminary result of three-component 1,1-heterodifunctionalization with hypervalent iodines. (B) This work: 1-fluoro-1-sulfonyloxylation of alkenes with optimized hypervalent iodines.

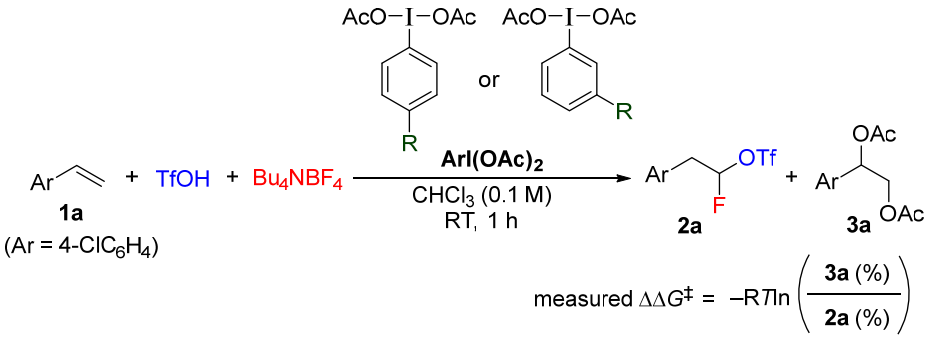
Herein, we report the 1-fluoro-1-sulfonyloxylation of alkenes with sulfonic acids and Bu_4NBF_4 using our designed hypervalent iodines (Figure 2.2B). Regression analysis based on a linear free-energy relationship (LFER) model optimized a substituent (R) on $ArI(OAc)_2$. Because of a synergistic effect of its *ortho* and *para* substituents, $ArI(OAc)_2$ (**AD**) substituted with *o*-{2,4-$(CF_3)_2C_6H_3$} and *p*-NO_2 was found to be the most efficient reagent.

2-2. Results and Discussion

To simplify the regression analysis, we investigated *para*- or *meta*-substituted hypervalent iodines ($ArI(OAc)_2$ **A**–**L**) by considering only electronic perturbation factors in the reactions among alkene (**1a**), TfOH, and Bu_4NBF_4. The yields (**2a** + **3a**) and selectivity (**2a**:**3a**) of the products are shown in Table 2.1. The *para* and *meta* substituents clearly influenced the selectivity. A simple regression analysis based on an LFER was carried out using Hammett substituent constants (Figure 2.3).[16] Parameter $\Delta\Delta G^{\ddagger}$ is defined as –

R*T*ln[selectivity (**3a**/**2a**)]. A plot of the $\Delta\Delta G^{\ddagger}$ values vs the parameter σ_p shows a linear correlation with a positive slope (ρ = 1.87) (Figure 2.3, left). The parameter σ_m also shows a good correlation with the measured $\Delta\Delta G^{\ddagger}$ values (ρ = 1.92) (Figure 2.3, right). These results suggest that an electron-withdrawing substituent at either *para* or *meta* position facilitated 1-fluoro-1-sulfonyloxylation.

Table 2.1. Selectivity, yield, and measured $\Delta\Delta G^{\ddagger}$ in the reaction of 1a, TfOH, Bu_4NBF_4, and *p*/*m*-substituted forms of $ArI(OAc)_2$.



$$\text{measured } \Delta\Delta G^{\ddagger} = -RT\ln\left(\frac{\textbf{3a}\ (\%)}{\textbf{2a}\ (\%)}\right)$$

entry	$ArI(OAc)_2$ R		selectivity (2a:3a)	yield (%) (2a + 3a)	measured $\Delta\Delta G^{\ddagger}$ (kcal/mol)	$\sigma_{p,m}$
1	H	A	22 : 78	46	-0.75	0.00
2	*p*-Me	B	8 : 92	75	-1.42	-0.17
3	*p*-NO_2	C	63 : 37	67	0.30	0.78
4	*p*-CO_2Me	D	47 : 53	57	-0.06	0.45
5	*p*-CN	E	61 : 39	62	0.27	0.66
6	*p*-CF_3	F	73 : 27	48	0.58	0.54
7	*p*-Ph	G	18 : 82	62	-0.89	-0.01
8	*m*-Me	H	13 : 87	75	-1.09	-0.07
9	*m*-NO_2	I	71 : 29	56	0.53	0.71
10	*m*-CO_2Me	J	61 : 39	46	0.26	0.37
11	*m*-CN	K	52 : 48	63	0.06	0.56
12	*m*-CF_3	L	53 : 47	68	0.07	0.43

1a (0.2 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), $ArI(OAc)_2$ (0.3 mmol), $CHCl_3$ (2 mL), RT, 1 h. Yields of **2a** and **3a** were determined by ^{1}H NMR using $CHBr_3$ as an internal standard.

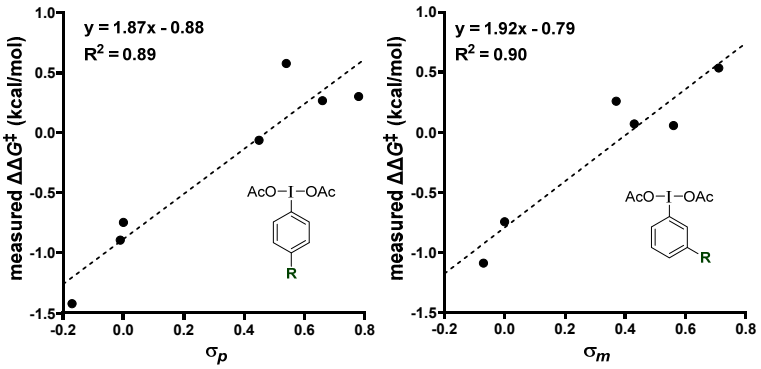
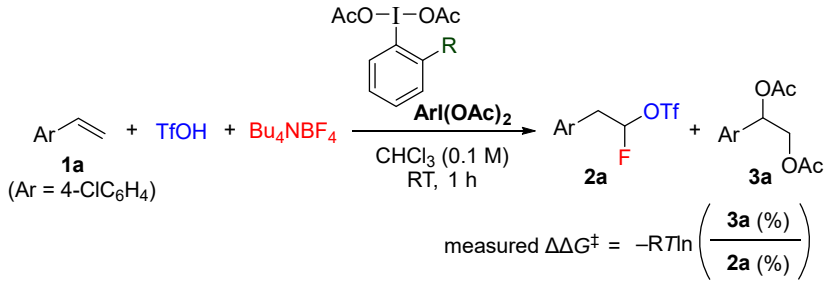


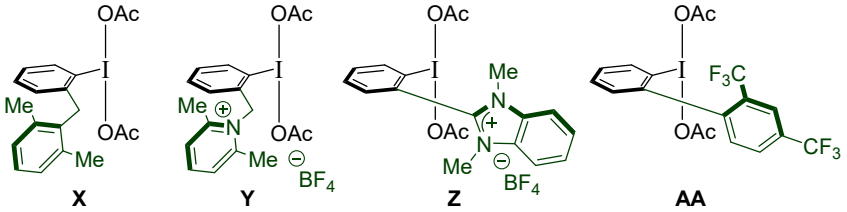
Figure 2.3. Correlations between Hammett substituent constants and measured $\Delta\Delta G^{\ddagger}$ values for *p*/*m*-substituted forms of $ArI(OAc)_2$.

We next focused on *ortho*-substituted ArI(OAc)$_2$, considering further positive influences of *ortho* effects which are known to enhance the reactivity and selectivity in hypervalent iodine chemistry.[12,17] A multivariate regression analysis using various parameters derived by density functional theory (DFT) calculation was conducted (see parameters in Chapter 2-4).[18] The measured $\Delta\Delta G^{\ddagger}$ values was obtained by conducting the experiments with eight hypervalent iodines (**M–T**) (Table 2.2, entries 1 and 2–9). Then, a suitable regression model ($R^2 = 0.97$) was generated by stepwise linear regression using the measured $\Delta\Delta G^{\ddagger}$

Table 2.2. Selectivity, yield, measured $\Delta\Delta G^{\ddagger}$, and predicted $\Delta\Delta G^{\ddagger}$ in the reaction using **1a**, TfOH, Bu_4NBF_4, and *o*-substituted forms of ArI(OAc)$_2$.



entry	ArI(OAc)$_2$ R		selectivity (2a:3a)		yield (%) (2a + 3a)	measured $\Delta\Delta G^{\ddagger}$ (kcal/mol)	predicted $\Delta\Delta G^{\ddagger}$ (kcal/mol)
training set							
1	H	**A**	22	78	46	-0.75	-0.77
2	*o*-Me	**M**	18	82	57	-0.90	-0.88
3	*o*-NO_2	**N**	61	39	66	0.25	0.25
4	*o*-*t*Bu	**O**	29	71	42	-0.53	-0.56
5	*o*-CN	**P**	64	36	66	0.33	0.17
6	*o*-CF_3	**Q**	62	38	77	0.29	0.31
7	*o*-F	**R**	49	51	74	-0.03	0.03
8	*o*-Br	**S**	46	54	70	-0.10	0.02
9	*o*-Mes	**T**	41	59	73	-0.21	-0.21
external validations							
10	*o*-Et	**U**	21	79	66	-0.76	-0.64
11	*o*-Cl	**V**	48	52	69	-0.05	0.03
12	*o*-Ph	**W**	29	71	76	-0.52	-0.18
13	*o*-CH_2(2,6-diMeC_6H_3)	**X**	39	61	51	-0.26	-0.08
external predictions							
14	*o*-CH_2(2,6-diMePy)BF_4	**Y**	70	30	54	0.50	0.21
15	*o*-imidazolyl•BF_4	**Z**	75	25	48	0.64	0.45
16	*o*-2,4(CF_3)$_2C_6H_3$	**AA**	66	34	64	0.38	0.17



1a (0.2 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), ArI(OAc)$_2$ (0.3 mmol), $CHCl_3$ (2 mL), RT, 1 h. Yields of **2a** and **3a** were determined via ^{1}H NMR using $CHBr_3$ or CH_2Br_2 as an internal standard.

values as a training set, for which the Sterimol B_5 value of the *ortho* substituent (B_5), the NBO charge of the iodine atom (NBO_I), and the IR carbonyl stretching frequency ($\nu_{C=O}$) were important descriptors (Figure 2.4, training set). To verify the model, external validation sets, including four hypervalent iodines ($ArI(OAc)_2$ **U–X**) were examined (Table 2.2, entries 10–13), and found to well fit the model (Figure 2.4). In the case of an *ortho*-iodo biaryl structure (**W**), the side-reactions such as well-known cyclization[7e] did not occur, so the influence of such side-reactions was ruled out. For B_5 values, increasing steric demand of the *ortho* substituent increased the preference toward 1-fluoro-1-sulfonyloxylation. The NBO_I and $\nu_{C=O}$ values reflect electronic effects, and electron-withdrawing groups were observed to facilitate the 1,1-selectivity, which is consistent with the results of the Hammett plot of *para* and *meta* substituents. Thus, our regression model suggests that a bulky electron-withdrawing group at the *ortho* position improves selectivity. Therefore, the pyridinium (**Y**), imidazolium (**Z**),[12] and 2,4-$(CF_3)_2C_6H_3$ (**AA**) moieties were chosen as promising groups for external predictions. As per the predicted $\Delta\Delta G^{\ddagger}$ values, these moieties experimentally afforded greater selectivity than the training set (Table 2.2, entries 14–16; Figure 2.4, external predictions).

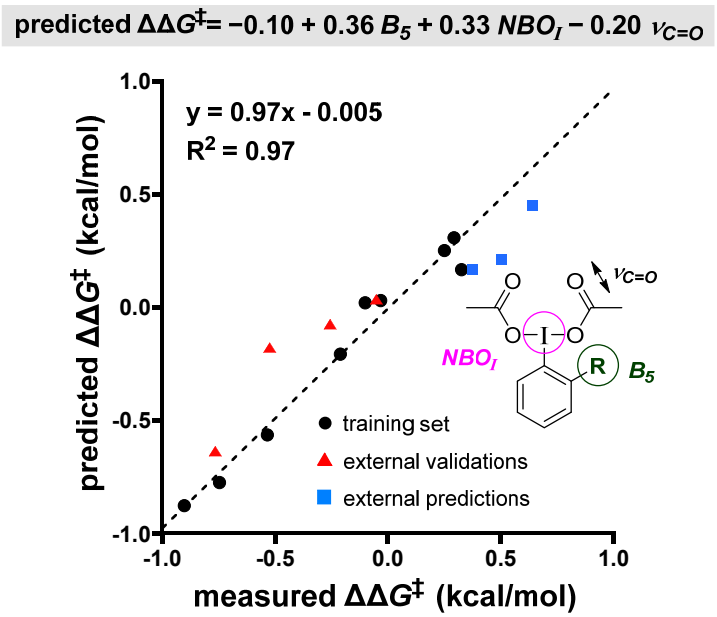
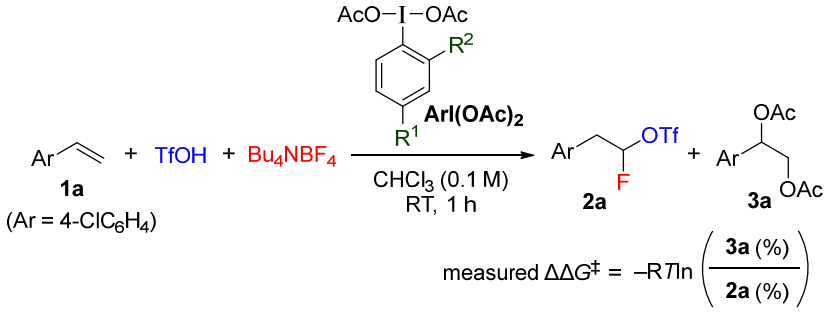
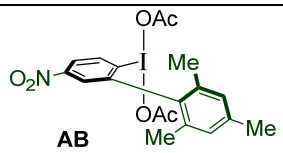
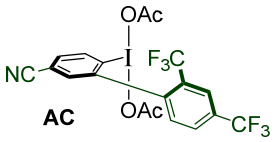
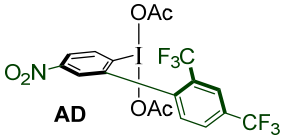


Figure 2.4. Predicted versus measured $\Delta\Delta G^{\ddagger}$ for *o*-substituted forms of $ArI(OAc)_2$.

Finally, we designed sterically and electronically controlled *ortho*- and *para*-disubstituted $ArI(OAc)_2$ using the insights gained from the regression analysis of monosubstituted $ArI(OAc)_2$. An electron-withdrawing effect of *ortho*- and *para*-substituents, and bulkiness at an *ortho*-position are crucial. Thus, three hypervalent iodines with NO_2 or CN group at the *para* position and a mesityl (Mes) or 2,4-$(CF_3)_2C_6H_3$ group at the *ortho* position were synthesized and evaluated (Table 2.3). $ArI(OAc)_2$ (**AB**) with *o*-Mes and *p*-NO_2 groups demonstrated greater selectivity (entry 1) than the corresponding mono-substituted analogs (Table 2.1, entry 3 or Table 2.2, entry 9). $ArI(OAc)_2$ (**AC**), with *o*-2,4-$(CF_3)_2C_6H_3$ and *p*-CN groups, afforded even better selectivity, and *o*-{2,4-$(CF_3)_2C_6H_3$}- and *p*-NO_2-substituted $ArI(OAc)_2$ (**AD**) gave the best result (Table 2.3, entries 2 and 3).

Table 2.3. Selectivity, yield, measured $\Delta\Delta G^{\ddagger}$, and predicted $\Delta\Delta G^{\ddagger}$ in the reaction using *o*- and *p*-disubstituted forms of $ArI(OAc)_2$.



entry	$ArI(OAc)_2$	selectivity (**2a**:**3a**)	yield (%) (**2a** + **3a**)	measured $\Delta\Delta G^{\ddagger}$ (kcal/mol)
1	 **AB**	72 : 28	57	0.55
2	 **AC**	79 : 21	56	0.76
3	 **AD**	80 : 20	59	0.79

1a (0.2 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), $ArI(OAc)_2$ (0.3 mmol), $CHCl_3$ (2 mL), RT, 1 h. Total yields of **2a** and **3a** were determined via ^{1}H NMR using $CHBr_3$ as an internal standard.

On the basis of the insights obtained from the regression analyses, the reaction mechanism was proposed (Figure 2.5). $ArI(OAc)_2$ reacts with TfOH to give ArI(OTf)OAc (**6**) (step I).[19] Coordination of styrene **1k** to the I center gives intermediate **7** and TfO^- (step II), and then, **7** changes to benzylic cation **8**. In path a, the nucleophilic attack of TfO^- to **8** affords intermediate **9**. Substitution of the iodine atom by the benzene ring gives phenonium ion (**10**). The ring-opening of **10** by an F^- ion of BF_4^- occurs at the electrophilic α-carbon atom of TfO group, affording 1-fluoro-1-sulfonyloxy product (**2**). A deuterium labeling experiment supported the participation of a phenonium ion (see Chapter 2-4). In path b, rearrangement of the AcO group from an iodine atom to a benzylic carbon atom in **8** occurs; finally, 1,2-diacetoxy product (**3**) is obtained through intermediate **12**. Path b is a common mechanism in hypervalent iodine chemistry.[20] The electron-withdrawing effect of substituents (R^1 and R^2) destabilizes intermediate **11** because of a cationic iodine center and disfavors path b. Steric repulsion between a bulky *ortho*-substituent and Ph group could inhibit the pseudorotation on the iodine atom for the rearrangement of the AcO group to **8′** in path b (Figure 2.5, bottom).[21]

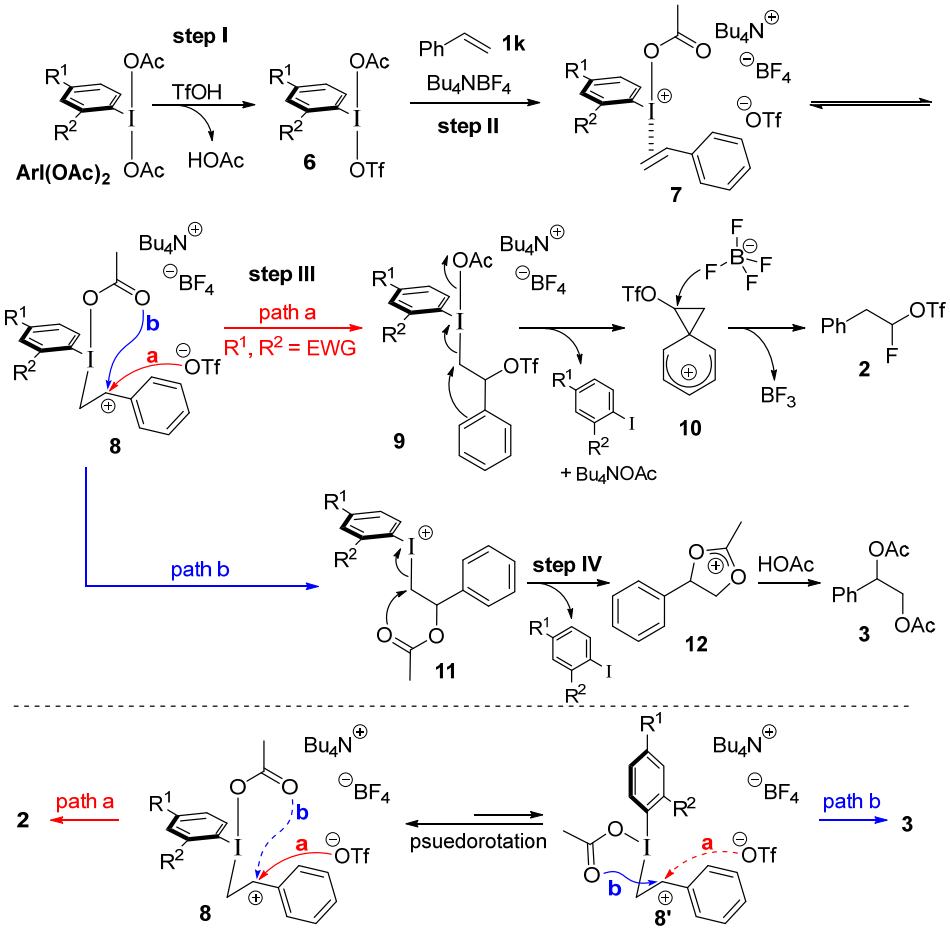
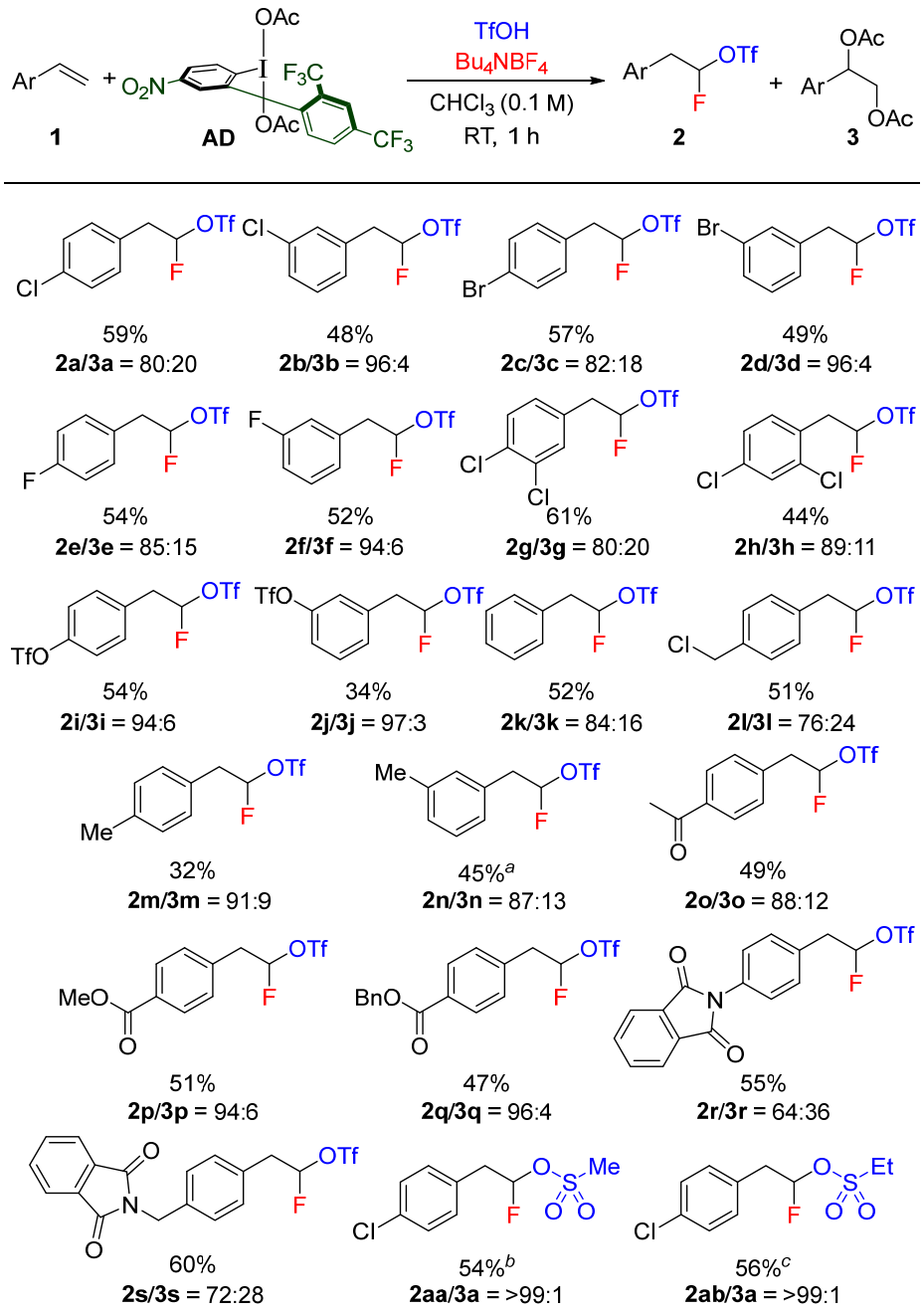


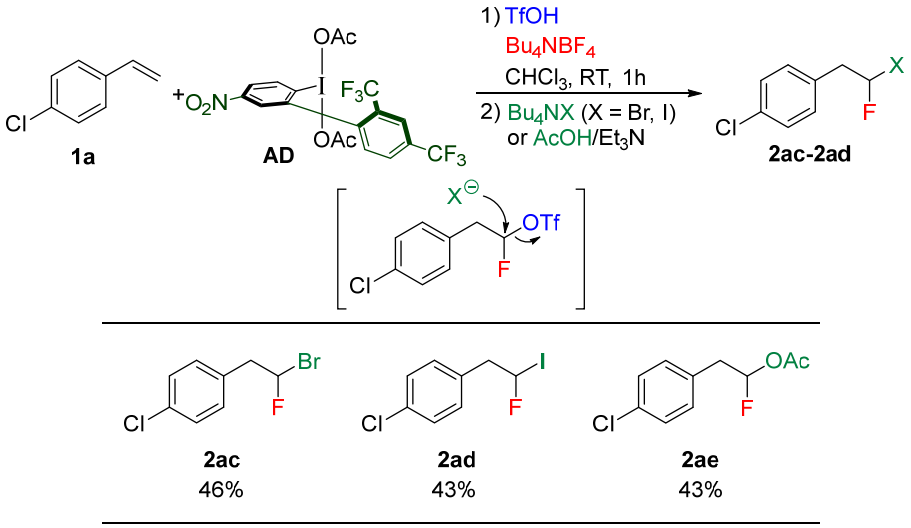
Figure 2.5. Plausible reaction mechanism.

The scope of the styrenes using $ArI(OAc)_2$ (**AD**) was investigated (Scheme 2.1). Styrenes with halogeno and TfO groups on the benzene ring afforded the desired products (**2a–2j**). An alkyl substituent on the benzene ring slightly decreased the yield (**2m** and **2n**), however, a benzylic chloride moiety was tolerated (**2l**). Styrenes with acyl, methoxycarbonyl, and benzyloxycarbonyl groups gave the corresponding products (**2o–2q**). The phthaloyl-substituted substrates smoothly underwent 1-fluoro-1-sulfonyloxylation (**2r** and **2s**). $MeSO_3H$ and $EtSO_3H$ instead of TfOH (**2aa** and **2ab**) gave excellent selectivity. In all the entries, undesired polymerization of **1** occurred because of the acidic conditions, limiting the yields of **2** to a moderate level.

We substituted the TfO group with other functional groups with reference to Dolbier's work[14] (Scheme 2.2). After 1-fluoro-1-sulfonyloxylation of **1a** under the optimal conditions, the addition of Bu_4NBr or Bu_4NI gave the 1-bromo-1-fluoro- or 1-fluoro-1-iodoalkane (**2ac** or **2ad**). In addition, treatment with $AcOH/NEt_3$ facilitated the substitution of TfO with AcO (**2ae**). These alkanes are useful as fluoroalkylene building blocks.[22,23]

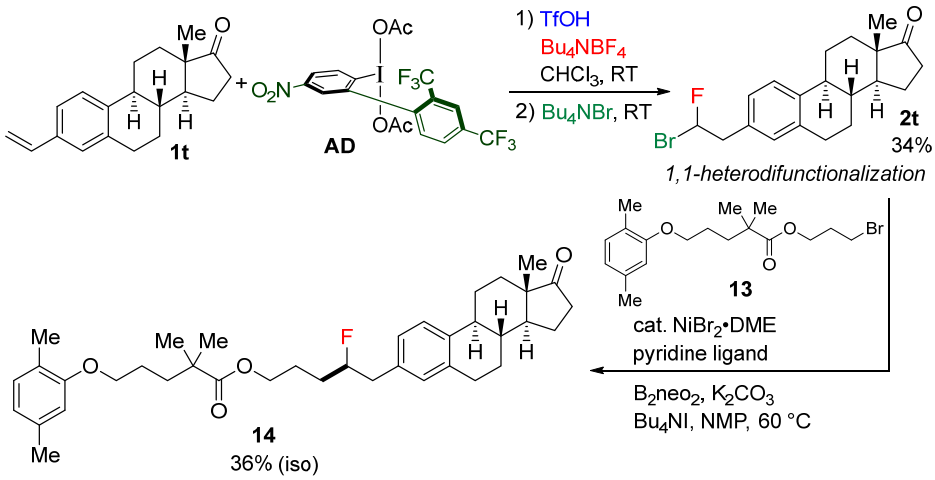


Scheme 2.1. Scope of styrenes; **1a** (0.2 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), $ArI(OAc)_2$ (0.3 mmol), $CHCl_3$ (2 mL), RT, 1 h. Total yields of **2a** and **3a** were determined by ^1H NMR using $CHBr_3$ as an internal standard.



Scheme 2.2. Synthesis of fluoroalkylene derivatives; **1a** (0.2 mmol), $ArI(OAc)_2$ (**AD**) (0.3 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), $CHCl_3$ (2 mL), RT, 1 h; then, Bu_4NBr, Bu_4NI or $AcOH/Et_3N$, RT, 1 h.

Compounds composed of bioactive substances connected by a linker are known to help overcome obstacles encountered in therapies.[24] We demonstrated a feasible method to synthesize fluoroalkylene-tethered bioactive derivatives using our method.[25] Vinyl estrone (**1t**) was converted into 1-bromo-1-fluoroalkane (**2t**) in a one-pot procedure with $ArI(OAc)_2$ (**AD**), followed by the addition of Bu_4NBr (Scheme 2.3). Finally, fluorinated estrone derivative (**14**) was obtained via a Ni-catalyzed reductive alkyl–alkyl coupling reaction[22a] of **2t** with gemfibrozil derivative (**13**).[26]



Scheme 2.3. Synthesis of a monofluorinated-alkylene-tethered bioactive compound.

2-3. Conclusion

The 1-fluoro-1-sulfonyloxylation of styrenes with RSO_3H and Bu_4NBF_4 mediated by *o*-{2,4-$(CF_3)_2C_6H_3$}- and *p*-NO_2-substituted $ArI(OAc)_2$ (**AD**) was achieved. Regression analysis of the substituents suggested the importance of the electron-withdrawing effect and bulkiness in facilitating 1-fluoro-1-sulfonyloxylation. A feasible one-pot synthesis of fluorine-containing building blocks and the synthesis of fluoroalkylene-tethered bioactive compound were demonstrated.

2-4. Experimantal Section

General Information

NMR spectra were recorded on JEOL-AL400, JEOL-ECS400, JEOL-ECZL400 (400 MHz for ^{1}H, 100 MHz for ^{13}C and 377 MHz for ^{19}F). Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 ppm for ^{1}H NMR) and the middle peak of triplet of $CDCl_3$ (δ = 77.00 ppm for ^{13}C NMR) as an internal reference, and CF_3COOH (δ = -76.55 ppm for ^{19}F NMR) as an external reference. Coupling constants were quoted in Hz (J). ^{1}H NMR spectroscopy splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). New compounds were characterized by ^{1}H, ^{13}C, ^{13}C off-resonance techniques, COSY, HMQC, and HMBC. Infrared (IR) spectra were recorded on a JASCO FT/IR-6200 Fourier transform infrared spectrophotometer. Column chromatography was performed on silica gel (MERK C60). Purification by recycle HPLC was performed on SHIMADZU recycle HPLC system (SPD-20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) and Japan Analytical Industry Co. (NEXT recycling preparative HPLC). High-resolution mass spectra were recorded on a JEOL JMS-700 and JMS-T100LP (TOF analyzer with ESI or DART ionization sources). Reactions were carried out in dry solvents under nitrogen atmosphere, unless otherwise stated. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), FUJIFILM Wako Pure Co., Ltd., KISHIDA Chemical Co., Ltd. NMR Yields and values of ratio **2**/**3** in crude products were determined by ^{1}H NMR using internal standard ($CHBr_3$).

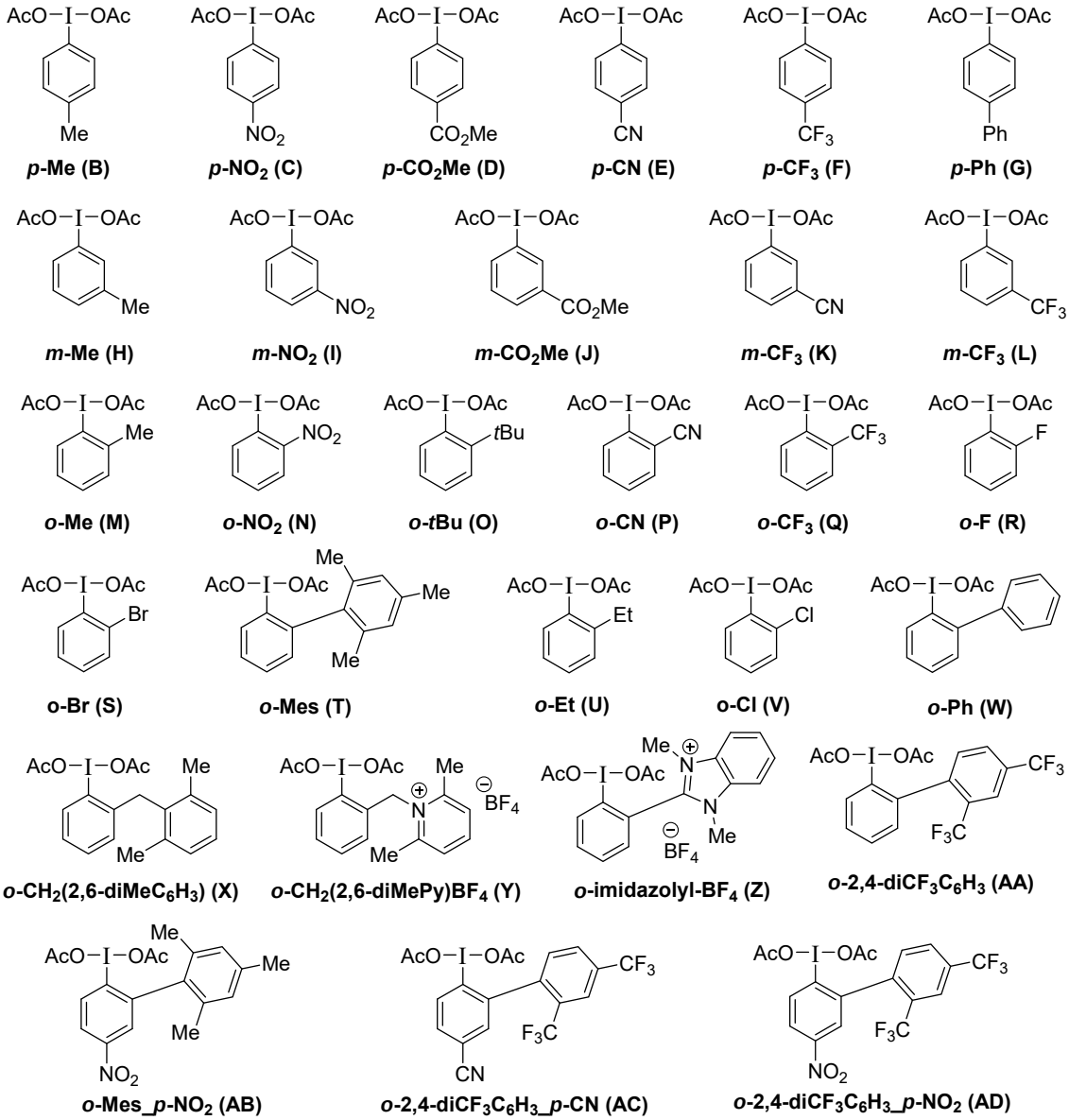
Materials

Iodoarene diacetates

Iodobenzene diacetates were prepared by general procedure unless otherwise noted. **P, R, U, V, AA-AD** are new compounds. **C**[27], **N**[28], **O**[12], **T**[12], **X**[12], **Y**[12] and **Z**[12] were synthesized according to reported procedures and analytical data were good agreement with those papers. Other iodobenzene diacetates (**B**[29], **D**[30], **E**[31], **F**[32], **G**[32], **H**[32], **I**[30], **J**[33], **K**[34], **L**[34], **M**[34], **Q**[34], **S**[34], **W**[35]) are known compounds and those analytical data were good agreement with the reported data.

General Procedure

To a round-bottom flask with iodoarene (5.00 mmol) was added 9% AcOOH in AcOH (10 mL) and reaction mixtures were stirred at room temperature over 9 h. The peracetic acid was removed under reduced pressure and the precipitated solid was washed with hexane or ether. The washed solid was dried under vacuum to give a white solid.



***p*-Me (B)** ***p*-NO_2 (C)** ***p*-CO_2Me (D)** ***p*-CN (E)** ***p*-CF_3 (F)** ***p*-Ph (G)**

***m*-Me (H)** ***m*-NO_2 (I)** ***m*-CO_2Me (J)** ***m*-CF_3 (K)** ***m*-CF_3 (L)**

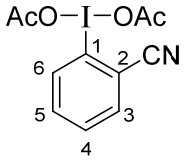
***o*-Me (M)** ***o*-NO_2 (N)** ***o*-*t*Bu (O)** ***o*-CN (P)** ***o*-CF_3 (Q)** ***o*-F (R)**

o-Br (S) ***o*-Mes (T)** ***o*-Et (U)** **o-Cl (V)** ***o*-Ph (W)**

***o*-CH_2(2,6-diMeC_6H_3) (X)** ***o*-CH_2(2,6-diMePy)BF_4 (Y)** ***o*-imidazolyl-BF_4 (Z)** ***o*-2,4-di$CF_3C_6H_3$ (AA)**

***o*-Mes_*p*-NO_2 (AB)** ***o*-2,4-di$CF_3C_6H_3$_*p*-CN (AC)** ***o*-2,4-di$CF_3C_6H_3$_*p*-NO_2 (AD)**

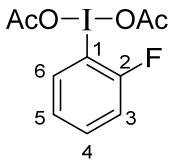
(P) (2-cyanophenyl)-λ^3-iodanediyl diacetate



Prepared by general procedure from 2-cyanoiodobenzene (0.286 g, 1.25 mmol) and 9% peracetic acid to give a product as a white solid (0.191 g, 44%).

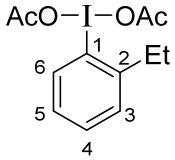
IR: (KBr) 2232 (CN), 1649 (C=O) cm^{-1}; mp: 96-98 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): 8.32-8.30 (m, 1H, 6-H), 7.93-7.91 (m, 1H, 3-H), 7.77-7.70 (m, 2H, 4-H and 5-H), 2.02 (s, 6H, OAc x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 177.1 (s, *C*OCH_3), 137.4 (d, C-6), 134.8 (d), 134.5 (d), 132.3 (d), 124.3 (s, C-2), 118.4 (s, C-1), 117.4 (s, CN), 20.3 (q, CO*C*H_3 x 2); HRMS (ESI+): Calculated ($C_{11}H_{10}NO_4INa$): 369.95467 ([M + Na]$^+$) Found: 369.95452

(R) (2-fluorophenyl)-λ^3-iodanediyl diacetate



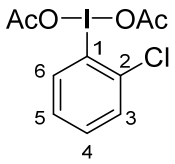
Prepared by general procedure from 2-fluoroiodobenzene (1.09 g, 4.92 mmol) and peracetic acid to give a product as a white solid (1.02 g, 61%).
IR: (KBr) 1642 (C=O) cm^{-1}; mp: 125-127 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): 8.16-8.12 (m, 1H, 6-H), 7.66-7.61 (m, 1H, 4-H), 7.40 (dd, J = 8.3, 1.4 Hz, d, $^3J_{HF}$ = 8.3 Hz, 1H, 3-H), 7.28 (td, J = 7.7, 1.3 Hz, 1H, 5-H), 1.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 177.1 (s, *C*OCH$_3$ x 2), 159.5 (s, d, $^1J_{CF}$ = 254 Hz, C-2), 137.1 (d, C-6), 134.9 (d, d, $^3J_{CF}$ = 7.2 Hz, C-4), 126.5 (d, d, $^4J_{CF}$ = 3.6 Hz, C-5), 116.6 (d, d, $^2J_{CF}$ = 23.0 Hz, C-3), 109.3 (s, d, $^2J_{CF}$ = 23.0 Hz, C-1), 20.4 (q, CO*C*H$_3$ x 2); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -95.2; HRMS (ESI+) Calculated ($C_{10}H_{10}O_4FINa$): 362.95000 ([M + Na]$^+$) Found: 362.95052

(U) (2-ethylphenyl)-λ^3-iodanediyl diacetate



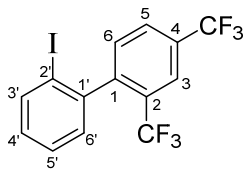
Prepared by general procedure from 2-ethyliodobenzene (1.13 g, 4.85 mmol) and 9% peracetic acid to give a product as a white solid (1.52 g, 90%).
IR: (KBr) 1657 (C=O) cm^{-1}; mp: 135-136 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): 8.20 (dd, J = 8.1, 1.2 Hz, 1H, 6-H), 7.59 (td, J = 7.7, 1.2 Hz, 1H, 4-H), 7.53 (dd, J = 7.7, 1.8 Hz, 1H, 3-H), 7.29-7.25 (m, 1H, 5-H), 3.01 (q, J = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 1.98 (s, 6H, COC*H*$_3$ x 2), 1.34 (t, J = 7.5 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 176.5 (s, *C*OCH$_3$), 145.8 (s, C-2), 137.7 (d, C-6), 133.0 (d, C-4), 129.5 (d, C-3), 128.6 (d, C-5), 127.0 (s, C-1), 32.6 (t, *C*H$_2$CH$_3$), 20.4 (q, CO*C*H$_3$), 15.2 (q, CH$_2$*C*H$_3$); HRMS (ESI+) Calculated ($C_{12}H_{15}O_4INa$): 372.99072 ([M + Na]$^+$) Found: 372.99059

(V) (2-chlorophenyl)-λ^3-iodanediyl diacetate



Prepared by general procedure from 2-chloroiodobenzene (1.24 g, 5.18 mmol) and peracetic acid to give a product as a white solid (1.46 g, 79%).
IR: (KBr) 1645 (C=O) cm^{-1}; mp: 180-197 ºC (sublimated); ^{1}H NMR (400 MHz, $CDCl_3$): 8.24 (dd, J = 7.8, 1.4 Hz, 1H, 6-H), 7.73 (dd, J = 7.8, 1.4 Hz, 1H, 3-H), 7.58 (td, J = 7.8, 1.4 Hz, 1H, 4-H), 7.36 (td, J = 7.8, 1.4 Hz, 1H, 5-H), 2.00 (s, 6H, OAc x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 177.0 (s, *C*OCH$_3$ x 2), 138.5 (d, C-6), 137.1 (s, C-1), 133.9 (d, C-4), 129.9 (d, C-3), 129.0 (d, C-5), 125.1 (s, C-2), 20.4 (q, CO*C*H$_3$ x 2); HRMS (ESI+) Calculated ($C_{10}H_{10}O_4NaClI$): 378.92045 ([M + Na]$^+$) Found: 378.92084

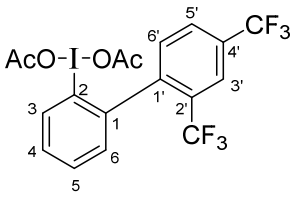
(AA-S1) 2'-iodo-2,4-bis(trifluoromethyl)-1,1'-biphenyl



A solution of 1,3-bis(trifluoromethyl)benzene (1.27 g, 5.93 mmol) in THF (20 mL) was cooled to -78 °C in a dry ice/acetone bath. *n*-BuLi (2.4 mL of a 2.5 M solution in *n*-hexane, 6 mmol) was added via a dropping funnel, and stirring was continued for 1 h at the same temperature. 1-Bromo-2-iodobenzene was then added dropwise at -78 °C. After 3 h, the solution was allowed to reach ambient temperature and then quenched by water (10 mL). The mixture was extracted with EtOAc. The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by flash column chromatography (only hexane, column length 20 cm, diameter 2.6 cm) and recycle GPC ($CHCl_3$) to give the titled compound as a colorless liquid (0.661 g, 27%).
IR: (neat) 3056 (C-H), 1277 (CF_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.03 (s, 1H, 3-H), 7.95 (d, J = 8.2 Hz, 1H, 3'-H), 7.87 (d, J = 8.4 Hz, 1H, 5-H), 7.42-7.40 (m, 2H, 5'-H and 6-H), 7.23 (d, J = 8.2 Hz, 1H, 6'-H), 7.13 (td, J = 8.2, 1.5 Hz, 1H, 4'-H); ^{13}C NMR (100 MHz, $CDCl_3$): 146.4 (s, C-1), 142.5 (s, C-1'), 138.9 (d, C-3'), 133.0 (d), 130.6 (s, q, $^2J_{CF}$ = 33.6 Hz), 129.9 (d, C-4'), 129.6 (d, C-6'), 129.2 (s, q, $^2J_{CF}$ = 32.5 Hz),

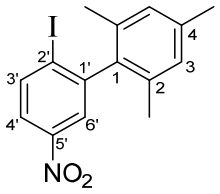
128.2 (d, C-5), 127.5 (d), 123.34 (d, C-3), 123.33 (s, q, $^1J_{CF}$ = 274 Hz, CF_3), 122.9 (s, q, $^1J_{CF}$ = 276 Hz, CF_3), 98.6 (s, C-2'); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -57.6 (s, 3F, CF_3), -61.6 (s, 3F, CF_3); HRMS (EI) Calculated ($C_{14}H_7F_6I$): 415.9497 ($[M]^+$) Found: 415.9492

(AA) (2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



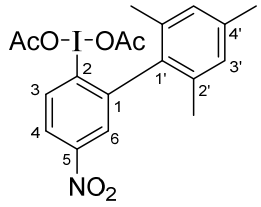
Prepared by general procedure from 2'-iodo-2,4-bis(trifluoromethyl)-1,1'-biphenyl (0.634 g, 1.52 mmol) and peracetic acid to give a product as a white solid (0.601 g, 75%).
mp: 134-135 ºC; IR: (KBr) 3062 (C-H), 1655 (C=O), 1269 (C-F), 1129 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.40 (d, *J* = 8.0 Hz, 1H, 3-H), 8.04 (s, 1H, 3'-H), 7.89 (d, *J* = 8.0 Hz, 5'-H), 7.73-7.70 (m, 2H, 5-H and 6'-H), 7.57-7.53 (m, 2H, 4-H and 6-H), 1.94 (s, 6H, OAc); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (s, *C*OCH_3 x 2), 142.4 (s, C-1'), 140.9 (s, C-1), 137.7 (d, C-3), 133.0 (d, C-6'), 131.8 (d, C-5), 131.7 (s, q, $^2J_{CF}$ = 34.0 Hz), 130.9 (d), 130.6 (d), 130.0 (s, q, $^2J_{CF}$ = 32.6 Hz), 128.0 (d, C-5'), 124.7 (s, C-2), 123.8 (d, C-3'), 123.0 (s, q, $^1J_{CF}$ = 274 Hz, CF_3), 122.9 (s, q, $^1J_{CF}$ = 276 Hz, CF_3), 20.1 (s, CO*C*H_3); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -56.1 (s, 3F, CF_3), -61.8 (s, 3F, CF_3); HRMS (ESI+) Calculated ($C_{18}H_{13}O_4F_6INa$): 556.96549 ($[M + Na]^+$) Found: 556.96495

(AB-S1) 2'-iodo-2,4,6-trimethyl-5'-nitro-1,1'-biphenyl



To a three-necked round bottom flask with a reflux condenser was added 2-bromo-4-nitroaniline (2.18 g, 10.0 mmol), $MesB(OH)_2$ (2.47 g, 15.1 mmol), K_2CO_3 (3.51 g, 25.4 mmol), $Pd(PPh_3)_4$ (0.117 g, 0.101 mmol), EtOH (6 mL), toluene (9 mL) and H_2O (3 mL). The suspension was degassed under reduced pressure and filled with N_2. The mixture was stirred at 90 ºC for 5 days. The reaction mixture was filtered with celite, extracted with EtOAc, washed with H_2O and brine. The collected organic layer was dried over Na_2SO_4. Then, the solution was filtered and organic volatiles were removed under reduced pressure. The crude was purified by flash column chromatography (hexane/EtOAc = 65:35) to give 2',4',6'-trimethyl-5-nitro-[1,1'-biphenyl]-2-amine (1.62 g, 63%) as a yellow solid. 2',4',6'-Trimethyl-5-nitro-[1,1'-biphenyl]-2-amine (1.03 g, 4.03 mmol) was added to a solution of *p*-TsOH•H_2O (2.78 g, 14.6 mmol) in MeCN (16 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (0.711 g, 10.3 mmol) and KI (2.10 g, 12.7 mmol) in H_2O (20 mL) was added gradually. The reaction mixture was stirred for 12 hours at room temperature and then quenched by water and $NaHCO_3$ aq. The mixture was extracted with EtOAc. The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by flash column chromatography (hexane/EtOAc = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a white solid (0.546 g, 37%).
mp: 140-141 °C; IR: (KBr) 2916 (C-H), 1519 (NO_2), 1356 (NO_2) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.16 (d, *J* = 8.3 Hz, 1H, 3'-H), 7.99 (d, *J* = 2.7 Hz, 1H, 6'-H), 7.89 (dd, *J* = 8.3, 2.7 Hz, 1H, 4'-H), 6.98 (s, 2H, 3-H x 2), 2.37 (s, 3H, 4-Me), 1.92 (s, 6H, 2-Me x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 148.4 (s), 148.1 (s), 140.2 (d, C-3'), 139.2 (s), 138.4 (s), 135.1 (s), 128.4 (d, C-3), 124.1 (d, C-6'), 122.9 (d, C-4'), 109.8 (s, C-2'), 21.2 (q, 4-Me), 20.3 (q, 2-Me); HRMS: (ESI+) Calculated ($C_{15}H_{14}NO_2INa$): 389.99614 ($[M]^+$) Found: 389.99760

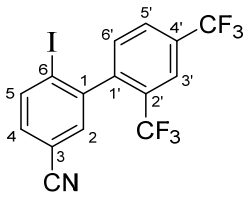
(AB) (2',4',6'-trimethyl-5-nitro-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



Prepared by a modified general procedure (rt, 2 h then 40 °C, 2 h) from 2'-iodo-2,4,6-trimethyl-5'-nitro-1,1'-biphenyl (0.679 g, 1.85 mmol) and peracetic acid (7 mL) to give a product as a white solid (0.371 g, 41%).

mp: 123-124 ºC; IR: (KBr) 3064 (C-H), 1642 (C=O), 1536 (NO_2), 1281 (NO_2) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.56 (d, J = 9.2 Hz, 1H, 3-H), 8.27-8.24 (m, 2H, 4-H and 6-H), 6.95 (s, 2H, 3'-H x 2), 2.35 (s, 3H, 4'-Me), 2.02 (s, 6H, 2'-Me x 2), 1.93 (s, 6H, OAc x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 176.5 (s, *C*OCH$_3$ x 2), 150.1 (s), 147.2 (s), 139.4 (s), 139.3 (d, C-3), 136.0 (s, overlapping), 132.6 (s), 128.6 (d, C-3'), 125.7 (d), 124.1 (d), 21.2 (q, 4'-Me), 20.4 (q, 2'-Me), 20.2 (q, CO*C*H$_3$ x 2); HRMS (ESI+) Calculated ($C_{19}H_{20}NO_6INa$): 508.02275 ([M + Na]$^+$) Found: 508.02323

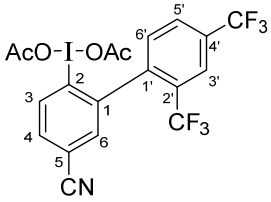
(AC-S1) 6-iodo-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-3-carbonitrile



To a three-necked round bottom flask with a reflux condenser was added 4-amino-3-bromobenzonitrile (1.96 g, 10.0 mmol), 2,4-bis(trifluoromethyl)phenylboronic acid (3.27 g, 12.7 mmol), K_2CO_3 (4.77 g, 34.5 mmol), $Pd(PPh_3)_4$ (1.05 g, 0.909 mmol), EtOH (17 mL), toluene (33 mL) and H_2O (17 mL). The suspension was degassed under reduced pressure and filled with N_2. The mixture was stirred at 90 ºC for 12 h. The reaction mixture was filtered with celite, extracted with EtOAc, washed with H_2O and brine. The collected organic layer was dried over Na_2SO_4. Then, the solution was filtered and organic volatiles were removed under reduced pressure. The crude was purified by flash column chromatography (hexane/EtOAc = 70:30) to give 6-amino-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-3-carbonitrile (2.98 g, 91%) as a solid. 6-Amino-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-3-carbonitrile (1.20 g, 3.64 mmol) was added to a solution of *p*-TsOH•H_2O (2.11 g, 11.1 mmol) in MeCN (15 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (0.630 g, 9.13 mmol) and KI (1.89 g, 11.3 mmol) in H_2O (18 mL) was added gradually. The reaction mixture was stirred for 12 hours at room temperature and then quenched by water and $NaHCO_3$ aq. The mixture was extracted with EtOAc. The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by flash column chromatography (hexane/ EtOAc = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a solid (1.07 g, 67%).

mp: 65-66 °C; IR: (KBr) 3057 (C-H), 2229 (CN), 1128 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.12 (d, J = 8.0 Hz, 1H, 5-H), 8.07 (s, 1H, 3'-H), 7.93 (d, J = 8.4 Hz, 1H, 5'-H), 7.51 (s, 1H, 2-H), 7.42-7.40 (m, 2H, 4-H and 6'-H); ^{13}C NMR (100 MHz, $CDCl_3$): 144.2 (s), 144.0 (s), 140.1 (d, C-5), 132.64 (d), 132.59 (d), 132.2 (d, C-2), 131.5 (s, q, $^2J_{CF}$ = 34.0 Hz), 129.2 (s, q, $^2J_{CF}$ = 31.5 Hz), 128.7 (d, C-5'), 123.6 (d, C-3'), 123.1 (s, q, $^1J_{CF}$ = 274 Hz, CF_3), 122.6 (s, q, $^1J_{CF}$ = 276 Hz, CF_3), 117.6 (s, CN), 112.0 (s, C-3), 105.1 (s, C-6); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -57.9 (s, 3F, CF_3), -61.8 (s, 3F, CF_3); HRMS: (EI) Calculated ($C_{15}H_6F_6NI$) 440.9449 ([M]$^+$) Found: 440.9442

(AC) (5-cyano-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate

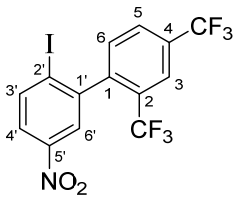


Prepared by a modified general procedure (40 °C) from 6-iodo-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-3-carbonitrile (1.07 g, 2.43 mmol) and peracetic acid (9 mL). The mixture was washed with ether and hexane to give a product as a white solid (0.621 g, 46%).

mp: 135-136 ºC; IR: (KBr) 2238 (CN), 1648 (C=O), 1282, 1129 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (d, J = 8.8 Hz, 1H, 3-H), 8.08 (s, 1H, 3'-H), 7.94 (d, J = 8.0 Hz, 1H, 5'-H), 7.82-7.80 (m, 2H, 4-H and 6-H), 7.69 (d, J = 8.0 Hz, 1H, 6'-H), 1.95 (s, 3H, COC*H*$_3$ x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 176.5 (s, *C*OCH$_3$ x 2), 142.2 (s, C-1), 140.4 (s, C-1'), 138.6 (d, C-3), 133.9

(d), 133.5 (d), 132.7 (d, C-6'), 132.6 (s, q, $^2J_{CF}$ = 34.0 Hz), 130.1 (s, q, $^2J_{CF}$ = 31.7 Hz), 128.8 (s, C-2), 128.4 (d, C-5'), 124.2 (d, C-3'), 122.8 (s, q, $^1J_{CF}$ = 264 Hz, CF_3), 122.7 (s, q, $^1J_{CF}$ = 277 Hz, CF_3), 116.6 (s, CN), 116.1 (s, C-5), 20.1 (q, CO*C*H$_3$ x 2); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -55.9 (s, 3F, CF_3), -61.9 (s, 3F, CF_3); HRMS (ESI+) Calculated ($C_{19}H_{12}NO_4F_6INa$): 581.96074 ([M + Na]$^+$) Found: 581.96003

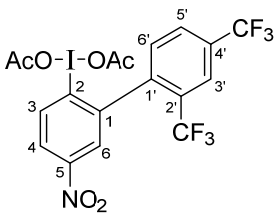
(AD-S1) 2'-iodo-5'-nitro-2,4-bis(trifluoromethyl)-1,1'-biphenyl



To a three-necked round bottom flask with a reflux condenser was added 2-bromo-4-nitroaniline (3.92 g, 18.1 mmol), 2,4-bis(trifluoromethyl)phenylboronic acid (6.89 g, 26.7 mmol), K_2CO_3 (9.50 g, 68.8 mmol), $Pd(PPh_3)_4$ (2.08 g, 1.80 mmol), EtOH (33 mL), toluene (67 mL) and H_2O (33 mL). The suspension was degassed under reduced pressure and filled with N_2. The mixture was stirred at 90 ºC for 12 h. The reaction mixture was filtered with celite, extracted with EtOAc, washed with H_2O and brine. The collected organic layer was dried over Na_2SO_4. Then, the solution was filtered and organic volatiles were removed under reduced pressure. The crude was purified by flash column chromatography (hexane/EtOAc = 65:35) to give 5-nitro-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-2-amine (5.16 g, 82%) as a yellow solid. 5-Nitro-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-2-amine (1.57 g, 4.48 mmol) was added to a solution of *p*-TsOH•H_2O (2.66 g, 14.0 mmol) in MeCN (18 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (1.02 g, 14.5 mmol) and KI (2.39 g, 14.4 mmol) in H_2O (22 mL) was added gradually. The reaction mixture was stirred for 12 hours at room temperature and then quenched by water and $NaHCO_3$ aq. The mixture was extracted with EtOAc. The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by flash column chromatography (hexane/ EtOAc = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow solid (1.59 g, 77%).

mp: 68-69 °C; IR: (KBr) 3083 (C-H), 1524 (NO_2), 1345 (NO_2) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.18 (d, *J* = 8.8 Hz, 1H, 3'-H), 8.10-8.09 (m, 2H, 6'-H and 3-H), 7.99 (dd, *J* = 8.8, 2.8 Hz, 1H, 4'-H), 7.95 (d, *J* = 8.0 Hz, 1H, 5-H), 7.44 (d, *J* = 8.0 Hz, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): 147.4 (s, C-5'), 144.2 (s), 144.1 (s), 140.2 (d, C-3'), 132.6 (d, C-6), 131.6 (s, q, $^2J_{CF}$ = 34.0 Hz), 129.3 (s, q, $^2J_{CF}$ = 31.1 Hz), 128.7 (d, C-5), 124.3 (d, C-4'), 124.0 (d, C-6'), 123.7 (d, C-3), 123.1 (s, q, $^1J_{CF}$ = 274 Hz, CF_3), 122.7 (s, q, $^1J_{CF}$ = 276 Hz, CF_3), 107.4 (s, C-2'); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -57.9 (s, 3F, CF_3), -61.8 (s, 3F, CF_3); HRMS: (EI) Calculated ($C_{14}H_6NO_2F_6I$) 460.9347 ([M]$^+$) Found: 460.9353

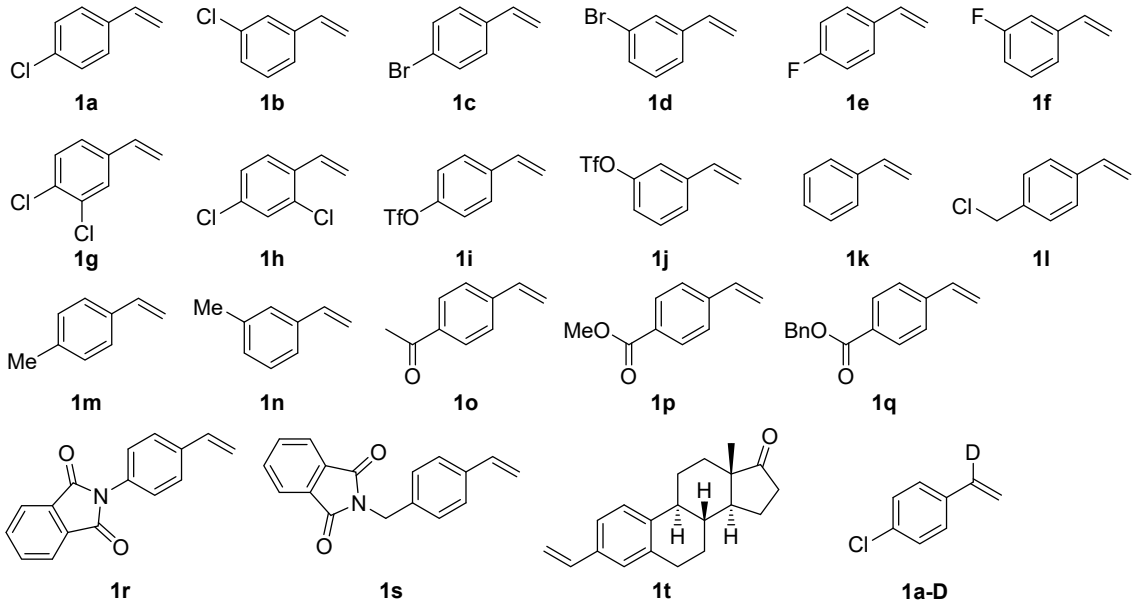
(AD) (5-nitro-2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-l3-iodanediyl diacetate



Prepared by a modified general procedure (40 °C) from 2'-iodo-5'-nitro-2,4-bis(trifluoromethyl)-1,1'-biphenyl (4.93 g, 10.7 mmol) and peracetic acid (30 mL). The mixture was washed with ether and hexane to give a product as a white solid (4.29 g, 69%).

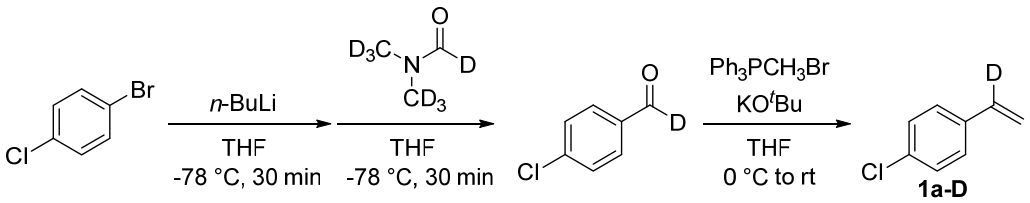
mp: 101-102 ºC; IR: (KBr) 3066 (C-H), 1645 (C=O), 1540 (NO_2), 1284 (NO_2) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.59 (d, *J* = 9.2 Hz, 1H, 3-H), 8.37-8.34 (m, 2H, 4-H and 6-H), 8.10 (s, 1H, 3'-H), 7.95 (d, *J* = 8.0 Hz, 1H, 5'-H), 7.72 (d, *J* = 8.0 Hz, 1H, 6'-H), 1.95 (s, 6H, COC*H*$_3$ x 2); ^{13}C NMR (100 MHz, $CDCl_3$): 176.5 (s, *C*OCH$_3$ x 2), 149.1 (s, C-5), 142.8 (s, C-1), 140.4 (s, C-1'), 139.1 (d, C-3), 132.73 (d, C-6'), 132.69 (s, q, $^2J_{CF}$ = 34.4 Hz), 130.19 (s, C-2), 130.17 (s, q, $^2J_{CF}$ = 32.0 Hz), 128.4 (d, C-5'), 125.5 (d), 125.3 (d), 124.3 (d, C-3'), 122.8 (s, q, $^1J_{CF}$ = 275 Hz, CF_3), 122.7 (s, q, $^1J_{CF}$ = 276 Hz, CF_3), 20.1 (q, CO*C*H$_3$ x 2); ^{19}F NMR (377 MHz, $CDCl_3$, TFA as an external standard): -55.9 (s, 3F, CF_3), -61.9 (s, 3F, CF_3); HRMS (ESI+) Calculated ($C_{18}H_{12}NO_6F_6INa$): 601.95057 ([M + Na]$^+$) Found: 601.94971

Styrenes



All styrenes are known compounds. **1a-1f, 1j, 1j-1l, 1q** are commercially available reagents. **1g**[36], **1h**[37], **1i**[37], **1m**[10b], **1n**[38], **1o**[39], **1p**[40], **1r**[37], **1s**[41], **1t**[37] were prepared according to the literatures, and the spectral data are in good agreement with the reports. **1a-D** was synthesized by the following procedure and the spectral data are in good agreement with the reports.[42]

Preparation of 1a-D

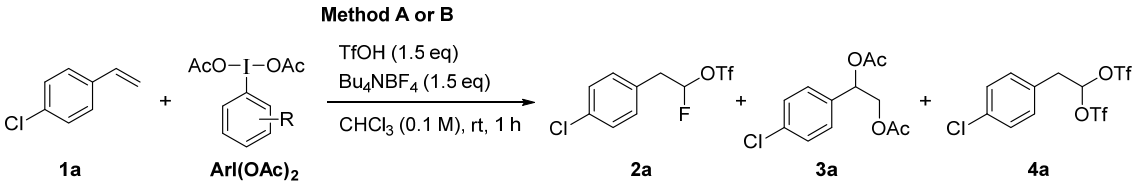


To a THF (30 mL) solution of 1-bromo-4-chlorobenzene (0.984 g, 5.14 mmol) in three-necked round bottom flask with a stirring bar and a dropping funnel were added *n*-BuLi in hexane (1.6 M, 8.8 mL, 5.50 mmol) under N_2 atmosphere at -78 ºC. The reaction mixture was stirred for 30 min at -78 ºC. d_7-Dimethylformamide (0.43 mL, 5.50 mmol) was slowly added to the reaction mixture and the reaction mixture was stirred for 30 min at -78 ºC. The reaction mixture was warmed to room temperature and quenched by NH_4Cl aq. and extracted with ether. The collected organic layers were dried over $MgSO_4$ and the organic volatiles were removed under reduced pressure. The crude was purified chromatography on silica gel (hexane/EtOAc = 8:2) to afford 4-chlorobenzaldehyde-*formyl*-d_1 (0.219 g, 30%) as a white solid. To a dried bottom round flask with a stirring bar were added methyltriphenylphosphonium bromide (0.631 g, 1.77 mmol), KO^{t}Bu (0.223 g, 1.99 mmol) and THF (6 mL). The mixture was stirred for 1 h at room temperature. The mixture was cooled to 0 ºC and a THF solution of 4-chlorobenzaldehyde-*formyl*-d_1 (0.196 g, 1.39 mmol) was added. The reaction mixture was gradually warmed to room temperature and stirred overnight. The mixture was diluted with EtOAc and water and extracted with EtOAc. The combined organic layer was wash with water and dried over $MgSO_4$. The organic volatiles were removed under reduced pressure. The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford α-*deuterio*-4-chlorostyrene (**1a-D**) as a colorless liquid (0.0788 g, 41%).

^{1}H NMR (400 MHz, $CDCl_3$): 7.34 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.7 Hz, 2H), 5.72 (t, J = 2.7 Hz, 1H), 5.27-5.26 (m, 1H)

General Procedure

1,1-heterodifunctionalization of 1a with $ArI(OAc)_2$, TfOH and Bu_4NBF_4 (Table 2.1, 2.2 and 2.3)



Methods A or B were conducted depending on the type of $ArI(OAc)_2$. Yields of 1-(4-chlorophenyl)ethane-1,2-diyl diacetate (**3a**) were determined by ^1H NMR according to the reported spectral data[43]. The yield of 1,1-bis(trifluoromethanesulfonyloxy)-2-(4-chlorophenyl)ethane (**4a**) in crude products was determined by ^1H NMR spectra based on the reported spectrum of 2-phenylethane-1,1-diyl bis(trifluoromethanesulfonate)[44].

Method A

To a two-necked flask with a stirring bar was added $ArI(OAc)_2$ (0.300 mmol, 1.5 equiv) Bu_4NBF_4 (0.0988 g, 0.300 mmol, 1.50 equiv) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol, 1.50 equiv) was added to the mixture. **1a** (0.0277 g, 0.200 mmol, 1.00 equiv) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard. (When ***o*-*t*Bu (O)** was used, CH_2Br_2 was used as an internal standard.)

Method B

To a two-necked flask with a stirring bar was added $ArI(OAc)_2$ (0.300 mmol, 1.50 equiv), Bu_4NBF_4 (0.0988 g, 0.300 mmol, 1.50 equiv), $CHCl_3$ (2 mL) and **1a** (0.0277 g, 0.200 mmol, 1.00 equiv). TfOH (26.3 μL, 0.300 mmol, 1.50 equiv) was slowly added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard.

1,1- heterodifunctionalization of styrenes with *o*-{2,4-$(CF_3)_2C_6H_3$}- and *p*-NO_2-substituted $ArI(OAc)_2$ (AD) and TfOH (Scheme 2.1)

To a two-necked flask with a stirring bar was added **AD** (1.50 equiv, 0.300 mmol), Bu_4NBF_4 (1.50 equiv, 0.300 mmol), $CHCl_3$ (2 mL) and corresponding styrene (1.00 equiv, 0.200 mmol). TfOH (26.3 μL, 0.300 mmol, 1.50 equiv) was slowly added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq. and extracted with ether. The combined organic layers were dried over Na_2SO_4. After solvent was removed under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard. The crude residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the title compound.

One-pot synthesis of 1-fluoroalkane (Scheme 2.2 and 2.3)

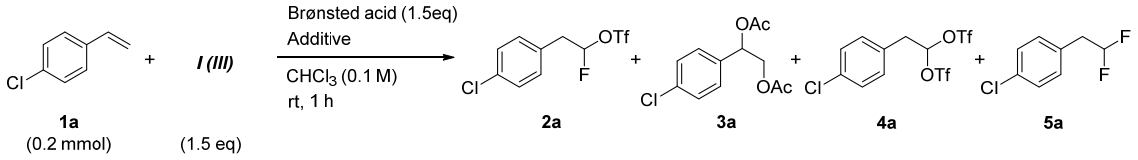
To a two-necked flask with a stirring bar was added **AD** (1.50 equiv, 0.300 mmol), Bu_4NBF_4 (1.50 equiv, 0.300 mmol), $CHCl_3$ (2 mL) and corresponding styrene (1.00 equiv, 0.200 mmol). TfOH (1.50 equiv, 0.300 mmol) was slowly added to the mixture. After stirring for 1 h at room temperature, the corresponding nucleophile was added to the reaction mixture and stirred for further 1 h. The reaction was quenched with

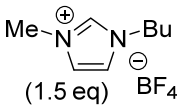
Na_2SO_3 aq. and extracted with ether. The combined organic layers were dried over Na_2SO_4. After solvent was removed under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard. The crude residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the targeted compound.

Optimization of reaction conditions (Table 2.S1)

All entries were conducted with Method A in General Procedure. The reaction conditions with Bu_4NBF_4 (1.5 eq) with $PhI(OAc)_2$ gave the product **2a** in only 10% yield and preferentially gave 36% yield of **3a** (entry 1). The use of 3 equivalent amount of Bu_4NBF_4 exclusively afforded 62% yield of **3a** (entry 2). These results indicate that the excess amount of BF_4 salt interferes 1,1-heterodifunctionalization. 1-Butyl-3-methylimidazolium tetrafluoroborate instead of Bu_4BF_4 lowered the yield of **2a** (entry 3). Iodosyl benzene suppressed the formation of **3a**, but the yield of **2a** was low (entry 4). The reaction among $ArI(OAc)_2$ **I**, TfOH, and Bu_4NBF_4 gave the product **2a** in 40% yield (entry 5) and the reaction without BF_4 salt gave the 1,1-homodifunctionalization product **4a** (entry 6). HBF_4•OEt_2 as a fluorine source additive also yielded the product **2a** (entry 7). HBF_4•OEt_2 as a Brønsted acid gave the 1,2-diacetoxylation product **3a** in 22% yield in the absence of additives (entry 8) and 1-fluoro-1-sulfonylation product **2a** in 37% yield in the presence of Bu_4NOTf (entry 9). A low temperature condition didn't improve the yield of **2a** compared with entry 5 (entry 10).

Table 2.S1. Reaction optimization of 1-fluoro-1-sulfonyloxylation.



entry	*I (III)*	Brønsted acid	Additive	Yield (%) 2a	3a	4a	5a
1	$PhI(OAc)_2$	TfOH	Bu_4NBF_4 (1.5 eq)	10	36	0	0
2	$PhI(OAc)_2$	TfOH	Bu_4NBF_4 (3.0 eq)	0	62	8	0
3	$PhI(OAc)_2$	TfOH	 (1.5 eq)	6	64	8	0
4	PhI=O	TfOH	Bu_4NBF_4 (1.5 eq)	8	0	8	0
5	**I**	TfOH	Bu_4NBF_4 (1.5 eq)	40	16	16	0
6	**I**	TfOH	none	0	4	53	0
7	**I**	TfOH	HBF_4•OEt_2 (1.5 eq)	27	8	2	6
8	**I**	HBF_4•OEt_2	none	0	22	0	7
9	**I**	HBF_4•OEt_2	Bu_4NOTf (1.5 eq)	37	27	0	<1
10[a]	**I**	TfOH	Bu_4NBF_4 (1.5 eq)	27	7	0	0

[a] -40 °C

Regression Analysis for Optimization of ArI(OAc)$_2$

Measured $\Delta\Delta G^{\ddagger}$ was calculated by a following formula;

$$\text{measured } \Delta\Delta G^{\ddagger} = -RT\ln\left(\frac{\textbf{Yield of 3}\boldsymbol{a}}{\textbf{Yield of 2}\boldsymbol{a}}\right) \quad (T = 293.15 \text{ K})$$

Simple regression analysis

Simple regression analysis for *para*- and *meta*-substituted ArI(OAc)$_2$ was carried out. Hammett substituent constants (σ) were referred to the reported data.[16]

Multi variate Regression Analysis (Table 2.2 and Figure 2.4)

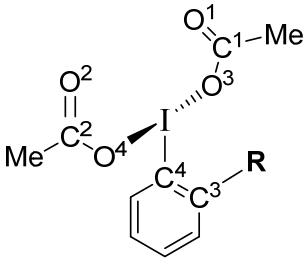
Multivariate regression analysis for *ortho*-substituted forms of ArI(OAc)$_2$ (**A, M-Z, AA**) was carried out.

Calculation for Molecular Descriptors by DFT Calculation Study

All calculations were performed with Gaussian 16, Revision C.01. Quantum chemical calculations were performed under vacuum at 298 K and 1 bar. The geometry optimizations were carried out at ωB97X-D level of theory with a mixed basis set; 6-311+G(d, p) for C, H, O, N, F, Cl, Br and Lanl2DZ for I. **Y** and **Z** were calculated as cations except BF_4 anion ($\mathbf{Y}^+$ and $\mathbf{Z}^+$). All molecular geometries were fully optimized. Stationary points and minima on the potential energy surface were identified by vibrational analysis. Natural bond orbital analysis was performed under the optimized geometries using the NBO version 3.1 program as including in Gaussian. Sterimol parameters of substituents on iodoarene diacetates (L, B_1, B_5) were calculated by *DBSTEP* as Van der Waals radii[45].

Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2019.

Summary of the referred parameters of ArI(OAc)$_2$



17 types of parameters, NBO(I), NBO(C^4), NBO(C^1), NBO(C^2), NBO(O^1), NBO(O^2), $v_{C=O}$, $I_{C=O}$, L, B_1, B_5, ∠(C^3-C^4-I-O^3), ∠(R-C^3-C^4), ∠(C^3-C^4-I), bond (I-C^4), HOMO, and LUMO were evaluated. ∠(C^3-C^4-I-O^3) is smaller than ∠(C^3-C^4-I-O^4).

An NBO(X) means NBO charge on an X atom. $v_{C=O}$ means a frequency of C=O. $I_{C=O}$ means an infrared of C=O. L, B_1 and B_5 mean sterimol parameters (L, the length measured along the axis of the bond between the substituent and the parent molecule; B_1, the minimal radius measured perpendicular to the bond axis used to measure L; B_5, the maximal radius measured perpendicular to the same bond axis). ∠(W-X-Y-Z) means a dihedral angle that consists of W, Y, X and Z atoms. ∠(X-Y-Z) means an angle that consists of X, Y and Z atoms. Bond (X-Y) means a bond length of X-Y bond. HOMO and LUMO mean absolute energy values of HOMO and LUMO orbitals (eV).

Table 2.S2. Summary of $ArI(OAc)_2$ parameters from DFT calculation.

		NBO(I)	NBO(C^4)	NBO(C^1)	NBO(C^2)	NBO(O^1)	NBO(O^2)	$\nu_{C=O}$	$I_{C=O}$	L	B_1	B_5	∠(C^3-C^4-I-O^3)	∠(R-C^3-C^4)	∠(C^3-C^4-I)	bond (I-C^4)	HOMO	LUMO
Training set																		
H	**A**	1.3708	-0.25993	0.80097	0.80097	-0.64961	-0.64961	1761.64	609.8665	2.17	1.09	1.09	89.99714	121.08892	118.82489	2.11259	-0.34673	-0.01863
o-Me	**M**	1.3588	-0.25263	0.80129	0.80137	-0.64753	-0.64844	1763.97	613.3383	3.20	1.70	2.11	71.15700	123.52827	119.99111	2.12244	-0.34679	-0.01875
o-NO_2	**N**	1.42752	-0.26984	0.81119	0.80447	-0.63918	-0.64557	1764.61	512.9198	3.56	1.55	2.60	49.08904	123.15243	123.35343	2.12232	-0.35504	-0.04338
o-tBu	**O**	1.35166	-0.24052	0.80024	0.80025	-0.64890	-0.64892	1761.77	597.1032	4.29	2.83	3.28	90.43795	126.66375	124.86384	2.13272	-0.34561	-0.01619
o-CN	**P**	1.40773	-0.22321	0.80386	0.80389	-0.64678	-0.64665	1758.22	545.0614	4.13	1.70	1.70	89.39356	122.29632	120.43639	2.11334	-0.35346	-0.03154
o-CF_3	**Q**	1.39575	-0.23171	0.80255	0.80255	-0.64912	-0.64913	1756.95	558.9483	3.48	2.09	2.72	90.30793	122.95012	122.80289	2.12182	-0.35029	-0.02398
o-F	**R**	1.40312	-0.33789	0.80200	0.80201	-0.64962	-0.64959	1758.39	573.1483	2.81	1.47	1.47	89.66243	120.12431	119.68418	2.10094	-0.34948	-0.02176
o-Br	**S**	1.39836	-0.29712	0.80223	0.80223	-0.64926	-0.64925	1758.71	576.0394	3.72	1.83	1.83	89.61489	122.89874	122.30280	2.11123	-0.34748	-0.02180
o-Mes	**T**	1.38042	-0.24622	0.80679	0.80215	-0.64317	-0.64804	1767.14	542.6898	7.49	2.16	4.46	72.04994	123.25699	119.72309	2.12511	-0.31663	-0.01417
External validations																		
o-Et	**U**	1.35565	-0.24440	0.80079	0.80094	-0.64799	-0.64851	1763.58	619.7478	4.36	1.70	3.23	73.24015	122.25662	120.17401	2.12469	-0.34625	-0.01788
o-Cl	**V**	1.40002	-0.29712	0.80220	0.80221	-0.64929	-0.64926	1758.58	575.6975	3.49	1.75	1.75	89.65415	122.28560	121.62075	2.10925	-0.34905	-0.02203
o-Ph	**W**	1.37934	-0.24359	0.80195	0.80056	-0.64839	-0.64785	1762.22	578.9761	6.45	1.70	3.24	87.33529	123.39647	119.80715	2.11688	-0.33461	-0.01659
o-CH_2(2,6-diMeC_6H_3)	**X**	1.35663	-0.25212	0.80099	0.80133	-0.64640	-0.64754	1765.15	650.9675	4.96	1.70	6.01	70.49439	122.32587	119.98031	2.12419	-0.32346	-0.01977
External predictions																		
o-CH_2(2,6-diMePy)$^+$	**Y**$^+$	1.38023	-0.25789	0.80142	0.80544	-0.62959	-0.62810	1766.22	489.3688	4.80	1.70	6.00	62.50660	120.39849	121.17461	2.12864	-0.43873	-0.15809
o-imidazolyl$^+$	**Z**$^+$	1.40037	-0.24036	0.80222	0.80539	-0.62822	-0.63010	1761.08	385.1544	7.98	1.94	4.21	56.87224	122.43780	120.90500	2.12826	-0.44836	-0.13228
o-2,4-di$CF_3C_6H_3$	**AA**	1.38022	-0.23883	0.80404	0.80203	-0.64334	-0.64762	1763.40	536.0076	7.76	2.21	4.99	59.29749	122.97560	120.99408	2.12939	-0.35210	-0.02386

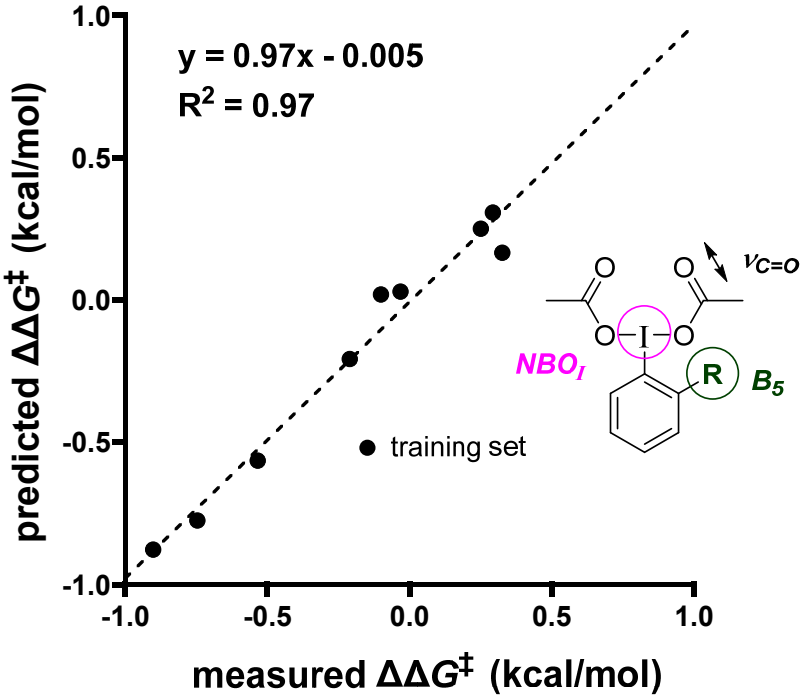
Mathematical Study (Table 2.2 and Figure 2.4)

Stepwise linear regression analyses were performed with EZR[46], which is a graphical user interface for R version 4.1.2[47]. Parameters used in the model were normalized as Z-scores using the formula: $Z = (X - \mu)/\sigma$, where Z is the normalized parameter, X is the parameter, μ is the mean, and σ is the standard deviation.

Equation 2.S1. Model in Figure S1 and Figure 4.

$$\text{predicted } \Delta\Delta G^{\ddagger} = -0.10 + 0.36\, B_5 + 0.33\, NBO_I - 0.20\, \nu_{C=O}$$

Figure 2.S1. Predicted versus measured $\Delta\Delta G^{\ddagger}$ for *ortho*-substituted forms of $ArI(OAc)_2$ (training set).



Coefficients:

	Estimate Std.	Error	t value	Pr(>|t|)
(Intercept)	-0.10498	0.04283	-2.451	0.05785 .
B5	0.35658	0.06136	5.812	0.00213 **
NBO.I.	0.32508	0.03021	10.759	0.00012 ***
v.C.O.	-0.20328	0.03709	-5.481	0.00276 **

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.09606 on 5 degrees of freedom

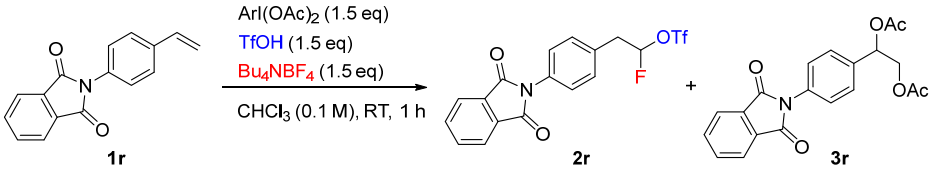
Multiple R-squared: 0.9722, Adjusted R-squared: 0.9555

F-statistic: 58.29 on 3 and 5 DF, p-value: 0.0002598

Complementary use of AD and Z (Table 2.S3 and Table 2.S4)

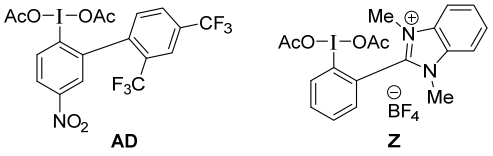
1,1-Heterodifunctionalization of **1r** with $ArI(OAc)_2$ (**AD**) showed comparatively low selectivity (Scheme 1 and Table 2.S8, entry 1). In order to improve the selectivity, we examined the use of $ArI(OAc)_2$ (**Z**), which gave the best selectivity among *ortho*-substituted hypervalent iodines $ArI(OAc)_2$. The reaction using **Z** resulted in a slightly better selectivity than that of **AD**. (entry 2). Furthermore, the conditions using **Z** without Bu_4NBF_4 gave a much better selectivity (entry 3), in which BF_4^- making a pair with the imidazolium moiety worked as a fluorine source.

Table 2.S3. Reaction of **1r** with **AD** or **Z**



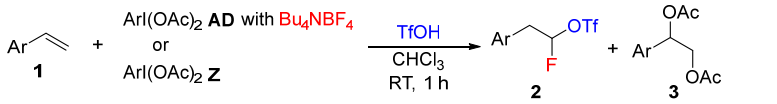
entry	$ArI(OAc)_2$	Selectivity (2r / 3r)	Yield (%) (2r + 3r)
1	**AD**	64 : 34	55
2	**Z**	69 : 31	45
3[a]	**Z**	78 : 22	49

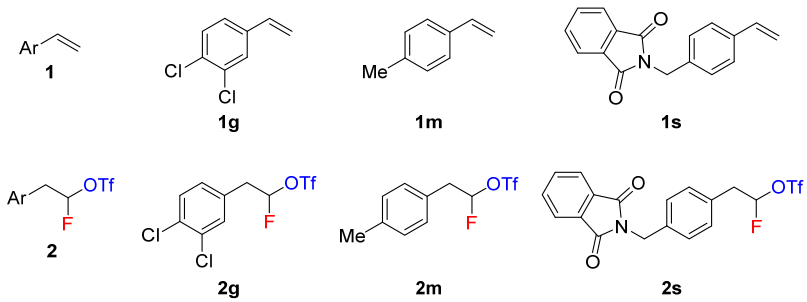
[a]Without Bu_4NBF_4



Therefore, we examined some styrenes in the 1,1-heterodifunctionalization using **Z** under the conditions without Bu_4NBF_4, and then found that the reactions using **1g**, **1m** and **1s** afforded better results than those with **AD** (Table 2.S4).

Table 2.S4. Substrate scope (**2p, 2q, 2s**) with **AD** or **Z**

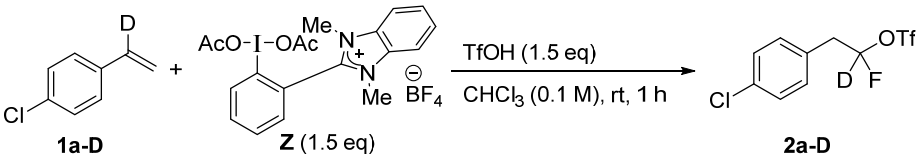




$ArI(OAc)_2$			
AD[a]	61% **2g/3g** = 80:20	32% **2m/3m** = 91:9	60% **2s/3s** = 72:28
Z[b]	57% **2g/3g** = 96:4	30% **2m/3m** = 100:0	45% **2s/3s** = 84:16

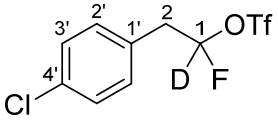
[a] **1** (0.2 mmol), $Ar(OAc)_2$ **AD** (0.3 mmol), TfOH (0.3 mmol), Bu_4NBF_4 (0.3 mmol), $CHCl_3$ (2 mL), RT, **1** h
[b] **1** (0.2 mmol), $Ar(OAc)_2$ **Z** (0.3 mmol), TfOH (0.3 mmol), $CHCl_3$ (2 mL), RT, **1** h

Deuterium labeling experiment



We investigated the formation of the phenonium ion using α-*deuterio*-4-chlorostyrene. According to modified General Procedure, **1a-D** was converted into **2a-D**. The result of migration of the deuterium showed the evidence of the formation of a phenonium ion as well as the related 1,1-difunctionalization work[48].

(2a-D) 1-*deuterio*-1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-chlorophenyl)ethane

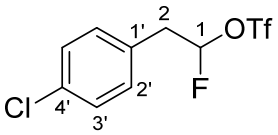


To a two-necked flask with a stirring bar was added $ArI(OAc)_2$ (**Z**) (0.169 g, 0.305 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, α-*deuterio*-4-chlorostyrene (**1a-D**) (0.0288 g, 0.206 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (52%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless oil (0.0170 g, 27%).

IR: (neat) 1424, 1218, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.35 (d, J = 8.3 Hz, 2H, 3'-H), 7.19 (d, J = 8.3 Hz, 2H, 2'-H), 3.32-3.18 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 134.4 (s), 131.3 (d, C-2'), 129.3 (d, C-3'), 129.3 (s), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.0 (s, d, $^1J_{CF}$ = 247 Hz, t, $^1J_{CD}$ = 28.4 Hz, C-1), 39.6 (t, d, $^2J_{CF}$ = 21.7 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (s, 3F, CF_3), -118.7--118.9 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_6DClF_4O_3S$): 306.9803, Found: 306.9799

Products

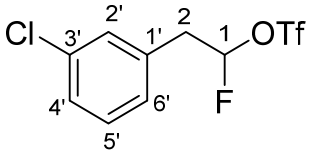
(2a) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-chlorophenyl)ethane



Prepared according to General Procedure using 4-chlorostyrene (**1a**) (0.0275 g, 0.198 mmol), **AD** (0.172 g, 0.297 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.105 g, 0.319 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by $CHBr_3$ as an internal standard (47%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0182 g, 30%).

IR: (neat) 1425, 1219, 1142, 895 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.35 (d, J = 8.4 Hz, 2H, 3'-H), 7.19 (d, J = 8.4 Hz, 2H, 2'-H), 6.21 (t, J = 5.2 Hz, d, $^2J_{HF}$ = 54.0 Hz, 1H, 1-H), 3.33-3.18 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 134.4 (s, C-4'), 131.3 (d, C-3'), 129.33 (d, C-2'), 129.33 (s, C-1'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.3 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 39.8 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.94 (3F, CF_3), -118.1 (1F, 1-F); HRMS (EI, 70 eV) Calculated ($C_9H_7ClF_4O_3S$): 305.9741, Found: 305.9742

(2b) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(3-chlorophenyl)ethane

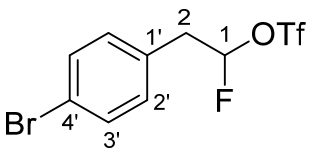


Prepared according to General Procedure using 3-chlorostyrene (**1b**) (0.0279 g, 0.201 mmol), **AD** (0.175 g, 0.302 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.102 g, 0.310 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by $CHBr_3$ as an internal standard (46%). The crude mixture was

purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0159 g, 26%).

IR: (neat) 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.35-7.29 (m, 2H, 4'-H and 5'-H), 7.26 (s, 1H, 2'-H), 7.14 (d, J = 6.6 Hz, 1H, 6'-H), 6.23 (t, J = 5.2 Hz, d, $^2J_{HF}$ = 53.9 Hz, 1H, 1-H), 3.33-3.18 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 135.0 (s, C-3'), 132.8 (s, d, $^3J_{CF}$ = 5.1 Hz, C-1'), 130.4 (d, C-5'), 130.1 (d, C-2'), 128.6 (d, C-4'), 128.1 (d, C-6'), 118.3 (s, q, $^1J_{CF}$ = 323 Hz, CF_3), 111.2 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 40.0 (t, d, $^2J_{CF}$ = 21.1 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.1 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_7ClF_4O_3S$): 305.9741 ($[M]^+$) Found: 305.9734

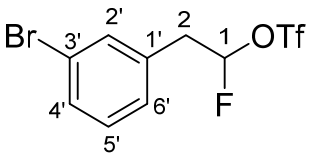
(2c) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-bromophenyl)ethane



Prepared according to General Procedure using 4-bromostyrene (**1c**) (0.0384 g, 0.210 mmol), $ArI(OAc)_2$ **AD** (0.177 g, 0.306 mmol), TfOH (26.3 µL, 0.300 mmol), Bu_4NBF_4 (0.104 g, 0.316 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (47%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0216 g, 29%).

IR: (neat) 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.50 (d, J = 8.2 Hz, 2H, 3'-H), 7.13 (d, J = 8.2 Hz, 2H, 2'-H), 6.21 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.31-3.16 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 132.3 (d, C-3'), 131.6 (d, C-2'), 129.8 (s, d, $^3J_{CF}$ = 5.7 Hz, C-1'), 122.5 (s, C-4'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.2 (d, d, $^1J_{CF}$ = 247.4 Hz, C-1), 39.8 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.92 (d, J = 9.2 Hz, 3F, CF_3), -118.01--118.30 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_7BrF_4O_3S$): 349.9235 ($[M]^+$) Found: 349.9240

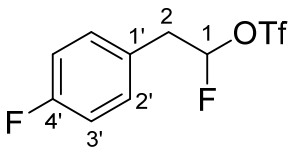
(2d) 1-fluoro-1-(trifluoromethanelsulfonyloxy)-2-(3-bromophenyl)ethane



Prepared according to a General Procedure using 3-bromostyrene (**1d**) (0.0382 g, 0.209 mmol), **AD** (0.174 g, 0.300 mmol), TfOH (26.3 µL, 0.300 mmol), Bu_4NBF_4 (0.101 g, 0.307 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (47%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0192 g, 26%).

IR: (neat) 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.48 (dt, J = 7.7, 1.6 Hz, 1H, 4'-H), 7.42 (s, 1H, 2'-H), 7.25 (t, J = 7.7 Hz, 1H, 5'-H), 7.19 (d, J = 7.7 Hz, 1H, 6'-H), 6.22 (t, J = 5.2 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.33-3.17 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 133.1 (s, d, $^3J_{CF}$ = 5.9 Hz, C-1'), 133.0 (d, C-2'), 131.5 (d, C-4'), 130.7 (d, C-5'), 128.6 (d, C-6'), 123.1 (s, C-3'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.2 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 40.0 (t, d, $^2J_{CF}$ = 21.9 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.1 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_7BrF_4O_3S$): 349.9235 ($[M]^+$) Found: 349.9242

(2e) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-fluorophenyl)ethane

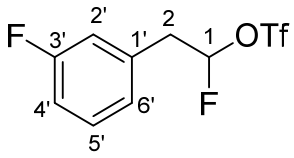


Prepared according to General Procedure using 4-fluorostyrene (**1e**) (0.0225 g, 0.184 mmol), **AD** (0.175 g, 0.302 mmol), TfOH (26.3 µL, 0.300 mmol), Bu_4NBF_4 (0.100 g, 0.304 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed ^1H NMR using $CHBr_3$ as an internal standard (46%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0147 g, 27%).

IR: (neat) 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.22 (d, J = 8.6 Hz, d, $^4J_{HF}$ = 5.1 Hz, 2H, 2'-H), 7.06 (d, J = 8.6 Hz, d, $^3J_{HF}$ = 8.6 Hz, 2H, 3'-H), 6.20 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.33-3.18 (m, 2H,

2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 162.7 (s, d, $^1J_{CF}$ = 247.6 Hz, C-4'), 131.6 (d, d, $^3J_{CF}$ = 8.4 Hz, C-2'), 126.7 (s, d, $^3J_{CF}$ = 5.9 Hz, d, $^4J_{CF}$ = 3.3 Hz, C-1'), 118.3 (s, q, $^1J_{CF}$ = 320.4 Hz, CF_3), 116.1 (d, d, $^2J_{CF}$ = 21.8 Hz, C-3'), 111.6 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 39.6 (t, d, $^2J_{CF}$ = 21.8 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -75.0 (d, *J* = 6.1 Hz, 3F, CF_3), -113.9 (q, *J* = 8.1 Hz, 1F, 4'-F), -117.9--118.2 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_7F_5O_3S$): 290.0036 ($[M]^+$) Found: 290.0041

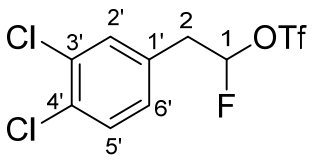
(2f) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(3-fluorophenyl)ethane



Prepared according to General Procedure using 3-fluorostyrene (**1f**) (0.0258 g, 0.211 mmol), **AD** (0.173 g, 0.309 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.101 g, 0.307 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (49%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0188 g, 31%).

IR: (neat) 1251 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.34 (t, *J* = 7.9 Hz, d, $^4J_{HF}$ = 5.9 Hz, 1H, 5'-H), 7.07-7.03 (m, 2H, 4'-H and 6'-H), 6.97 (d, $^3J_{HF}$ = 9.4 Hz, 1H, 2'-H), 6.23 (t, *J* = 5.2 Hz, d, $^2J_{HF}$ = 54.0 Hz, 1H, 1-H), 3.36-3.20 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0 (s, d, $^1J_{CF}$ = 247 Hz, C-3'), 133.2 (s, t, $^3J_{CF}$ = 6.6 Hz, C-1'), 130.7 (d, d, $^3J_{CF}$ = 9.1 Hz, C-5'), 125.6 (d, d, $^4J_{CF}$ = 3.3 Hz, C-6'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 117.0 (d, d, $^2J_{CF}$ = 21.3 Hz, C-2'), 115.4 (d, d, $^2J_{CF}$ = 20.5 Hz, C-4'), 111.3 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 40.1 (t, d, $^2J_{CF}$ = 22.1 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -112.2 (dd, *J* = 15.3, 9.1 Hz, 1F, 3'-F), -117.7--118.0 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_7F_5O_3S$): 290.0036 ($[M]^+$) Found: 290.0043

(2g) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(3,4-dichlorophenyl)ethane



<u>The conditions with **AD**</u>

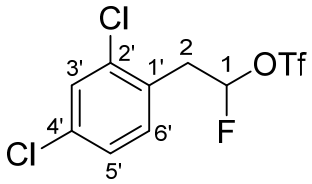
Prepared according to General Procedure using 3,4-dichlorostyrene (**1g**) (0.0350 g, 0.202 mmol), **AD** (0.173 g, 0.300 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.101 g, 0.306 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (49%).

<u>The conditions with **Z**</u>

To a two-necked flask with a stirring bar was added **Z** (0.173 g, 0.312 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, 3,4-dichlorostyrene (**1g**) (0.0334 g, 0.193 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (55%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0211 g, 32%).

IR: (neat) 1250 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.45 (d, *J* = 8.3 Hz, 1H, 5'-H), 7.36 (d, *J* = 2.2 Hz, 1H, 2'-H), 7.10 (dd, *J* = 8.3, 2.2 Hz, 1H, 6'-H), 6.22 (t, *J* = 5.1 Hz, d, $^2J_{HF}$ = 53.8 Hz, 1H, 1-H), 3.32-3.17 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 133.3 (s), 132.8 (s), 131.9 (d, C-2'), 131.1 (d, C-5'), 131.0 (s, d, $^3J_{CF}$ = 5.1 Hz, C-1'), 129.3 (d, C-6'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 110.7 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 39.5 (t, d, $^2J_{CF}$ = 21.9 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.1 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_6Cl_2F_4O_3S$): 339.9351 ($[M]^+$) Found: 339.9348

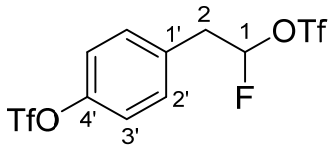
(2h) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(2,4-dichlorophenyl)ethane



Prepared according to General Procedure using 2,4-dichlorostyrene (**1h**) (0.0345 g, 0.199 mmol), **AD** (0.176 g, 0.304 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.103 g, 0.313 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (39%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0195 g, 29%).

IR: (neat) 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.46 (d, J = 2.1 Hz, 1H, 3'-H), 7.27 (dd, J = 8.4, 2.1 Hz, 1H, 5'-H), 7.23 (d, J = 8.4 Hz, 1H, 6'-H), 6.31 (t, J = 5.4 Hz, d, $^2J_{HF}$ = 53.9 Hz, 1H, 1-H), 3.50-3.32 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 135.3 (s, d, $^3J_{CF}$ = 4.9 Hz, C-1'), 133.2 (d), 129.9 (d, C-3'), 127.9 (d), 127.8 (s), 127.7 (s), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 110.0 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 37.7 (t, d, $^2J_{CF}$ = 22.1 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.0 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_6Cl_2F_4O_3S$): 339.9351 ($[M]^+$) Found: 339.9359

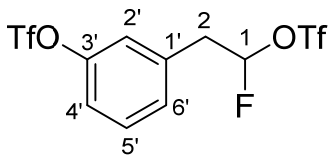
(2i) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{4-(trifluoromethanesulfonyloxy)phenyl}ethane



Prepared according to General Procedure using 4-vinylphenyl trifluoromethanesulfonate (**1i**) (0.0492 g, 0.195 mmol), **AD** (0.178 g, 0.307 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.107 g, 0.325 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (51%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0274 g, 33%).

IR: (neat) 1250, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.36 (d, J = 8.7 Hz, 2H, 2'-H), 7.30 (d, J = 8.7 Hz, 2H, 3'-H), 6.24 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 53.9 Hz, 1H, 1-H), 3.40-3.25 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 149.5 (s, C-4'), 131.9 (d, C-2'), 131.6 (s, d, J = 5.7 Hz, C-1'), 122.1 (d, C-3'), 118.8 (s, q, $^1J_{CF}$ = 321.2 Hz, CF_3), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 110.9 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 39.7 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -72.8 (3F, CF_3), -75.0 (3F, CF_3), -118.1--118.4 (1F, 1-F); HRMS (DART+) Calculated ($C_{10}H_{11}NO_6F_7S_2$) 437.99105 ($[M + NH_4]^+$) Found: 437.99103

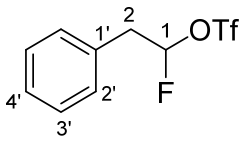
(2j) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{3-(trifluoromethanesulfonyloxy)phenyl}ethane



Prepared according to a General Procedure using 3-vinylphenyl trifluoromethanesulfonate (**1j**) (0.0490 g, 0.194 mmol), **AD** (0.170 g, 0.304 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.105 g, 0.319 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (33%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0304 g, 33%).

IR: (neat) 1250, 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.48 (t, J = 8.0 Hz, 1H, 5'-H), 7.32-7.27 (m, 2H, 4'-H and 6'-H), 7.20 (s, 1H, 2'-H), 6.26 (t, J = 4.9 Hz, d, $^2J_{HF}$ = 53.8 Hz, 1H, 1-H), 3.41-3.26 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 149.9 (s, C-3'), 133.7 (s, d, $^3J_{CF}$ = 5.9 Hz, C-1'), 131.0 (d, C-5'), 130.1 (d), 123.0 (d, C-2'), 121.4 (d), 118.9 (s, q, $^1J_{CF}$ = 321 Hz, CF_3), 118.3 (s, q, $^1J_{CF}$ = 321 Hz, CF_3), 110.6 (d, d, $^1J_{CF}$ = 247.3 Hz, C-1), 39.9 (t, d, $^2J_{CF}$ = 21.9 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -72.9 (3F, CF_3), -74.9 (3F, CF_3), -118.4--118.6 (1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{10}H_7F_7O_6S_2$): 419.9572 ($[M]^+$) Found: 419.9574

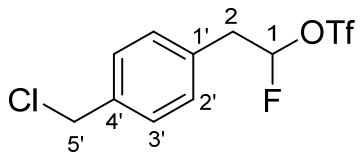
(2k) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-phenylethane



Prepared according to General Procedure using styrene (**1k**) (0.0201 g, 0.193 mmol), **AD** (0.176 g, 0.305 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.103 g, 0.311 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (43%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless oil (0.0152 g, 29%). The spectra of the product were good accordance with reported data.[14]

^1H NMR (400 MHz, $CDCl_3$): 7.40-7.33 (m, 3H), 7.25 (d, J = 7.8 Hz, 2H), 6.23 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.36-3.20 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 131.0 (d, $^3J_{CF}$ = 5.7 Hz, C-1'), 129.9, 129.1, 128.3, 118.3 (q, $^1J_{CF}$ = 320 Hz, CF_3), 111.9 (d, $^1J_{CF}$ = 247 Hz, C-1), 40.5 (d, $^2J_{CF}$ = 20.5 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -75.0 (3F, CF_3), -117.4--117.7 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_8O_3F_4S$): 272.0130 ($[M]^+$) Found: 272.0129

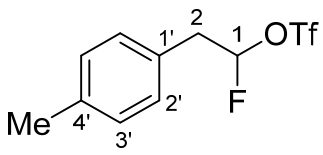
(2l) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{4-(chloromethyl)phenyl}ethane



Prepared according to General Procedure using 4-vinylbenzylchloride (**1l**) (0.0305 g, 0.200 mmol), **AD** (0.180 g, 0.310 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.102 g, 0.310 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (39%). In the procedure using **AD**, however, the compound **2l** was not able to be separated from 2'-iodo-5'-nitro-2,4-bis(trifluoromethyl)-1,1'-biphenyl, which was a by-product ArI from **AD**, by flash silica gel column chromatography and recycle GPC. Therefore, the characterization data were obtained from compound **2l** prepared from the reaction using $ArI(OAc)_2$ **Z**. To a two-necked flask with a stirring bar was added **Z** (0.170 g, 0.307 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, **1l** (0.0307 g, 0.201 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0179 g, 28%).

IR: (neat) 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.40 (d, J = 7.8 Hz, 2H, 3'-H), 7.25 (d, J = 7.8 Hz, 2H, 2'-H), 6.23 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 54.0 Hz, 1H, 1-H), 4.59 (s, 2H, 5'-H_2), 3.36-3.20 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 137.7 (s, C-4'), 131.2 (s, d, $^3J_{CF}$ = 6.0 Hz, C-1'), 130.3 (d, C-2'), 129.3 (d, C-3'), 118.3 (s, q, $^1J_{CF}$ = 319.8 Hz, CF_3), 111.6 (d, d, $^1J_{CF}$ = 247.7 Hz, C-1), 45.8 (t, C-5'), 40.1 (t, d, $^2J_{CF}$ = 20.5 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.1 (m, 1F, 1-F); HRMS (DART+) Calculated ($C_{10}H_9F_4O_3S$): 285.02030 ($[M - Cl]^+$) Found: 285.02122

(2m) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-methylphenyl)ethane



<u>The conditions with **AD**</u>

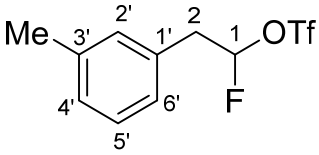
Prepared according to General Procedure using 4-methylstyrene (**1m**) (0.0236 g, 0.200 mmol), **AD** (0.178 g, 0.307 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.105 g, 0.318 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (29%).

<u>The conditions with **Z**</u>

To a two-necked flask with a stirring bar was added **Z** (0.174 g, 0.314 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, 4-methylstyrene (**1m**) (0.0228 g, 0.193 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (30%).

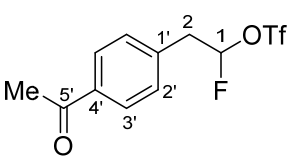
The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0065 g, 12%).
IR: (neat) 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.17 (d, J = 8.2 Hz, 2H, 2'-H), 7.13 (d, J = 8.2 Hz, 2H, 3'-H), 6.20 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.36-3.15 (m, 2H, 2-H_2), 2.35 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): 138.1 (s, C-4'), 129.80 (d), 129.76 (d), 127.9 (s, d, $^3J_{CF}$ = 5.7 Hz, C-1'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 112.1 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 40.1 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2), 21.2 (q, Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -75.0 (3F, CF_3), -117.6--117.9 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{10}H_{10}F_4O_3S$): 286.0287 ($[M]^+$) Found: 286.0285

(2n) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(3-methylphenyl)ethane



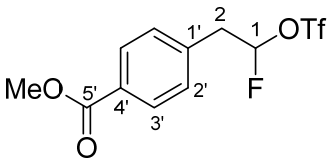
Prepared according to General Procedure using 3-methylstyrene (**1n**) (0.0237 g, 0.201 mmol), **AD** (0.174 g, 0.300 mmol), TfOH (26.3 μL, 0.310 mmol), Bu_4NBF_4 (0.103 g, 0.313 mmol) and $CHCl_3$ (2 mL). (The reaction time was 5 min.) The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (39%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 9:1) to afford the product as a colorless liquid (0.0142 g, 25%).
IR: (neat) 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.25 (t, J = 7.6 Hz, 1H, 5'-H), 7.14 (d, J = 7.3 Hz, 1H, 4'-H), 7.05-7.03 (m, 2H, 2'-H and 6'-H), 6.21 (t, J = 5.4 Hz, d, $^2J_{HF}$ = 54.2 Hz, 1H, 1-H), 3.32-3.15 (m, 2H, 2-H_2), 2.35 (s, 3H, 5-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 138.9 (s, C-3'), 130.9 (s, d, $^3J_{CF}$ = 6.0 Hz, C-1'), 130.6 (d, C-2'), 129.0 (d, C-5'), 129.0 (d, C-4'), 126.9 (d, C-6'), 118.3 (s, q, $^1J_{CF}$ = 319 Hz, CF_3), 112.1 (d, d, $^1J_{CF}$ = 249 Hz, C-1), 40.4 (t, d, $^2J_{CF}$ = 21.1 Hz, C-2), 21.4 (q, Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -75.1 (3F, CF_3), -117.2--117.5 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{10}H_{10}F_4O_3S$): 286.0287 ($[M]^+$) Found: 286.0280

(2o) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-(4-acetylphenyl)ethane



Prepared according to General Procedure using 1-(4-vinylphenyl)ethan-1-one (**1o**) (0.0298 g, 0.204 mmol), **AD** (0.176 g, 0.304 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.103 g, 0.313 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (43%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless oil (0.0260 g, 41%).
IR: (neat) 1685 (C=O), 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.97 (d, J = 8.2 Hz, 2H, 3'-H), 7.37 (d, J = 8.2 Hz, 2H, 2'-H), 6.27 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.43-3.27 (m, 2H, 2-H_2), 2.62 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): 197.6 (s, C-5'), 137.0 (s, C-4'), 136.1 (s, d, $^3J_{CF}$ = 5.7 Hz, C-1'), 130.3 (d, C-2'), 129.1 (d, C-3'), 118.3 (s, q, $^1J_{CF}$ = 321 Hz, CF_3), 111.1 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 40.3 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2), 26.8 (q, Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.8--118.1 (1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{11}H_{10}F_4O_4S$): 314.0236 ($[M]^+$) Found: 314.0233

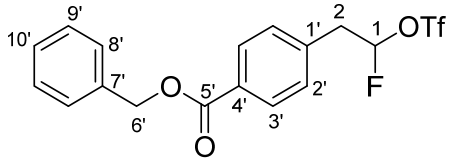
(2p) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{4-(methoxycarbonyl)phenyl}ethane



Prepared according to General Procedure using methyl 4-vinylbenzoate (**1p**) (0.0349 g, 0.215 mmol), **AD** (0.178 g, 0.306 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.101 g, 0.306 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (48%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0270 g, 38%).
IR: (neat) 1722 (C=O), 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.04 (d, J = 8.3 Hz, 2H, 3'-H), 7.34 (d, J = 8.3 Hz, 2H, 2'-H), 6.26 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 53.8 Hz, 1H, 1-H), 3.93 (s, 3H, OMe), 3.42-3.26 (m, 2H, 2-

H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 166.7 (s, C-5'), 135.9 (s, d, $^3J_{CF}$ = 5.9 Hz, C-1'), 130.3 (d, C-3'), 130.2 (s, C-4'), 130.0 (d, C-2'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.2 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 52.4 (q, OMe), 40.3 (t, d, $^2J_{CF}$ = 21.1 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.8 (3F, CF_3), -117.4--117.7 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{11}H_{10}F_4O_5S$): 330.0185 ($[M]^+$) Found: 330.0179

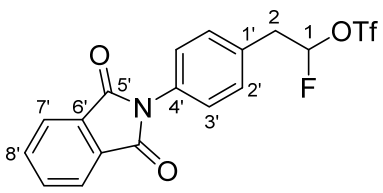
(2q) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{4-(benzyloxycarbonyl)phenyl}ethane



Prepared according to General Procedure using benzyl 4-vinylbenzoate (**1q**) (0.0470 g, 0.197 mmol), **AD** (0.173 g, 0.299 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.105 g, 0.319 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (45%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) and recycle HPLC (hexane/EtOAc = 8:2) to afford the product as a colorless oil (0.0105 g, 13%).

IR: (neat) 1718 (C=O), 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.08 (d, J = 8.2 Hz, 2H, 3'-H), 7.45 (d, J = 7.2 Hz, 2H, 8'-H), 7.42-7.36 (m, 3H, 9'-H and 10'-H), 7.33 (d, J = 8.2 Hz, 2H, 2'-H), 6.26 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 5.37 (s, 2H, 6'-H_2), 3.41-3.26 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 166.0 (s, C-5'), 136.1 (s, d, $^3J_{CF}$ = 5.7 Hz, C-1'), 136.0 (s, C-7'), 130.5 (d, C-3'), 130.2 (s, C-4'), 130.1 (d, C-2'), 128.8 (d), 128.5 (d), 128.4 (d, C-8'), 118.3 (s, q, $^1J_{CF}$ = 319 Hz, CF_3), 111.1 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 67.1 (t, C-6'), 40.3 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$ external standard: TFA in D_2O): -74.9 (3F, CF_3), -117.7--118.0 (1F, 1-F); HRMS (ESI+) Calculated ($C_{17}H_{14}O_5F_4SNa$) 429.03903 ($[M + Na]^+$) Found: 429.03732

(2r) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-{4-(1,3-dioxoisoindolin-2-yl)phenyl}ethane



<u>The conditions with **AD**</u>

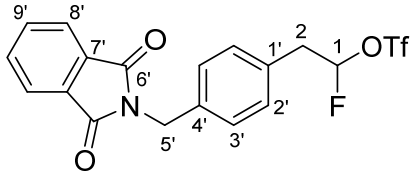
Prepared according to General Procedure using 2-(4-vinylphenyl)isoindoline-1,3-dione (**1r**) (0.0500 g, 0.201 mmol), **AD** (0.179 g, 0.310 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.102 g, 0.311 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (35%).

<u>The conditions with **Z**</u>

To a two-necked flask with a stirring bar was added **Z** (0.172 g, 0.310 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, 2-(4-vinylphenyl)isoindoline-1,3-dione (**1r**) (0.0494 g, 0.198 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (38%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a yellow solid (0.0242 g, 29%).

mp: 86-89 ºC; IR: (KBr) 1717 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): 7.96 (dd, J = 5.3, 2.9 Hz, 2H, 7'-H), 7.81 (dd, J = 5.3, 2.9 Hz, 2H, 8'-H), 7.49 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H), 6.28 (t, J = 5.1 Hz, d, $^2J_{HF}$ = 54.1 Hz, 1H, 1-H), 3.42-3.26 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 167.2 (s, C-5'), 134.7 (d, C-8'), 131.82 (s), 131.76 (s), 130.8 (s, d, $^3J_{CF}$ = 4.9 Hz, C-1'), 130.7 (d), 127.0 (d), 124.0 (d, C-7'), 118.3 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.4 (d, d, $^1J_{CF}$ = 248 Hz, C-1), 40.1 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.9 (3F, CF_3), -118.1 - -118.3 (1F, 1-F); HRMS (DART+) Calculated ($C_{17}H_{12}NO_5F_4S$): 418.03668 ($[M + H]^+$) Found: 418.03557

(2s) 1-fluoro-1-(trifluoromethanesulfonyloxy)-2-[4-{(1,3-dioxoisoindolin-2-yl)methyl}phenyl]ethane



The conditions with **AD**

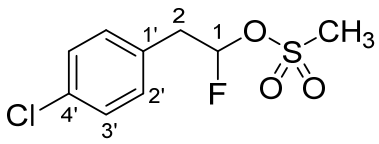
Prepared according to General Procedure using 2-(4-vinylbenzyl)isoindoline-1,3-dione (**1s**) (0.0540 g, 0.205 mmol), **AD** (0.165 g, 0.300 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.102 g, 0.309 mmol) and $CHCl_3$ (2 mL). The crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (43%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a yellow solid (0.0371 g, 42%).

The conditions with **Z**

To a two-necked flask with a stirring bar was added **Z** (0.165 g, 0.299 mmol) and $CHCl_3$ (2 mL). TfOH (26.3 μL, 0.300 mmol) was added to the mixture. Then, 2-(4-vinylphenyl)isoindoline-1,3-dione (**1s**) (0.0535 g, 0.203 mmol) was added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq and extracted with ether. The combined organic layers were dried over Na_2SO_4. After removing of volatiles under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (38%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a yellow solid (0.0300 g, 34%).

mp: 79-80 ºC; IR: (KBr) 1719 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): 7.85 (dd, J = 5.5, 2.9 Hz, 2H, 8'-H), 7.71 (dd, J = 5.5, 2.9 Hz, 2H, 9'-H), 7.43 (d, J = 8.1 Hz, 2H, 2'-H), 7.20 (d, J = 8.1 Hz, 2H, 3'-H), 6.19 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 54.2 Hz, 1H, 1-H), 4.84 (s, 2H, 5'-H_2), 3.32-3.16 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 168.1 (s, C-6'), 136.5 (s, C-4'), 134.2 (d, C-9'), 132.2 (s, C-7'), 130.6 (s, d, $^3J_{CF}$ = 5.7 Hz, C-1'), 130.3 (d, C-3'), 129.4 (d, C-2'), 123.5 (d, C-8'), 118.2 (s, q, $^1J_{CF}$ = 320 Hz, CF_3), 111.7 (d, d, $^1J_{CF}$ = 247 Hz, C-1), 41.3 (t, C-5'), 40.1 (t, d, $^2J_{CF}$ = 21.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -75.0 (3F, CF_3), -117.9--118.2 (1F, 1-F); HRMS (DART+) Calculated ($C_{18}H_{17}N_2O_5F_4S$): 449.07888 ($[M + NH_4]^+$) Found: 449.08013

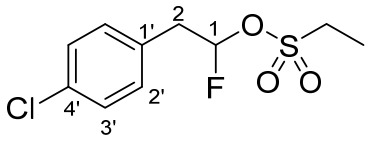
(2aa) 1-fluoro-1-(methanesulfonyloxy)-2-(4-chlorophenyl)ethane



To a two-necked flask with a stirring bar was added **AD** (0.178 g, 0.307 mmol), Bu_4NBF_4 (0.100 g, 0.304 mmol), $CHCl_3$ (2 mL) and 4-chlorostyrene (**1a**) (0.0265 g, 0.191 mmol). $MeSO_3H$ (0.0575 g, 0.598 mmol) was slowly added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq. and extracted with ether. The combined organic layers were dried over Na_2SO_4. After solvent was removed under reduced pressure, the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (54%). The crude was purified by column chromatography on silica gel (hexane/EtOAc = 5:5) to afford the product as a white solid (0.0225 g, 47%).

mp: 38-39 ºC; IR: (KBr) 1366, 1179, 975, 859, 800, 521 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.32 (d, J = 8.4 Hz, 2H, 3'-H), 7.19 (d, J = 8.4 Hz, 2H, 2'-H), 6.18 (t, J = 5.0 Hz, d, $^2J_{HF}$ = 57.6 Hz, 1H, 1-H), 3.19 (d, J = 5.0 Hz, 1H, 2-H), 3.15 (dd, J = 5.0, 2.0 Hz, 1H, 2-H), 3.07 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): 133.9 (s, C-4'), 131.4 (d, C-2'), 130.7 (s, d, $^3J_{CF}$ = 5.1 Hz, C-1'), 129.1 (d, C-3'), 108.4 (d, d, $^1J_{CF}$ = 234 Hz, C-1), 40.4 (q, d, $^4J_{CF}$ = 1.7 Hz, CH_3), 39.7 (t, d, $^2J_{CF}$ = 21.9 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -124.3--124.5 (m, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_9H_{10}ClFO_3S$): 252.0023 ($[M]^+$) Found: 252.0020

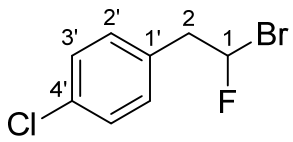
(2ab) 1-fluoro-1-(ethanesulfonyloxy)-2-(4-chlorophenyl)ethane



To a two-necked flask with a stirring bar was added **AD** (0.176 g, 0.304 mmol), Bu_4NBF_4 (0.105 g, 0.318 mmol), $CHCl_3$ (2 mL) and 4-chlorostyrene (**1a**) (0.0285 g, 0.206 mmol). $EtSO_3H$ (0.0653 g, 0.593 mmol) was slowly added to the mixture. After stirring for 1 h at room temperature, the reaction was quenched with Na_2SO_3 aq. and extracted with ether. The combined organic layers were dried over Na_2SO_4. After solvent was removed under reduced pressure, the crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (56%). The crude was purified by column chromatography on silica gel (hexane/EtOAc = 7:3) to afford the product as a white solid (0.0303 g, 55%).

IR: (neat) 1436 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.32 (d, J = 8.3 Hz, 2H, 3'-H), 7.19 (d, J = 8.3 Hz, 2H, 2'-H), 6.16 (t, J = 5.0 Hz, d, $^2J_{HF}$ = 57.2 Hz, 1H, 1-H), 3.20-3.13 (m, 4H, 2-H_2 and CH_2CH$_3$) 1.38 (t, J = 7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): 133.8 (s, C-4'), 131.3 (d, C-2'), 130.8 (s, d, $^3J_{CF}$ = 5.1 Hz, C-1'), 129.0 (d, C-3'), 108.0 (d, d, $^1J_{CF}$ = 234 Hz, C-1), 47.9 (t, CH$_2$CH$_3$), 39.8 (t, d, $^2J_{CF}$ = 21.9 Hz, C-2), 8.0 (q, CH$_2$$CH_3$); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): –123.7 (dt, J = 58.0, 15.3 Hz, 1F, 3-F); HRMS (EI+, 70 eV) Calculated ($C_{10}H_{12}ClFO_3S$): 266.0180 ([M]$^+$) Found: 266.0187

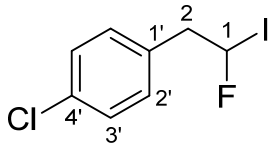
(2ac) 1-bromo-1-fluoro-2-(4-chlorophenyl)ethane



Prepared according to General Procedure using 4-chlorostyrene (**1a**) (0.0282 g, 0.203 mmol), **AD** (0.175 g, 0.302 mmol), TfOH (26.3 µL, 0.300 mmol), Bu_4NBF_4 (0.103 g, 0.312 mmol), $CHCl_3$ (2 mL). After 1 h, Bu_4NBr (0.193 g, 0.598 mmol) was added to the reaction mixture. The crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (46%). The crude mixture was purified by chromatography on silica gel (hexane) to afford the product as a colorless liquid (0.0186 g, 38%).

IR: (neat) 1494, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.32 (d, J = 8.3 Hz, 2H, 3'-H), 7.20 (d, J = 8.3 Hz, 2H, 2'-H), 6.53 (dd, J = 6.5, 4.5 Hz, d, $^2J_{HF}$ = 50.0 Hz, 1H, 1-H), 3.57-3.37 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 133.8 (s, C-4'), 132.9 (s, d, $^3J_{CF}$ = 4.0 Hz, C-1'), 131.2 (d, C-2'), 129.0 (d, C-3'), 94.0 (d, d, $^1J_{CF}$ = 255 Hz, C-1), 46.4 (t, d, $^2J_{CF}$ = 20.1 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard:TFA in D_2O): -132.2 (ddd, J = 50.0, 22.8, 17.3 Hz, 1F, 1-F); HRMS (EI+, 70 eV) Calculated (C_8H_7BrClF): 235.9404 ([M]$^+$) Found: 235.9405

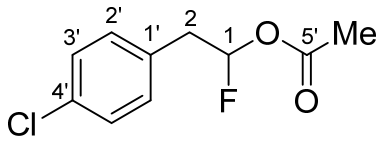
(2ad) 1-fluoro-1-iodo-2-(4-chlorophenyl)ethane



Prepared according to General Procedure using 4-chlorostyrene (**1a**) (0.0280 g, 0.202 mmol), **AD** (0.178 g, 0.307 mmol), TfOH (26.3 µL, 0.300 mmol), Bu_4NBF_4 (0.105 g, 0.319 mmol), and $CHCl_3$ (2 mL). After 1 h, Bu_4NI (0.231 g, 0.625 mmol) was added and the reaction mixture. The crude yield was confirmed by ^{1}H NMR using $CHBr_3$ as an internal standard (43%). The crude mixture was purified by chromatography on silica gel (hexane) and recycle HPLC (hexane) to afford the product as a white solid (0.0101 g, 18%).

mp: <30 ºC; IR: (KBr) 1490, 1154, 1092, 1065, 988, 731, 673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.31 (d, J = 8.4 Hz, 2H, 3'-H), 7.18 (d, J = 8.4 Hz, 2H, 2'-H), 6.87 (dd, J = 6.6, 4.8 Hz, d, $^2J_{HF}$ = 49.4 Hz, 1H, 1-H), 3.64-3.45 (m, 2H, 2-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): 134.3 (s, d, $^3J_{CF}$ = 3.4 Hz, C-1'), 133.7 (s, C-4'), 131.0 (d, C-2'), 129.0 (d, C-3'), 73.3 (d, d, $^1J_{CF}$ = 256 Hz, C-1), 49.0 (t, d, $^2J_{CF}$ = 20.3 Hz, C-2); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -138.1--138.3 (1F, 1-F); HRMS (EI+, 70 eV) Calculated (C_8H_7ClFI): 283.9270 ([M]$^+$) Found: 283.9263

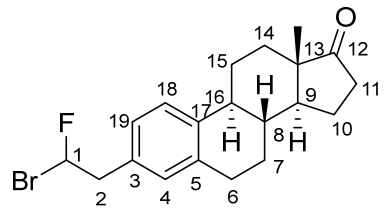
(2ae) 1-acetoxy-1-fluoro-2-(4-chlorophenyl)ethane



Prepared according to General Procedure using 4-chlorostyrene (**1a**) (0.0287 g, 0.207 mmol), **AD** (0.179 g, 0.309 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.102 g, 0.308 mmol) and $CHCl_3$ (2 mL). After 1 h, AcOH (50.0 μL, 0.800 mmol) and NEt_3 (112 μL, 0.800 mmol) were added to the reaction mixture. After 18 h, the reaction was quenched and the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (43%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) to afford the product as a colorless liquid (0.0180 g, 40%).

IR: (neat) 1771 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.30 (d, J = 8.4 Hz, 2H, 3'-H), 7.18 (d, J = 8.4 Hz, 2H, 2'-H), 6.43 (t, J = 5.3 Hz, d, $^2J_{HF}$ = 55.7 Hz, 1H, 1-H), 3.16-3.00 (m, 2H, 2-H_2), 2.11 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): 169.0 (s, C-5'), 133.4 (s, C-4'), 132.1 (s, d, $^3J_{CF}$ = 6.0 Hz, C-1'), 131.2 (d, C-2'), 128.9 (d, C-3'), 102.5 (d, d, $^1J_{CF}$ = 224 Hz, C-1), 39.3 (t, d, $^2J_{CF}$ = 24.2 Hz, C-2), 20.9 (q, Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard:TFA in D_2O): -128.0 (dt, J = 55.7, 17.5 Hz, 1F, 1-F); HRMS (EI+, 70 eV) Calculated ($C_{10}H_{10}ClFO_2$): 216.0353 ($[M]^+$) Found: 216.0351

(2t) (8*R*,9*S*,13*S*,14*S*)-3-(2-bromo-2-fluoroethyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[*a*]phenanthren-17-one

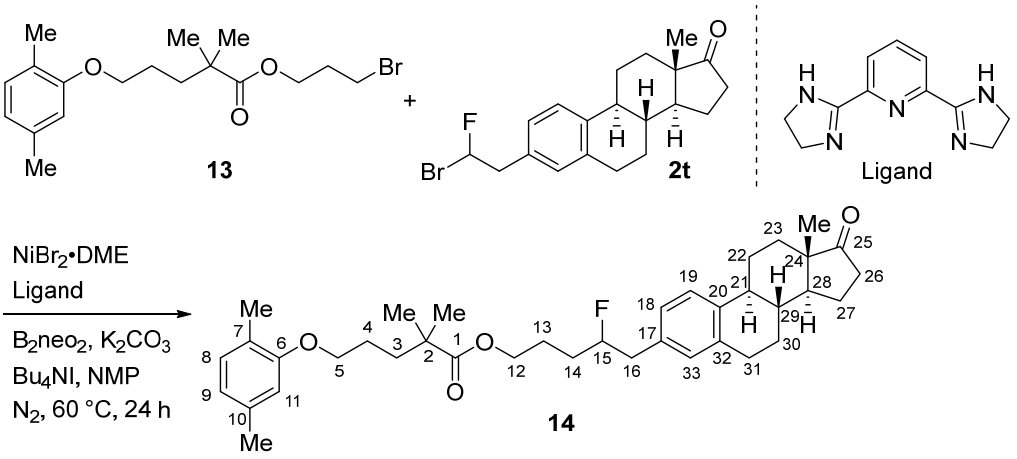


Prepared according to General Procedure using 3-vinylestrone (**1t**) (0.0556 g, 0.201 mmol), **AD** (0.167 g, 0.300 mmol), TfOH (26.3 μL, 0.300 mmol), Bu_4NBF_4 (0.106 g, 0.320 mmol) and $CHCl_3$ (2 mL) at RT. After 1 h, Bu_4NBr (0.194 g, 0.601 mmol) was added to the reaction mixture. After 1 h, the reaction was quenched and the crude yield was confirmed by ^1H NMR using $CHBr_3$ as an internal standard (34%). The crude mixture was purified by chromatography on silica gel (hexane/EtOAc = 8:2) and recycle HPLC (hexane/EtOAc = 8:2) to afford the product as a white solid (0.0212 g, 28%).

mp: 62-64 ºC; IR: (KBr) 2928 (C-H), 1737 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.27 (d, J = 8.0 Hz, 1H, 19-H), 7.04 (d, J = 8.0 Hz, 1H, 18-H), 6.99 (s, 1H, 4-H), 6.54 (dd, J = 6.9, 4.5 Hz, d, $^2J_{HF}$ = 50.3 Hz, 1H, 1-H), 3.56-3.33 (m, 2H, 2-H_2), 2.92 (dd, J = 8.9, 4.1 Hz, 2H, 6-H_2), 2.51 (dd, J = 19.1, 8.5 Hz, 1H), 2.45-2.40 (m, 1H), 2.33-2.26 (m, 1H), 2.20-1.95 (m, 4H), 1.69-1.40 (m, 6H), 0.91 (s, 3H, 13-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 221.0 (s, C-12), 139.3 (s, C-5), 137.0 (s, C-17), 132.1 (s, d, $^3J_{CF}$ = 3.3 Hz, C-3), 130.4 (d, d, $^4J_{CF}$ = 2.5 Hz, C-4), 127.1 (d, C-18), 125.9 (d, C-19), 94.6 (d, d, $^1J_{CF}$ = 254 Hz, C-1), 50.6 (d, C-9), 48.1 (s, C-13), 46.9 (t, d, $^2J_{CF}$ = 19.7 Hz, C-2), 44.4 (d, C-7), 38.2 (d, C-8), 36.0 (t), 31.7 (t, C-14), 29.5 (t, C-6), 26.6 (t), 25.8 (t), 21.7 (t), 14.0 (q, 13-Me); ^{19}F NMR (377 MHz, $CDCl_3$, external standard: TFA in D_2O): -131.2--131.5 (m, 1-F); HRMS (DART+) Calculated ($C_{20}H_{25}OFBr$): 379.10673 ($[M + H]^+$) Found: 379.10538

Reductive coupling reaction of C(sp^3)-F/C(sp^3)-F (Scheme 2.3)

(14) 4-fluoro-5-{(8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[*a*]phenanthren-3-yl}pentyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate



The gemfibrozil derivative (**13**) and ligand were synthesized according to the reference[22a]. The reported procedure was slightly modified[27]. In a glove box, $NiBr_2$•DME (3.7 mg, 0.012 mmol), ligand (2.6 mg, 0.012 mmol), B_2neo_2 (0.0444 g, 0.197 mmol), K_2CO_3 (0.0385 g, 0.279 mmol), Bu_4NI (0.0736 g, 0.199 mmol), compound **2t** (0.0370 g, 0.0975 mmol), **13** (0.0595 g, 0.160 mmol) and NMP (0.6 mL) were added to a 10 mL vessel with a stirring bar and the vessel was sealed. The vessel was warmed at 60 ºC and the reaction mixture was stirred for 24 h. The reaction mixture was allowed to room temperature and extracted with EtOAc, washed with brine and dried over Na_2SO_4. The volatiles were removed under reduced pressure and the crude mixture was purified by silica gel column chromatography and recycle HPLC to give the product as a colorless oil (0.0209 g, 36%).

IR: (neat) 2926 (C-H), 1737 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.21 (d, J = 8.1 Hz, 1H, 19-H), 7.00-6.97 (m, 2H, 8-H and 18-H), 6.94 (s, 1H, 33-H), 6.65 (d, J = 7.7 Hz, 1H, 9-H), 6.60 (s, 1H, 11-H), 4.77-4.59 (m, 1H, 15-H), 4.08 (t, J = 6.0 Hz, 2H, 12-H), 3.90 (t, J = 5.1 Hz, 2H, 5-H), 2.96-2.73 (m, 4H), 2.50 (dd, J = 18.9, 8.6 Hz, 1H), 2.43-2.38 (m, 1H), 2.35-2.24 (m, 4H), 2.19-1.80 (m, 8H), 1.78-1.40 (m, 13H), 1.19 (s, 6H, 2-Me x 2), 0.90 (s, 3H, 24-Me); ^{13}C NMR (100 MHz, $CDCl_3$): 221.2 (s, C-25), 177.9 (s, C-1), 157.0 (s, C-6), 138.2 (s), 136.7 (s), 136.6 (s), 134.6 (s, d, $^3J_{CF}$ = 5.0 Hz, C-17), 130.4 (d), 130.1 (d, C-33), 126.9 (d), 125.6 (d), 123.6 (s, C-7), 120.8 (d, C-9), 112.0 (d, C-11), 94.2 (d, d, $^1J_{CF}$ = 171 Hz, C-15), 68.0 (t, C-5), 64.1 (t, C-12), 50.6 (d, C-28), 48.1 (s, C-24), 44.4 (d), 42.2 (s), 41.2 (t, d, $^2J_{CF}$ = 22.2 Hz, C-16), 38.2 (d), 37.2 (t), 36.0 (t), 31.7 (t), 31.3 (t, d, $^2J_{CF}$ = 21.1 Hz, C-14), 29.5 (t), 26.6 (t), 25.8 (t), 25.3 (q, 2-Me x 2), 25.3 (t), 24.6 (t, d, $^3J_{CF}$ = 3.0 Hz, C-13), 21.7 (t), 21.6 (q, 10-Me), 15.9 (q, 7-Me), 14.0 (q, 24-Me); ^{19}F NMR (377 MHz, $CDCl_3$, TFA in D_2O as an external standard): -179.2- -179.6 (m, 1F, 15-F); HRMS (ESI+) Calculated ($C_{38}H_{51}O_4FNa$) 613.36636 ([M + Na]$^+$) Found: 613.36431

2-5. Reference

[1] a) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981; b) S. E. Denmark, W. E. Kuester, M. T. Burk, *Angew. Chem. Int. Ed.* **2012**, *51*, 10938; c) S. Wu, Y. Zhou, Z. Li, *Chem. Commun.* **2019**, *55*, 883.

[2] a) G. Yin, X. Mu, G. Liu, *Acc. Chem. Res.* **2016**, *49*, 2413; b) X.-W. Lan, N.-X. Wang, Y. Xing, *Eur. J. Org. Chem.* **2017**, 5821; c) X. Yang, S. J. Kalita, S. Maheshuni, Y.-Y. Huang, *Coord. Chem. Rev.* **2019**, *392*, 35; d) X. Bao, J. Li, W. Jiang, C. Huo, *Synthesis* **2019**, *51*, 4507; e) Z.-L. Li, G.-C. Fang, Q.-S. Gu, X.-Y. Liu, *Chem. Soc. Rev.* **2020**, *49*, 32.

[3] Recent reports for 1,1-heterodifunctionalization with carbon electrophiles; a) Y. Li, Y. Li, H. Shi, H. Wei, H. Li, I. Funes-Ardoiz, G. Yin, *Science* **2022**, *376*, 749; b) Y. Ano, N. Kawai, N. Chatani, *Chem. Sci.* **2021**, *12*, 12326; c) W. Wang, C. Ding, G. Yin, *Nat. Catal.* **2020**, *3*, 951; d) Y. Li, H. Wei, D. Wu,

Z. Li, W. Wang, G. Yin, *ACS Catal.* **2020**, *10*, 4888; reviews; e) Y. Li, D. Wu, H.-G. Cheng, G. Yin, *Angew. Chem. Int. Ed.* **2020**, *59*, 7990; f) S. Yang, Y. Chen, Z. Ding, *Org. Biomol. Chem.* **2020**, *18*, 6983.

[4] L. D. Elliott, J. W. Wrigglesworth, B. Cox, G. C. Lloyd-Jones, K. I. Booker-Milburn, *Org. Lett.* **2011**, *13*, 728.

[5] P. V. Balaji, S. Chandrasekaran, *Chem. Commun.* **2014**, *50*, 70.

[6] a) P. V. Balaji, S. Chandrasekaran, *Tetrahedron* **2016**, *72*, 1095; b) S. Yang, Y. Chen, Z. Yuan, F. Bu, C. Jiang, Z. Ding, *Org. Biomol. Chem.* **2020**, *18*, 9873.

[7] a) *Iodine Catalysis in Organic Synthesis* (Eds.: K. Ishihara, K. Muñiz), Wiley-VCH, Weinheim, **2022** b) *PATAI's Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds* (Eds.: B. Olofsson, I. Marek, Z. Rappoport) Wiley-Blackwell, **2019**; c) A. Yoshimura, V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328; d) T. Wirth, *Hypervalent Iodine Chemistry (Topics in Current Chemistry, 373)*, Springer, **2016**; e) N. Chatterjee, A. Goswami, *Eur. J. Org. Chem.* **2017**, 3023.

[8] R. M. Romero, T. H. Wöste, K. Muñiz, *Chem. Asian. J.* **2014**, *9*, 972.

[9] Examples of 1,2-homodifunctionalization: a) F. Scheidt, M. Schäfer, J. C. Sarie, C. G. Daniliuc, J. J. Molloy, R. Gilmour, *Angew. Chem. Int. Ed.* **2018**, *57*, 16431; b) J. C. Sarie, J. Neufeld, C. G. Daniliuc, R. Gilmour, *ACS Catal.* **2019**, *9*, 7232; c) S. Meyer, J. Häfliger, M. Schäfer, J. J. Molloy, C. G. Daniliuc, R. Gilmour, *Angew. Chem. Int. Ed.* **2021**, *60*, 6430.

[10] Recent reports for 1,1-homodifunctionalization: a) S. M. Banik, J. W. Medley, E. N. Jacobsen, *Science* **2016**, *353*, 51; b) F. Scheidt, J. Neufeld, M. Schäfer, C. Thiehoff, R. Gilmour, *Org. Lett.* **2018**, *20*, 8073; c) J. Häfliger, K. Livingstone, C. G. Daniliuc, R. Gilmour, *Chem. Sci.* **2021**, *12*, 6148.

[11] Recent reports for 1,2-heterodifunctionalization: a) C. Wata, T. Hashimoto, *J. Am. Chem. Soc.* **2021**, *143*, 1745; b) F. Wu, N. Kaur, N.-E. Alom, W. Li, *JACS Au* **2021**, *1*, 734; c) M. Schäfer, T. Stünkel, C. G. Daniliuc, R. Gilmour, *Angew. Chem. Int. Ed.* **2022**, *61*, e202205508.

[12] Y. Nishimoto, M. Fujie, J. Hara, M. Yasuda, *Org. Chem. Front.* **2021**, *8*, 3695.

[13] Reviews for fluorination using BF_4: a) A. J. Cresswell, S. G. Davies, P. M. Roberts, J. E. Thomson, *Chem. Rev.* **2015**, *115*, 566; b) Z.-Z. Han, C.-P. Zhang, *Adv. Synth. Catal.* **2020**, *362*, 4256.

[14] W. R. Dolbier Jr., M. Okamoto, *J. Fluorine Chem.* **2015**, *179*, 33.

[15] Pioneering example of substituent effects on I(III): R. M. Romero, J. A. Souto, K. Muñiz, *J. Org. Chem.* **2016**, *81*, 6118.

[16] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165.

[17] a) M. Uyanik, M. Akakura, K. Ishihara, *J. Am. Chem. Soc.* **2009**, *131*, 251; b) S. Ghosh, S. Pradhan, I. Chatterjee, *Beilstein J. Org. Chem.* **2018**, *14*, 1244; c) F. Berthiol, *Synthesis* **2015**, *47*, 587; d) A. Parra, *Chem. Rev.* **2019**, *119*, 12033.

[18] a) C. B. Santiago, A. Milo, M. S. Sigman, *J. Am. Chem. Soc.* **2016**, *138*, 13424; reviews; b) C. B. Santiago, J.-Y. Guo, M. S. Sigman, *Chem. Sci.* **2018**, *9*, 2398; c) J. M. Crawford, C. Kingston, F. D. Toste, M. S. Sigman, *Acc. Chem. Res.* **2021**, *54*, 3136.

[19] a) S. Izquierdo, S. Essafi, I. Rosal, P. Vidossich, R. Pleixats, A. Vallribera, G. Ujaque, A. Lledós, A. Shafir, *J. Am. Chem. Soc.* **2016**, *138*, 12747. b) Tania, S. D. Houston, L. Sharp-Bucknall, T. B. Poynder, M. Albayer, J. L. Dutton, *Chem. Eur. J.* **2020**, *26*, 15863.

[20] Y.-B. Kang, L. H. Gade, *J. Am. Chem. Soc.* **2011**, *133*, 3658.

[21] a) K. M. Lancer, G. H. Wiegand, *J. Org. Chem.* **1976**, *41*, 3360; b) J. Malmgren, S. Santoro, N. Jalalian, F. Himo, B. Olofsson, *Chem. Eur. J.* **2013**, *19*, 10334.

[22] Selected paper; a) J. Sheng, H.-Q. Ni, S.-X. Ni, Y. He, R. Cui, G.-X. Liao, K.-J. Bian, B.-B. Wu, X.-S. Wang, *Angew. Chem. Int. Ed.* **2021**, *60*, 15020; b) B.-B. Wu, J. Xu, Q. Gao, K.-J. Bian, G.-K. Liu, X.-S. Wang, *Angew. Chem. Int. Ed.* **2022**, e202208938; review; c) T. W. Butcher, W. M. Amberg, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2022**, *61*, e202112251.

[23] Pioneering work of direct synthesis of 1-bromo-1-fluoroalkanes: F. Chen, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2021**, *23*, 2364.

[24] a) M. Hasan, R. K. Leak, R. E. Stratford, D. P. Zlotos, P. A. Witt-Enderby, *Pharmacol. Res. Perspect.* **2018**, e00417; b) F. Wang, M. Li, C. Lin, S. Jin, H. Li, Y. Lu, H. Wang, H. Wang, X. Wang, *Bioorg. Med. Chem.* **2021**, *39*, 116131; c) Z. Fu, S. Li, S. Han, C. Shi, Y. Zhang, *Sig. Transduct. Target. Ther.* **2022**, *7*, 93.

[25] a) I. Ojima, *Fluorine in Medicinal Chemistry and Chemical Biology*, Wiley-Blackwell, Chichester, **2009**; b) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2013**, *52*, 8214; *Angew. Chem.* **2013**, *125*, 8372; c) D. O'Hagan, H. Deng, *Chem. Rev.* **2015**, *115*, 634.

[26] K. M. Gayler, J. M. Quintana, J. Mattke, M. A. Plunk, J. H. Kostyo, J. W. Karunananthan, H. Nguyen,

M. Shuda, L. D. Ferreira, H. Baker, A. L. Stinchcomb, I. Sharina, R. R. Kane, E. Martin, *Eur. J. Med. Chem.* **2021**, *224*, 113729.
[27] Y. Wu, S. Izquierdo, P. Vidossich, A. Lledós, A. Shafir, *Angew. Chem. Int. Ed.* **2016**, *55*, 7152.
[28] T. Baba, S. Takahashi, Y. Kambara, A. Yoshimura, V. N. Nemykin, V. V. Zhdankin, A. Saito, *Adv. Synth. Catal.* **2017**, *359*, 3860.
[29] Y. Minamitsuji, D. Kato, H. Fujioka, T. Dohi, Y. Kita, *Aust. J. Chem.* **2009**, *62*, 648.
[30] A. Watanabe, K. Miyamoto, T. Okada, T. Asawa, M. Uchiyama, *J. Org. Chem.* **2018**, *83*, 14262.
[31] M. Iinuma, K. Moriyama, H. Togo, *Synlett* **2012**, *23*, 2663.
[32] N. Miralles, R. M. Romero, E. Fernández, K. Muñiz, *Chem. Comm.* **2015**, *51*, 14068.
[33] J.-H. Chun, V. W. Pike, *J. Org. Chem.* **2012**, *77*, 1931.
[34] M. B. Haskali, S. Telu, Y.-S. Lee, C. L. Morse, S. Lu, V. W. Pike, *J. Org. Chem.***2016**, *81*, 297.
[35] H. Meng, L. Wen, Z. Xu, Y. Li, J. Hao, Y. Zhao, *Org. Lett.* **2019**, *21*, 5206.
[36] J. Cao, D. Lv, F. Yu, M.-F. Chiou, Y. Li, H. Bao, *Org. Lett.* **2021**, *23*, 3184-3189.
[37] S. Gülak, T. N. Gieshoff, A. J. von Wangelin, *Adv. Synth. Catal.* **2013**, *355*, 2197-2202.
[38] G. A. Molander, A. R. Brown, *J. Org. Chem.* **2006**, *71*, 9681-9686.
[39] G. G. Pawar, G. Singh, V. K. Tiwari, M. Kapur, *Adv. Synth. Catal.* **2013**, *355*, 2185-2190.
[40] A. Mori, Y. Miyakawa, E. Ohashi, T. Haga, T. Maegawa, H. Sajili, *Org. Lett.* **2006**, *8*, 3279.
[41] L. T. Ball, G. C. Lloyd-Jones, C. A. Russell, *Chem. Eur. J.* **2012**, *18*, 2931.
[42] W. J. Kerr, A. J. Morrison, M. Pazicky, T. Weber, *Org. Lett.* **2012**, *14*, 2250.
[43] J. Seayad, A. M. Seayad, C. L. L. Chai, *Org. Lett.* **2010**, *12*, 1412.
[44] W. R. Dolbier Jr., M. Okamoto, *J. Fluorine Chem.* **2014**, *167*, 96.
[45] Luchini, G.; Paton, R. S. DBSTEP: DFT Based Steric Parameters. 2022, DOI: 10.5281/zenodo.4702097
[46] Y. Kanda, *Bone Marrow Transplant* **2013**, *48*, 452.
[47] R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.
[48] N. O. Ilchenko, B. O. A. Tasch, K. J. Szabó, *Angew. Chem. Int. Ed.* **2014**, *53*, 12897.

Chapter 3: Sulfonyloxylation and Acetoxylation of Aryl C–H Proximal to λ^3-Iodanediyl Group on Biaryl Structures

3-1. Introduction

A biaryl structure is a ubiquitous motif in many fields such as natural product synthesis,[1] medicinal chemistry,[2] and ligand design.[3] Among C(sp^2)–H functionalizations,[4] a C–O bond-forming reaction such as acetoxylation is one of the most attractive methods to access complicated biaryl compounds. Organic hypervalent iodines[5] are promising oxidants to transform C–H to C–O bonds because they can do so via a metal-free process. Several examples of the acetoxylation and sulfonyloxylation of arenes have been reported (Figure 3.1a);[6,7,8] however, suitable substrates have been limited to arenes with strong electron-donating groups (e.g., –OMe and –NHAc) or polycyclic aromatic hydrocarbons, in which case biaryl substrates are not available. Kita and coworkers have reported that cationic I(III) species oxidize anisoles via an electron transfer process to give radical cation species that undergo nucleophilic addition of Me_3SiOAc to complete the acetoxylation of anisoles (Scheme 3.1b).[6b,9] On the basis of this pioneering study, a novel functionalization of biaryl compounds by intramolecular electron transfer between I(III) and

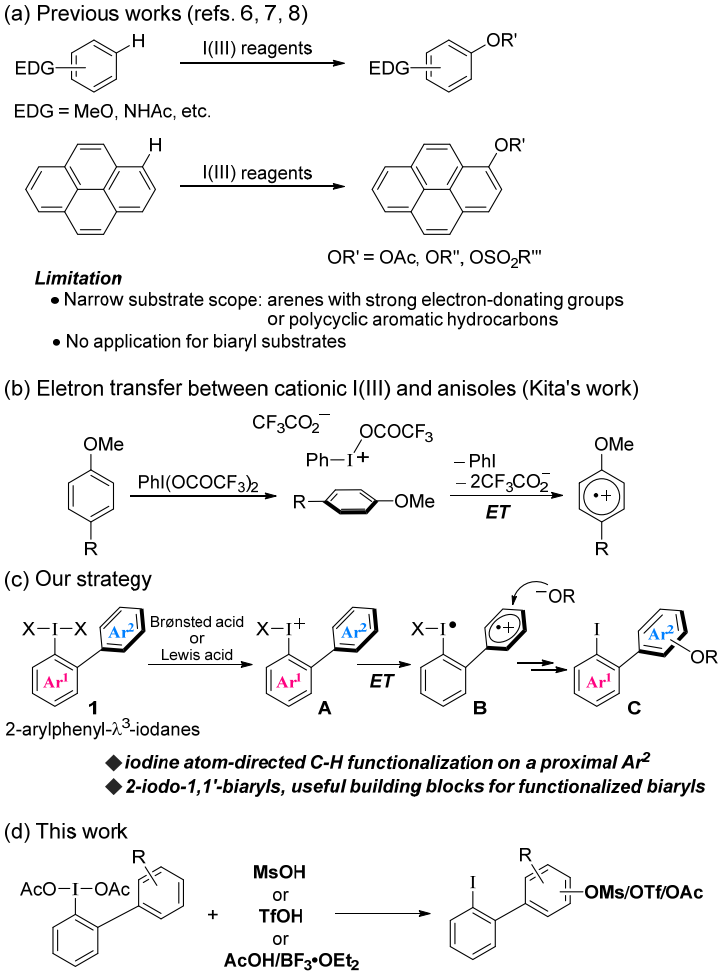


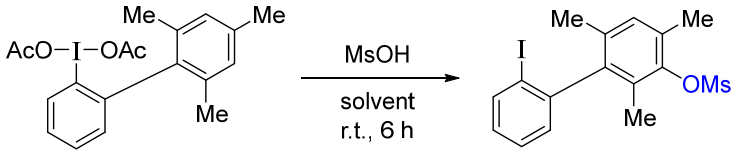
Figure 3.1. Transformation of an aryl C–H to a C–O bond by hypervalent iodine reagents.

proximal aryl groups in biaryl frameworks was designed. In our strategy (Figure 3.1c), the treatment of 2-arylphenyl-λ^3-iodanes (**1**) with a Brønsted acid or a Lewis acid generates a cationic I(III) (**A**);[5] intramolecular electron transfer (ET) then occurs from a proximal Ar^2 group to an I(III) center and gives radical cation (**B**), which is attacked by oxygen-nucleophilic reagents. In the overall process, the I(III) moiety guides the site-selective C–H functionalization on the 1-phenyl ring (Ar^2) of a 1-phenyl-2-iodobenzene structure (**1**).[10] In addition, because of their transformable C(sp^2)–I bonds, the obtained products are useful building blocks for diverse downstream routes to synthesize functionalized biaryl compounds. Herein, on the basis of this strategy, we demonstrate the selective sulfonyloxylation and acetoxylation of C–H bonds in a 2-aryl group of 2-arylphenyl-λ^3-iodanediyl diacetates (Figure 3.1d).

3-2. Results and Discussion

First, the mesyloxylation of 2-mesitylphenyl-λ^3-iodanediyl diacetate (**1a**) using methanesulfonic acid (MsOH) in CH_2Cl_2 (Table 3.1) was examined. MsOH was expected to function not only as a strong Brønsted acid to generate cationic I(III) but also as a nucleophile.[7c] An equimolar amount of MsOH gave only 2% yield of the desired product **2a** mesyloxylated at the proximal mesityl group (entry 1). Loading a greater amount of MsOH led to higher yields of **2a** (entries 2–5); finally, 5 equivalents of MsOH gave **2a** in 93% yield (entry 5). In our investigation of solvent effects, $CHCl_3$ and PhCl gave moderate yields and MeCN gave low yields (entries 6–8). Thus, the reaction conditions corresponding to entry 5 were chosen as the best protocol.

Table 3.1. Optimization of the conditions for the mesyloxylation of **1a**[a].



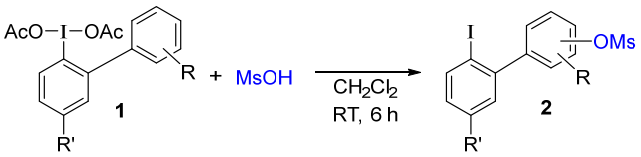
1a **2a**

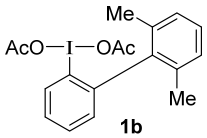
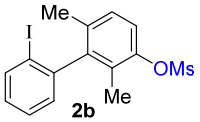
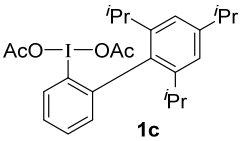
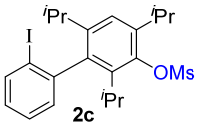
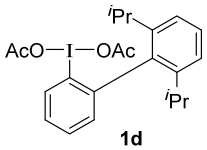
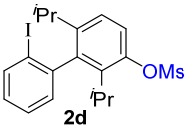
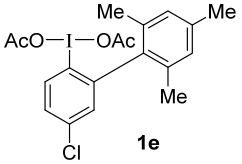
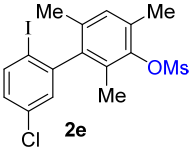
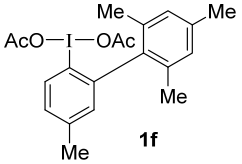
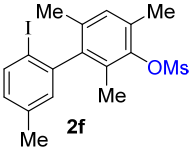
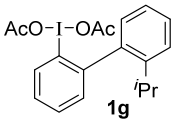
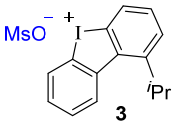
entry	MsOH (equiv)	solvent	yield of **2a**
1	1	CH_2Cl_2	2%
2	2	CH_2Cl_2	47%
3	2.5	CH_2Cl_2	65%
4	3	CH_2Cl_2	88%
5	5	CH_2Cl_2	93%
6	5	$CHCl_3$	72%
7	5	PhCl	74%
8	5	MeCN	12%

[a] **1a** (0.2 mmol), MsOH, solvent (5 mL), RT, 6 h. [b] Yield of **2a** was determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

The substrate scope of 2-arylphenyl-λ^3-iodanes (**1**) in mesyloxylation was investigated (Table 3.2). 2,6-Dimethylphenyl-substituted substrate (**1b**) was converted into **2b** in 77% yield, where the mesyloxylation occurred only at the 3′-position (entry 1). Mesyloxylation of 2,4,6-triisopropylphenyl and 2,6-diisopropylphenyl groups gave good results despite their large steric hindrance (entries 2 and 3). The reactions using substrates **1e** and **1f** bearing Me and Cl groups on a phenyl-λ^3-iodane framework proceeded well (entries 4 and 5). Substrate **1g** without a substituent at the 6′-position of the 2-aryl group gave no desired product because a well-known intramolecular cyclization[11] proceeded, giving dibenzo iodonium salt (**3**) (entry 6). In the experiments using 3- or 4-arylphenyl-λ^3-iodanes (see chapter 3-4), the desired functionalization reactions did not proceed, which suggests that it is important for the I(III) and aryl groups to be close to each other. 2-Aryl groups with electron-withdrawing substituents suppressed this mesyloxylation because of unfavorable electron transfer.

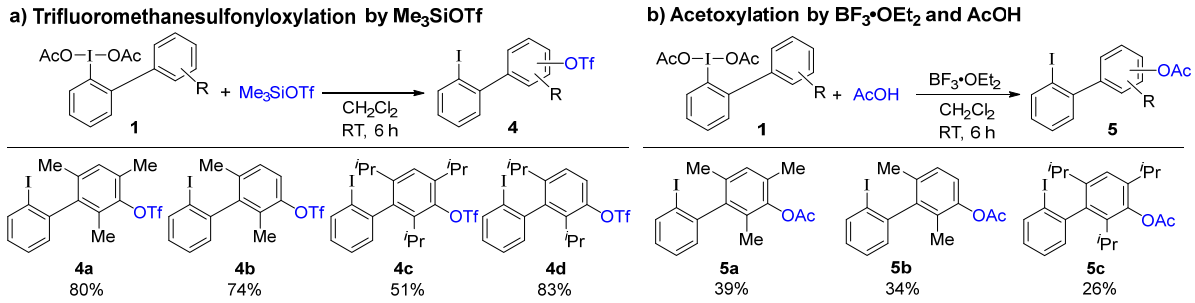
Table 3.2. Substrate scope and limitation of 2-arylphenyl-λ^3-iodanediyl diacetates (**1**) in mesyloxylation[a].



Entry	Substrate	Product	Yield
1	 **1b**	 **2b**	77%
2	 **1c**	 **2c**	57%
3	 **1d**	 **2d**	79%
4	 **1e**	 **2e**	77%
5	 **1f**	 **2f**	73%
6	 **1g**	 **3**	77%

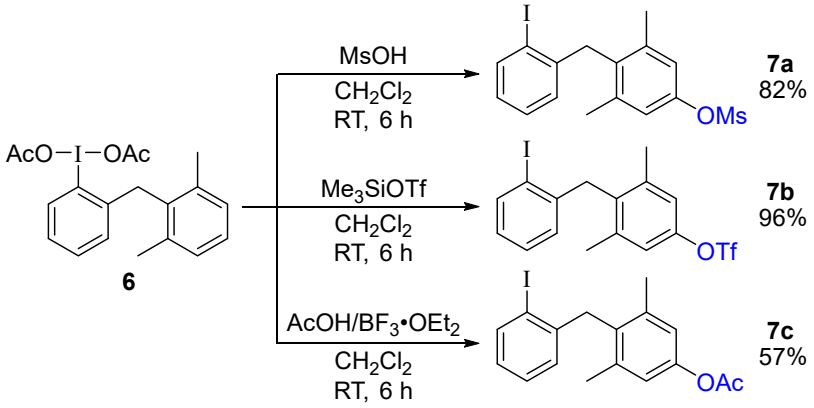
[a]**1** (0.2 mmol), MsOH (1 mmol), CH_2Cl_2 (5 mL), RT, 6 h. Isolated yields are shown.

Lewis acids as well as Brønsted acids generally activate aryl-λ^3-iodanediyl diacetates.[5] Thus, as a substitute for sulfonic acids, Me_3SiOTf was investigated as both a Lewis acid and a nucleophile (Scheme 3.1a). When substrate **1a** was treated with Me_3SiOTf (5 equiv), trifluoromethanesulfonyloxylation of the mesityl group proceeded to afford **4a** in 80% yield. Other aryl groups were also available to give the desired products **4b–4d**. Acetoxylation was accomplished using AcOH as a nucleophile and $BF_3{\cdot}OEt_2$ as a Lewis acid (Scheme 3.1b). Three types of λ^3-iodanes were examined, furnishing the acetoxylation products **5a–5c** in moderate yields.



Scheme 3.1. (a) C–H trifluoromethanesulfonyloxylation of biaryls (**1**). **1** (0.2 mmol), Me_3SiOTf (5 equiv), CH_2Cl_2 (5 mL), RT, 6 h; (b) C–H acetoxylation. **1** (0.2 mmol), AcOH (20 equiv), $BF_3{\cdot}OEt_2$ (2 equiv), CH_2Cl_2 (5 mL), RT, 6 h.

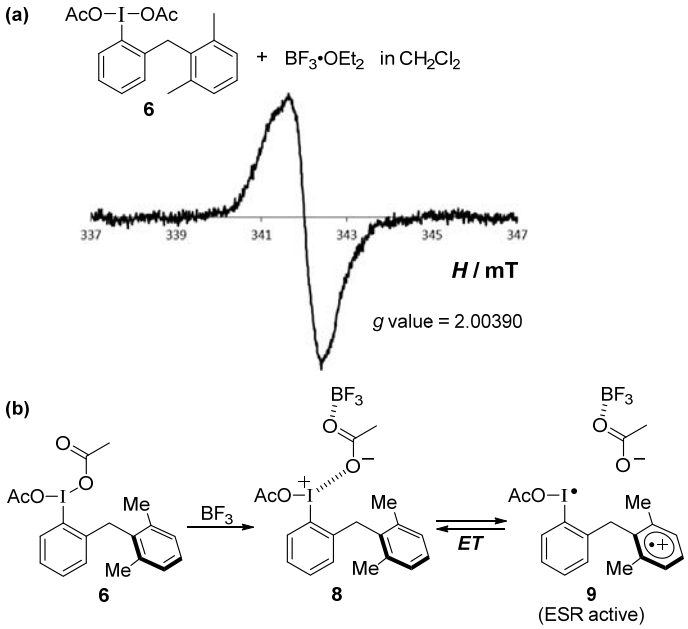
A 2-benzyl-1-iodobenzene structure having a C1 unit as a spacer is also applicable to this reaction system. In (2-arylmethylphenyl)-λ^3-iodanediyl diacetate (**6**), C–H functionalization by a proximal aryl group proceeded (Scheme 3.2). Substrate **6** underwent mesyloxylation, trifluoromethanesulfonyloxylation, and acetoxylation under each set of standard conditions to give the corresponding products **7a**, **7b**, and **7c**, respectively, in high yields. However, spacers longer than a C2 unit were not suitable.



Scheme 3.2. C–H functionalization in (2-arylmethylphenyl)-λ^3-iodanediyl diacetate.

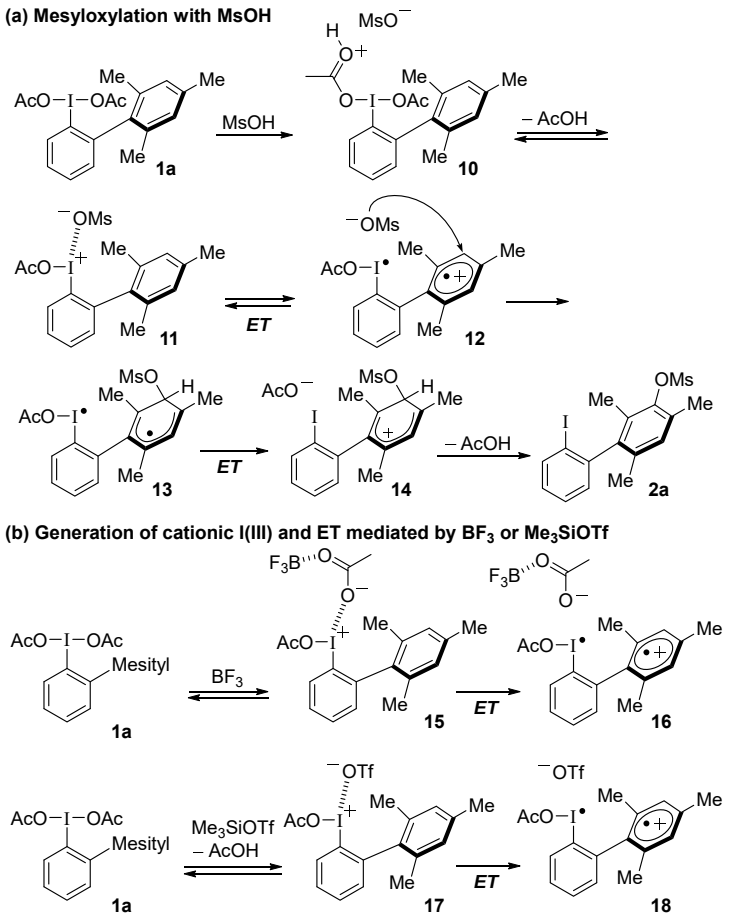
To verify our anticipated intramolecular electron transfer between a cationic I(III) center and a proximal Ar group, an electron spin resonance (ESR) study was carried out. A mixture of **6** and $BF_3{\cdot}OEt_2$ in CH_2Cl_2 solution at room temperature gave a signal without strong hyperfine coupling to hydrogens (Scheme 3.3a), whereas the combination of **1a** with MsOH or $BF_3{\cdot}OEt_2$ provided no significant information. The signal is

similar to that of an iodanyl radical reported by Kalek and coworkers,[12] which suggests the production of iodanyl radical species **9** with a radical cationic aryl group (Scheme 3.3b). The interaction of BF_3 with an AcO group on an I(III) atom generates cationic I(III) species (**8**);[13] sequential electron transfer then occurs from the 2,6-dimethylphenyl group to the cationic I(III) to generate ESR-active species (**9**). The observed signal is unsymmetrical despite the use of a solution sample, which indicates the signal of the radical cationic aryl group[14] overlaps that of the iodanyl radical.



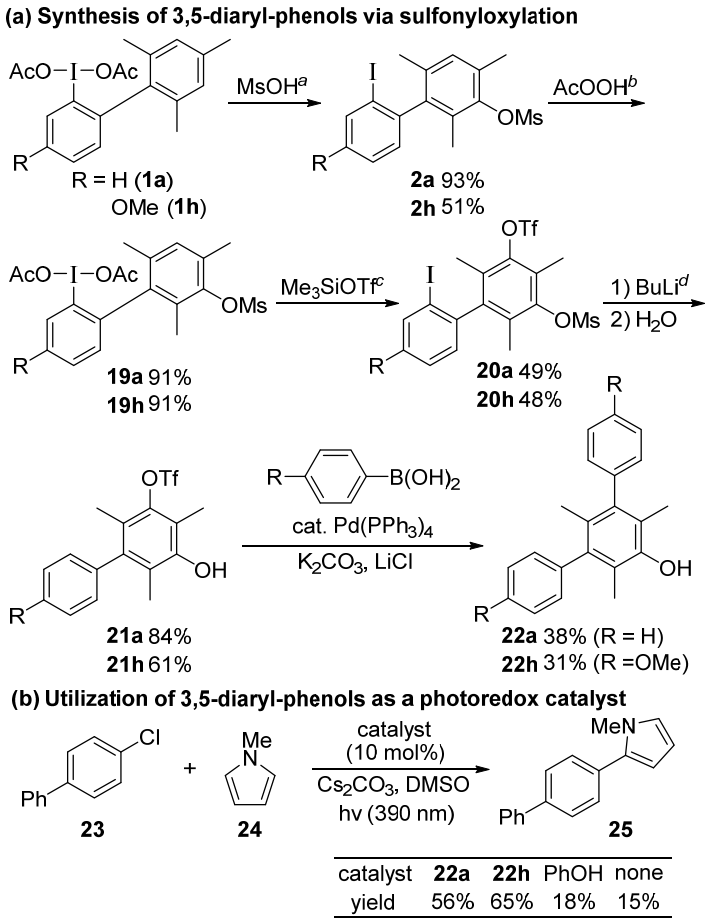
Scheme 3.3. ESR study for intramolecular electron transfer to give an iodanyl radical intermediate.

A plausible reaction mechanism for the mesyloxylation of **1a** with MsOH is illustrated in Scheme 3.4a. Protonation of **1a** by MsOH to form **10** accelerates the elimination of an AcO group to generate a cationic I(III) intermediate (**11**) that interacts with MsO^-.[15] An excess amount of MsOH would accelerate this step. Intramolecular electron transfer (ET) between the cationic I(III) center and mesityl group occurs to produce iodanyl radical intermediate (**12**), which has a radical cationic mesityl moiety. The nucleophilic addition of MsO^- to the mesityl group of **12** leads to biradical species (**13**), and then intramolecular ET in **13** followed by deprotonation in **14** provides product (**2a**). In the acetoxylation or trifluoromethanesulfonyloxylation reaction, BF_3 or Me_3Si^+ abstracts an AcO group from an I(III) center to generate cationic I(III) intermediate (**15** or **17**) (Scheme 3.4b). After the intramolecular ET, $AcOBF_3^-$ or TfO^- functions as a nucleophile, finally affording the corresponding functionalized products.



Scheme 3.4. Proposed reaction mechanisms.

A sequential process of mesyloxylation and trifluoromethanesulfonyloxylation was used for the synthesis of 3,5-diaryl-substituted phenols (Scheme 3.5a). Mesityl-substituted λ^3-iodane (**1a** or **1h**) underwent mesyloxylation, the obtained **2a** or **2h** was oxidized, and sequential treatment with Me_3SiOTf afforded **20a** or **20h**, respectively. Treatment with *n*-BuLi followed by H_2O removed both the methanesulfonyl and iodo groups, and then Suzuki–Miyaura cross-coupling of aryl triflates (**21**) with aryl boronic acids furnished 3,5-diaryl-2,4,6-trimethylphenols **22**. Recently, the photoredox catalytic activity of multi-substituted phenolates was reported.[16,17] Thus, we evaluated the performance of the synthesized **22** in the visible-light-mediated coupling of aryl chloride (**23**) with pyrrole (**24**) (Scheme 3.5b). Both **22a** and **22h** exhibited effective catalytic activity because of a visible-light absorption band and the high reduction potential of their corresponding phenolate forms (the estimated excited-state redox potential of phenolate form (**22a**$^-$), E(**22a**·/**22a**$^-$*), is −3.15 V and that of **22h**$^-$, E(**22h**·/**22h**$^-$*), is −3.13 V vs. SCE).[18] By contrast, PhOH, the phenolate form of which does not absorb visible light, did not work well in the reaction.



Scheme 3.5. Synthesis of 3,5-diaryl-phenols via mesyloxylation and trifluoromethanesulfonyloxylation, and their application as a photoredox catalyst.

3-3. Conclusion

In conclusion, iodane-mediated proximal aryl C–H sulfonyloxylation and acetoxylation on 2-iodo-1,1′-biphenyl and 1-benzyl-2-iodobenzene structures were achieved. MsOH, Me_3SiOTf, or BF_3 mediates the elimination of AcO^- from λ^3-iodanediyl diacetates to generate cationic I(III) species. An ESR study supported the key step where intramolecular electron transfer between the cationic I(III) and proximal aryl moieties provides an iodanyl radical intermediate with a radical cationic Ar moiety. The sequential process of two sulfonyloxylations allowed access to 3,5-diaryl-2,4,6-trimethylphenols that functioned as efficient photoredox catalysts in the coupling between an aryl bromide and *N*-methylpyrrole.

3-4. Experimantal Section

General Information

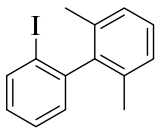
NMR spectra were recorded on JEOL-AL400, JEOL-ECS400, JEOL-ECZL400 (400 MHz for ^{1}H, 100 MHz for ^{13}C and 377 MHz for ^{19}F). Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 ppm for ^{1}H NMR) and the middle peak of triplet of $CDCl_3$ (δ = 77 ppm for ^{13}C NMR) as an internal reference, and CF_3COOH in D_2O (δ = -76.55 ppm for ^{19}F NMR) as an external reference. Coupling constants were quoted in Hz (J). ^{1}H NMR spectroscopy splitting patterns were designated as singlet

(s), doublet (d), triplet (t), quartet (q). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). New compounds were characterized by ^{1}H, ^{13}C, ^{13}C off-resonance, DEPT techniques, COSY, HMQC, HSQC, and HMBC. Differential pulse voltammetry measurements were performed with an ALS-600C electrochemical analyzer using a glassy carbon working electrode, a Pt counter electrode, and an $Ag/AgNO_3$ reference electrode at room temperature in DMSO containing 0.1 M nBu_4NBF_4 as the supporting electrolyte. Infrared (IR) spectra were recorded on a JASCO FT/IR-6200 Fourier transform infrared spectrophotometer. ESR spectra were recorded on a Bruker EMXmicro spectrometer. Purification by recycle HPLC was performed on SHIMADZU recycle HPLC system (SPD-20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) and Japan Analytical Industry Co. (NEXT recycling preparative HPLC). High-resolution mass spectra were recorded on a JEOL JMS-700 and JMS-T100LP (TOF analyzer with ESI or DART ionization sources). Reactions were carried out in dry solvents under nitrogen atmosphere, unless otherwise stated. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), FUJIFILM Wako Pure Co., Ltd., KISHIDA Chemical Co., Ltd.

Materials

λ^3-Iodanes **1a** and **6** were synthesized according to the reported literature (Y. Nishimoto, M. Fujie, J. Hara, M. Yasuda, *Org. Chem. Front.* **2021**, *8*, 3695). Other all λ^3-iodanes were prepared by following procedures and characterization data of them were described below.

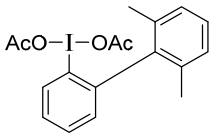
(S1) 2'-iodo-2,6-dimethyl-1,1'-biphenyl



This manipulation was carried out according to the reported method (N. Hartmann, M. Niemeyer, *Synth*. *Commun*. **2001**, *31*, 3839.). A solution of *o*-bromofluorobenzene (1.049 g, 5.99 mmol) in THF (8 mL) was cooled to -78 °C in a dry ice/acetone bath. *n*-BuLi (3.75 mL of a 1.6 M solution in *n*-hexane, 6 mmol) was added via a dropping funnel during a period of ca. 5 min, and stirring was continued for 30 min at the same temperature. A solution of (2,6-dimethylphenyl)magnesium bromide in THF (10 mL), freshly prepared from 2,6-dimethylphenyl bromide (1.066 g, 5.76 mmol) and Mg (0.174 g, 7.23 mmol) was then added dropwise at -78 °C during a period of ca. 5 min. The solution was slowly allowed to reach ambient temperature while stirring was continued overnight. The resulting mixture was cooled in an ice bath and iodine (3.046 g, 12.0 mmol) was added with rapid stirring. After 15 min the excess iodine was destroyed with a Na_2SO_3 solution. The mixture was extracted with chloroform (3 x 5 mL). The collected organic layer was dried (Na_2SO_4). The solvent was evaporated, and the residue was purified by column chromatography (only hexane, column length 20 cm, diameter 2.6 cm) and distillation under reduced pressure to give the white solid (1.010 g, 66%).

mp: 63-65 °C; IR: (KBr) 3060 (C-H), 2855 (C-H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.95 (dd, J = 8.0, 1.2 Hz, 1H), 7.42 (td, J = 8.0, 1.2 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.15-7.11 (m, 3H, 6-H), 7.04 (dd, J = 8.0, 1.2 Hz, 1H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.8 (s), 143.8 (s), 139.1 (d), 135.6 (s), 129.4 (d), 128.53 (d), 128.50 (d), 127.7 (d), 127.3 (d), 100.3 (s), 20.4 (q); HRMS (DART+) Calculated ($C_{14}H_{14}I$) 309.01347 ($[M + H]^+$) Found: 309.01435

(1b) (2',6'-dimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate

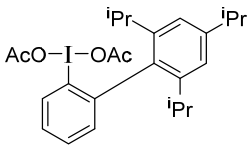


To the flame-dried flask was added 2'-iodo-2,6-dimethyl-1,1'-biphenyl (1.01 g, 3.27 mmol) and 9% peracetic acid (8 mL). The reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (1.28 g, 92%).

mp: 116-117 °C; IR: (KBr) 3060 (C-H), 2924 (C-H), 1646 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.39 (dd, J = 8.4, 0.9 Hz, 1H), 7.72 (td, J = 8.4, 0.9 Hz, 1H), 7.47-7.44 (m, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 7.5 Hz, 2H), 2.06 (s, 6H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.2 (s,

*C*OCH$_3$), 144.8 (s), 140.5 (s), 138.0 (d), 136.5 (s), 132.7 (d), 130.9 (d), 129.5 (d), 128.8 (d), 127.4 (d), 126.3 (s), 20.5 (q), 20.2 (q); HRMS (ESI+) Calculated ($C_{22}H_{27}O_4NaI$) 449.02202 ([M + Na]$^+$) Found: 449.02244

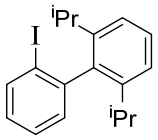
(1c) (2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-2,4,6-triisopropyl-1,1'-biphenyl (2.05 g, 5.05 mmol) and 9% peracetic acid (13.5 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (1.60 g, 61%).

mp: 119-121 °C; IR: (KBr) 2961 (C-H), 2866 (C-H), 1658 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.44 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.68 (td, *J* = 7.8, 1.2 Hz, 1H), 7.53 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.45 (td, *J* = 7.8, 1.2 Hz, 1H), 7.05 (s, 2H), 2.94 (septet, *J* = 6.8 Hz, 1H), 2.46 (septet, *J* = 6.8 Hz, 2H), 1.95 (s, 6H), 1.31 (d, *J* = 6.8 Hz, 6H), 1.18 (d, *J* = 6.8 Hz, 6H), 0.96 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.7 (C), 149.8 (C), 146.9 (C), 145.1 (C), 138.4 (CH), 135.7 (C), 131.9 (CH, two signals are overlapping), 129.6 (CH), 126.4 (CH), 120.8 (CH), 34.3 (CH), 30.4 (CH), 26.0 (CH_3), 24.0 (CH_3), 22.7 (CH_3), 20.7 (CH_3); HRMS (ESI+) Calculated ($C_{25}H_{33}O_4NaI$) 547.13157 ([M + Na]$^+$) Found: 547.13010

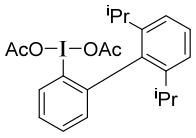
(S2) 2'-iodo-2,6-diisopropyl-1,1'-biphenyl



This manipulation was carried out according to the reported method (N. Hartmann, M. Niemeyer, *Synth*. *Commun*. **2001**, *31*, 3839.). A solution of *o*-bromofluorobenzene (5.21 g, 29.7 mmol) in THF (40 mL) was cooled to -78 °C in a dry ice/acetone bath. n-BuLi (18.8 mL of a 1.6 M solution in n-hexane, 30 mmol) was added via dropping funnel, and stirring was continued for 30 min at the same temperature. A solution of 2,6-*i*Pr$_2$C$_6$H$_3$MgBr in THF (50 mL), freshly prepared from 2,6-*i*Pr$_2$C$_6$H$_3$Br (7.24 g, 30.0 mmol) and Mg (0.782 g, 32.2 mmol) was then added dropwise at -78 °C. The solution was slowly allowed to reach ambient temperature while stirring was continued overnight. The resulting mixture was cooled in an ice bath and iodine (15.3 g, 60.3 mmol) was added with rapid stirring. After 15 min the excess iodine was destroyed with a Na_2SO_3 solution. The mixture was extracted with chloroform (3 x 5 mL). The collected organic layer was dried (Na_2SO_4). The solvent was evaporated and the residue was purified by recrystallization from ethanol to give a white needle crystal (1.77g, 16%).

mp: 125-126 °C; IR: (KBr) 2959 (C-H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.96 (d, *J* = 7.8 Hz, 1H), 7.43-7.38 (m, 2H, 5-H), 7.23 (d, *J* = 7.7 Hz, 2H), 7.18 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.05 (td, *J* = 7.8, 1.2 Hz, 1H), 2.40 (septet, *J* = 7.0 Hz, 2H), 1.23 (d, *J* = 7.0 Hz, 6H), 1.01 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 146.3 (s), 145.6 (s), 141.8 (s), 139.0 (d), 130.4 (d), 128.62 (d), 128.57 (d), 128.0 (d), 123.0 (d), 102.0 (s), 30.7 (d), 25.0 (q), 23.5 (q); HRMS (EI) Calculated ($C_{18}H_{21}I$) 364.0688 ([M]$^+$) Found: 364.0685

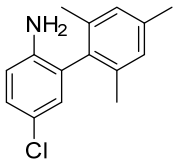
(1d) (2',6'-diisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-2,6-diisopropyl-1,1'-biphenyl (**S2**) (0.690 g, 1.89 mmol) and 9% peracetic acid (7 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (0.291 g, 32%).

mp: 110-113 °C; IR: (KBr) 2959 (C-H), 1651 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.45 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.70 (td, *J* = 7.5, 1.2 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.47 (td, *J* = 7.5, 1.2 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.22 (d, *J* = 7.7 Hz, 2H), 2.48 (septet, *J* = 6.8 Hz, 2H), 1.95 (s, 6H), 1.19 (d, *J* = 6.8 Hz, 6H), 0.97 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.8 (s), 147.4 (s), 144.7 (s), 138.6 (d), 138.2 (s), 132.1 (d), 131.8 (d), 129.9 (d), 129.8 (d), 126.2 (s), 122.9 (d), 30.6 (d), 26.1 (q), 22.8 (q), 20.8 (q); HRMS (ESI+) Calculated ($C_{22}H_{27}O_4NaI$) 505.08462 ([M + Na]$^+$) Found: 505.08670

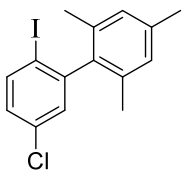
(S3) 5-chloro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine



This manipulation was carried out according to the reported method (T. G. Driver *et al*., *J. Org. Chem.* **2009**, *74*, 3225.). To the flame-dried three-necked flask was added 2,4,6-trimethylphenylboronic acid (0.852 g, 5.20 mmol), K_2CO_3 (2.22 g, 16.1 mmol), and $Pd(PPh_3)_4$ (0.451 g, 0.39 mmol) were then dissolved in 19 mL of toluene, 13 mL of H_2O, and 6.5 mL of EtOH. 2-bromo-4-chloroaniline (0.830 g, 4.02 mmol) and was added, and the resulting mixture was heated to 95 ˚C for 16 hours. After cooling, the solution was diluted with 30 mL of saturated aqueous NH_4Cl. The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 20 cm, diameter 2.6 cm) to give the titled compound as an orange solid (0.737 g, 75%).

mp: 79-80 °C; IR: (KBr) 3396 (NH_2), 3176 (C-H), 2921 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.11 (dd, J = 8.6, 2.2 Hz, 1H), 6.96 (s, 1H), 6.90 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 8.6 Hz, 1H), 3.41 (s, 2H), 2.32 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 142.3 (s), 137.5 (s), 136.8 (s), 133.5 (s), 129.5 (d), 128.5 (d), 127.9 (d), 127.6 (s), 122.8 (s), 116.0 (d), 21.1 (q), 20.0 (q); HRMS (EI) Calculated ($C_{15}H_{16}ClN$) 245.0971 ($[M]^+$) Found: 245.0967

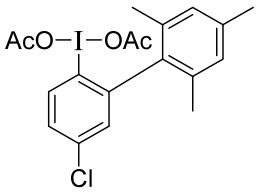
(S4) 5'-chloro-2'-iodo-2,4,6-trimethyl-1,1'-biphenyl



This manipulation was carried out according to the reported method (*Eur. J. Org. Chem.* **2019**, 696). 5-chloro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine (0.936 mmol, 0.230 g) was added to a solution of *p*-TsOH•H_2O (2.87 mmol, 0.545 g) in MeCN (4.4 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (2.36 mmol, 0.163 g) and KI (3.01 mmol, 0.498 g) in H_2O (5.6 mL) was added gradually. The reaction mixture was stirred for 3 hours at room temperature and then quenched by water (20 mL) and $NaHCO_3$ aq. The mixture was extracted with ethyl acetate (3 x 5 mL). The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5, column length 10 cm, diameter 2.6 cm) to give the titled compound as a white solid (0.147 g, 45%).

mp: 74-75 °C; IR: (KBr) 2975 (C-H), 2914 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.84 (d, J = 8.4 Hz, 1H), 7.10 (d, J = 2.6 Hz, 1H), 7.30 (dd, J = 8.4 Hz, 2.6 Hz, 1H), 6.94 (s, 2H), 2.34 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 147.8 (s), 140.05 (d), 139.98 (s), 137.8 (s), 135.3 (s), 134.7 (s), 129.7 (d), 128.7 (d), 128.2 (d), 98.1 (s), 21.2 (q), 20.2 (q); HRMS (EI) Calculated ($C_{15}H_{14}ClI$) 355.9829 ($[M]^+$) Found: 355.9829

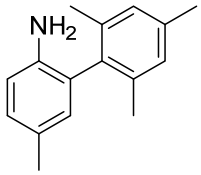
(1e) (5-chloro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-l3-iodanediyl diacetate



To the flame-dried flask was added 5'-chloro-2'-iodo-2,4,6-trimethyl-1,1'-biphenyl (**S4**) (0.198 g, 0.56 mmol) and 9% peracetic acid (2.0 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a pale yellow solid (0.174 g, 68%).

mp: 123-125 °C; IR: (KBr) 3057 (C-H), 2915 (C-H), 1648 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.31 (d, J = 7.5 Hz, 1H), 7.42-7.40 (m, 2H), 6.91 (s, 2H), 2.33 (s, 3H), 2.03 (s, 6H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (s, *C*OCH_3), 147.0 (s, C-5), 139.2 (d, C-3), 139.1 (s), 138.9 (s), 136.8 (s), 136.2 (s), 131.0 (d), 129.7 (d), 128.3 (d, C-9), 124.6 (s, C-1), 21.1 (q, 8-Me), 20.4 (q), 20.2 (q); HRMS (ESI+) Calculated ($C_{19}H_{20}O_4NaClI$) 496.99870 ($[M + Na]^+$) Found: 496.99908

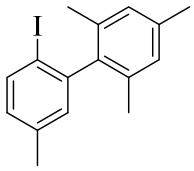
(S5) 5-methyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine



This manipulation was carried out according to the reported method (T. G. Driver *et al*., *J. Org. Chem.* **2009**, *74*, 3225.). To the flame-dried three-necked flask was added 2,4,6-trimethylphenylboronic acid (0.868 g, 5.29 mmol), K_2CO_3 (2.20 g, 16.0 mmol), and $Pd(PPh_3)_4$ (0.471 g, 0.41 mmol) were then dissolved in 19 mL of toluene, 13 mL of H_2O, and 6.5 mL of EtOH. 2-bromo-4-methylaniline (0.784 g, 4.24 mmol) and was added, and the resulting mixture was heated to 95 ˚C for 16 hours. After cooling, the solution was diluted with 30 mL of saturated aqueous NH_4Cl. The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 20 cm, diameter 2.6 cm) to give the titled compound as an orange solid (0.651 g, 61%).

IR: (neat) 3374 (NH_2), 2917 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 6.98-6.96 (m, 3H, 4-H), 6.73 (s, 1H), 6.71 (d, 1H), 3.28 (s, 2H), 2.32 (s, 3H), 2.26 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 141.0 (s), 137.0 (s), 136.9 (s), 135.0 (s), 130.4 (d), 128.5 (d), 128.3 (d, C-4), 127.6 (s), 126.3 (s), 115.1 (d), 21.1 (q), 20.6 (q), 20.2 (q); HRMS (EI) Calculated ($C_{16}H_{19}N$) 225.1518 ($[M]^+$) Found: 225.1517

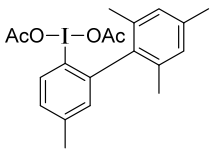
(S6) 2'-iodo-2,4,5',6-tetramethyl-1,1'-biphenyl



This manipulation was carried out according to the reported method (*Eur. J. Org. Chem.* **2019**, 696). 2',4',5,6'-Tetramethyl-[1,1'-biphenyl]-2-amine (0.41 mmol, 0.076 g) was added to a solution of *p*-TsOH•H_2O (1.21 mmol, 0.231 g) in MeCN (1.6 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (1.11 mmol, 0.163 g) and KI (0.76 mmol, 0.126 g) in H_2O (2.5 mL) was added gradually. The reaction mixture was stirred for 3 hours at room temperature and then quenched by water (10 mL) and $NaHCO_3$ aq. The mixture was extracted with ethyl acetate (3 x 5 mL). The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a colorless liquid (0.085 g, 62%).

IR: (neat) 3003 (C-H), 2918 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.79 (d, J = 8.1 Hz, 1H), 6.94 (m, 3H, 6-H), 6.85 (dd, J = 8.1, 2.0 Hz, 1H), 2.34 (s, 3H), 2.32 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.7 (s), 141.1 (s), 138.6 (d), 138.4 (s), 137.1 (s), 135.4 (s), 130.5 (d), 129.4 (d), 128.0 (d), 96.6 (s), 21.2 (q), 21.0 (q), 20.3 (q); HRMS (EI) Calculated ($C_{15}H_{14}ClI$) 336.0375 ($[M]^+$) Found: 336.0370

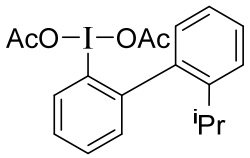
(1f) (2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-2,4,6-trimethyl-1,1'-biphenyl (**S6**) (0.460 g, 1.41 mmol) and 9% peracetic acid (5.3 mL). The reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (0.442 g, 70%).

mp: 113-115 °C; IR: (KBr) 3422 (C-H), 2921 (C-H), 1644 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.26 (d, J = 8.8 Hz, 1H), 7.25-7.23 (m, 2H), 6.90 (s, 2H), 2.47 (s, 3H), 2.33 (s, 3H), 2.02 (s, 6H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (s), 145.1 (s), 143.6 (s), 138.3 (s), 137.9 (d), 137.8 (s), 136.3 (s), 131.7 (d), 130.3 (d), 128.2 (d), 123.5 (s), 21.6 (q), 21.1 (q), 20.4 (q), 20.3 (q); HRMS (ESI+) Calculated ($C_{20}H_{23}O_4NaI$) 477.05332 ($[M + Na]^+$) Found: 477.05418

(1g) (2'-isopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2-iodo-2'-isopropyl-1,1'-biphenyl (0.308 g, 0.956 mmol) and 9% peracetic acid (3.7 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (0.342 g, 82%). mp: 130-131 °C; IR: (KBr) 2954 (C-H), 1641 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 8.37 (d, *J* = 7.7 Hz, 1H), 7.68 (td, *J* = 7.7, 1.2 Hz, 1H), 7.54 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.48-7.39 (m, 3H), 7.22-7.16 (m, 2H), 2.71 (septet, *J* = 6.9 Hz, 1H), 1.95 (s, 6H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (C), 146.7 (C), 145.6 (C), 139.8 (C), 137.4 (CH), 132.0 (CH), 130.9 (CH), 130.1 (CH), 129.6 (CH), 129.4 (CH), 126.6 (CH), 125.6 (CH), 124.9 (CH), 30.0 (CH), 25.4 (CH_3), 22.7 (CH_3), 20.4 (CH_3); HRMS (ESI+) Calculated ($C_{19}H_{21}O_4NaI$) 463.03767 ([M + Na]$^+$) Found: 463.03776

General Procedure

Procedure for methanesulfonyloxylation of 2-arylphenyl-λ^3-iodanediyl diacetate (1) (Table 2)

To a solution of 2-arylphenyl-λ^3-iodanediyl diacetate (**1**) (0.2 mmol) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (1.0 mmol). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography to give the desired product.

Procedure for triflation of 2-arylphenyl-λ^3-iodanediyl diacetate (1) (Scheme 1a)

To a solution of 2-arylphenyl-λ^3-iodanediyl diacetate (**1**) (0.2 mmol) in CH_2Cl_2 (5 mL) was added trimethylsilyl trifluoromethanesulfonate (1.0 mmol). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography to give the desired product.

Procedure for acetoxylation of 2-arylphenyl-λ^3-iodanediyl diacetate (1) (Scheme 1b)

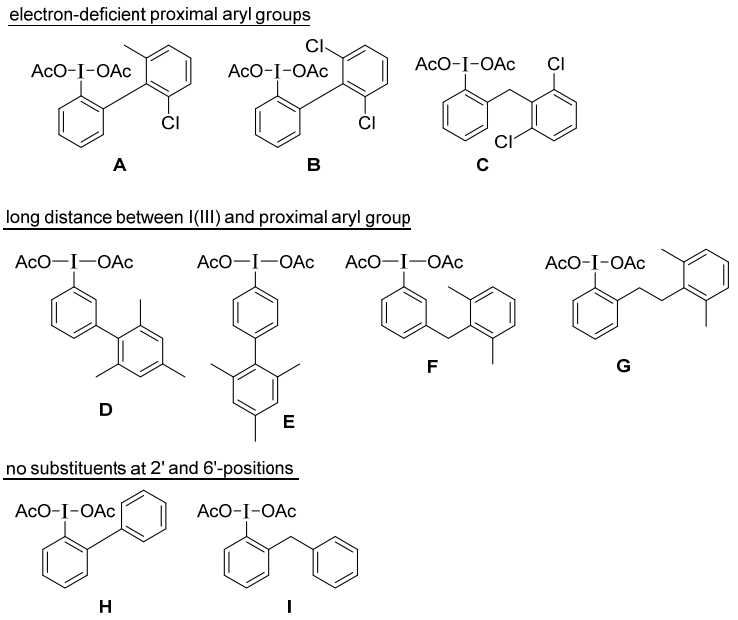
To a solution of 2-arylphenyl-λ^3-iodanediyl diacetate (**1**) (0.2 mmol) in CH_2Cl_2 (5 mL) was added BF_3•OEt_2 (0.4 mmol) and AcOH (1.0 mmol). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography to give the desired product.

Procedure for C–H functionalization of (2-arylmethylphenyl)-λ^3-iodanediyl diacetate (6) (Scheme 2)

C–H functionalization of (2-arylmethylphenyl)-λ^3-iodanediyl diacetate (**6**) were carried out by the same method as that of 2-arylphenyl-λ^3-iodanediyl diacetate (**1**).

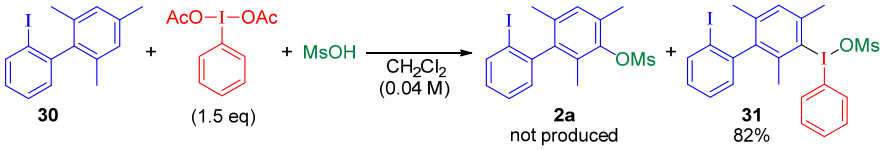
Limitation of Substrate Scope

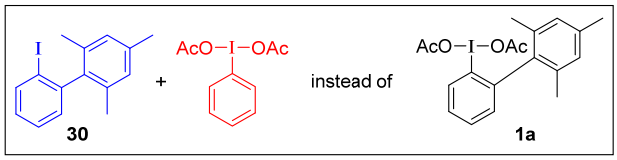
The following substrates (**A**-**I**) did not give the mesyloxylated products in the reaction using MsOH. In substrates (**A**, **B**, and **C**), electron transfer from an electron-deficient proximal aryl group to an I(III) center would not occur. In substrates (**D**-**G)**, the long distance between an I atom and a proximal aryl group would suppress electron transfer between them. In the reaction of substrate (**H** or **I**), a well-known intramolecular cyclization exclusively proceeded to give the corresponding dibenziodonium salt.



Use of $PhI(OAc)_2$ as an External Oxidant

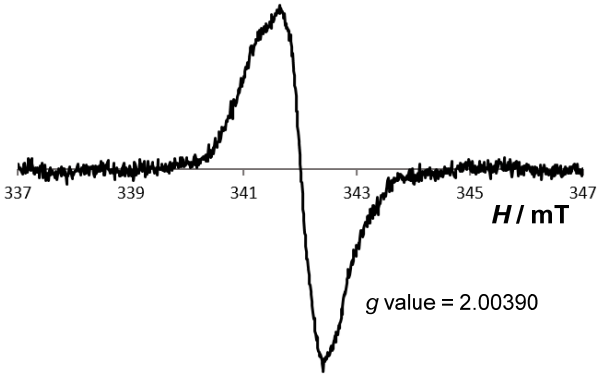
When using the combination of aryl iodide (**30**) with $PhI(OAc)_2$ instead of λ^3-iodanediyl diacetate (**1a**), in which $PhI(OAc)_2$ works as an external oxidant, mesyloxylated product 2a was not obtained and diaryl λ^3-iodane (**31**) was produced in 82% yield. This result suggests that λ^3-iodanes as an external oxidant is not effective.





ESR measurements

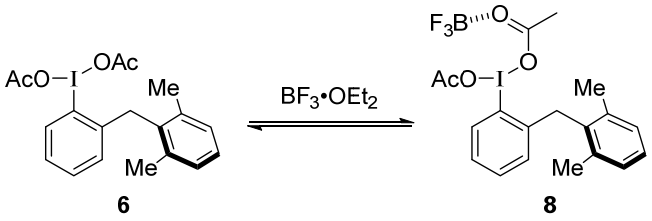
A sample solution was prepared from λ^3-iodanediyl diacetate (**6**) (0.0449 g, 0.1 mmol), $BF_3{\cdot}OEt_2$ (0.0291 g, 0.2 mmol), and CH_2Cl_2 (0.5 mL, 0.25 M).



ESR spectrum of a CH_2Cl_2 solution of λ^3-iodanediyl diacetate (**6**) and $BF_3{\cdot}OEt_2$. 9.593 GHz, *g*-value = 2.00390, Gain = 317000, sweep time = 5.1 min, modulation amplitude = 0.3 mT.

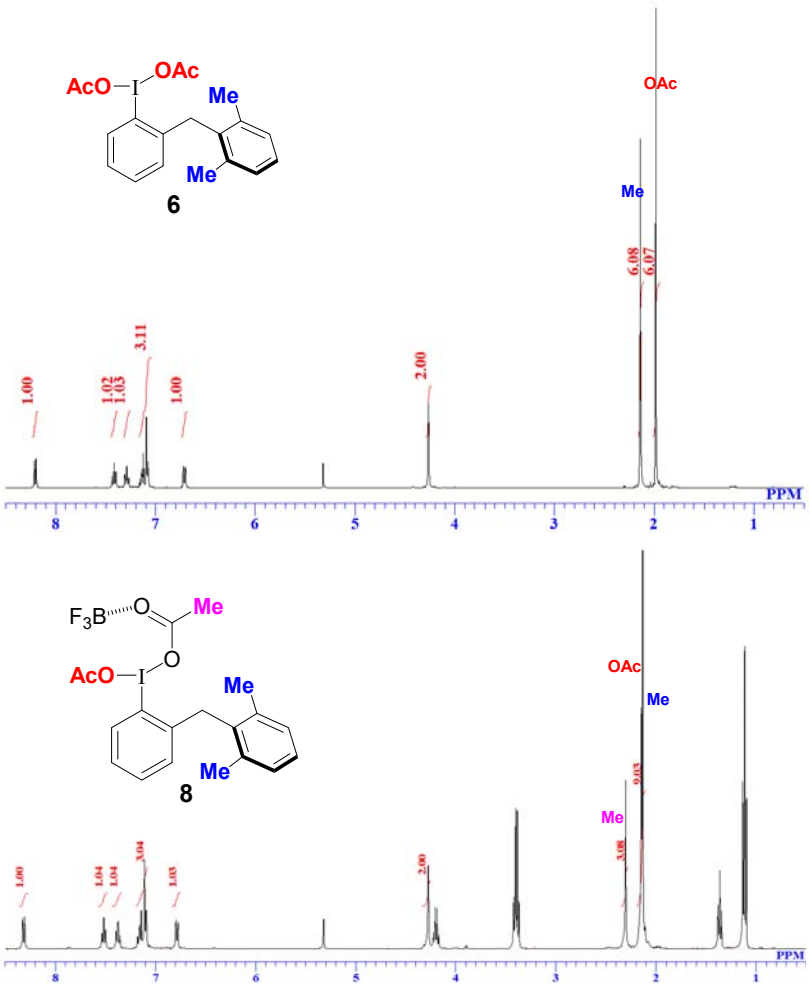
Observation of the Coordination of AcO group to BF_3

When BF_3•OEt_2 was added into a CD_2Cl_2 solution of iodoarene diacetate (**6**), in ^1H NMR CH_3 signals of AcO group shifted downfield more than original signals of **6**. And, the two signals of AcO groups appeared separately. Therefore, this result supported one of AcO groups coordinated to BF_3 and complex (**8**) was generated.



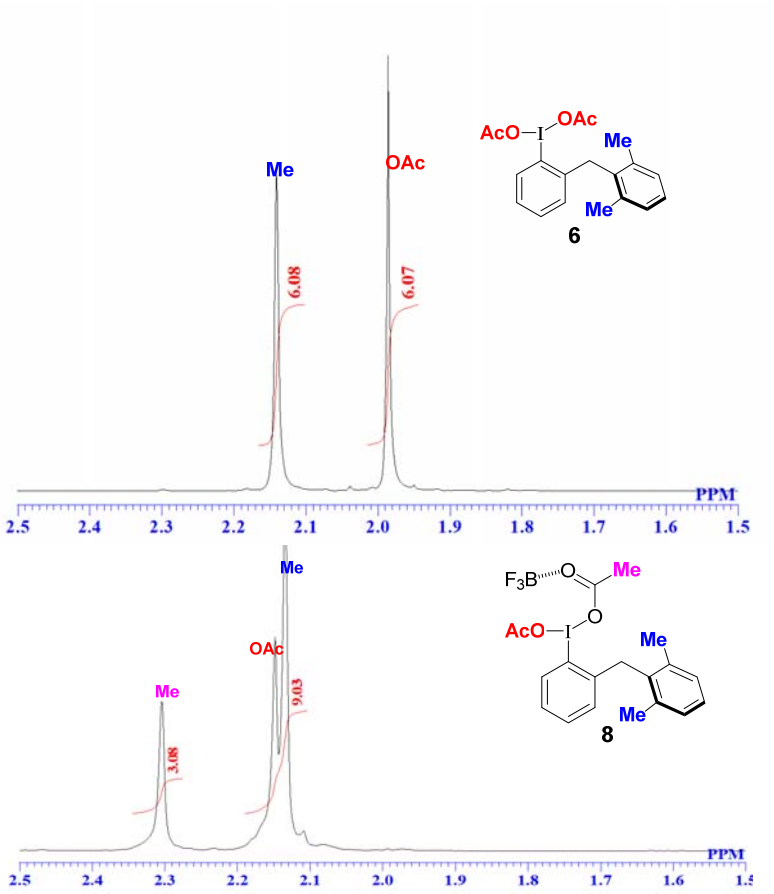
6 **8**

^1H NMR (400 MHz, in CD_2Cl_2 at –50 °C)
0.5 ppm ~ 8.5 ppm



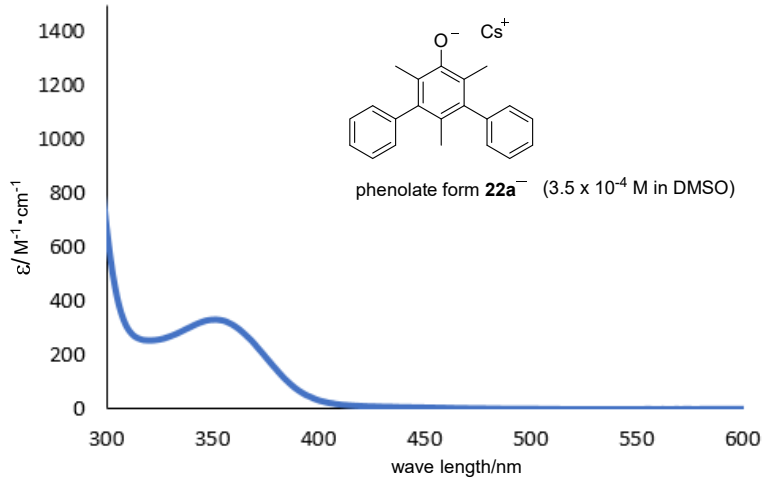
^{1}H NMR (400 MHz, in CD_2Cl_2 at –50 °C)

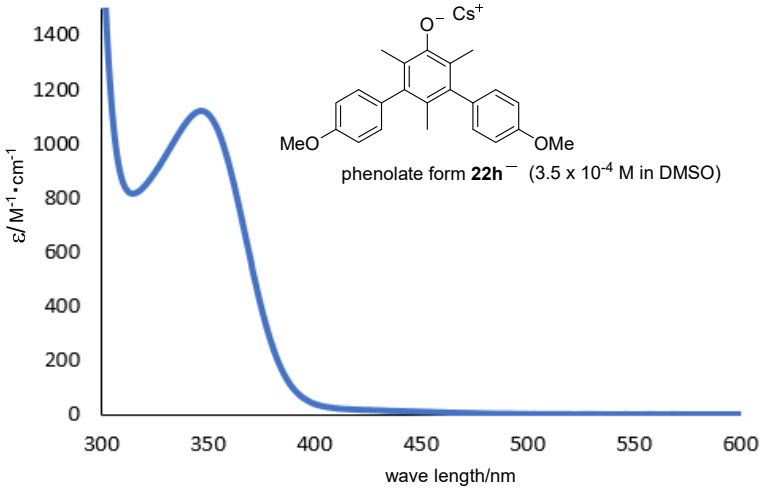
1.5 ppm ~ 2.5 ppm



UV- Visible Absorption Spectroscopy

The sample solution was prepared from a phenol compound, Cs_2CO_3 (1.5 equiv), and DMSO.





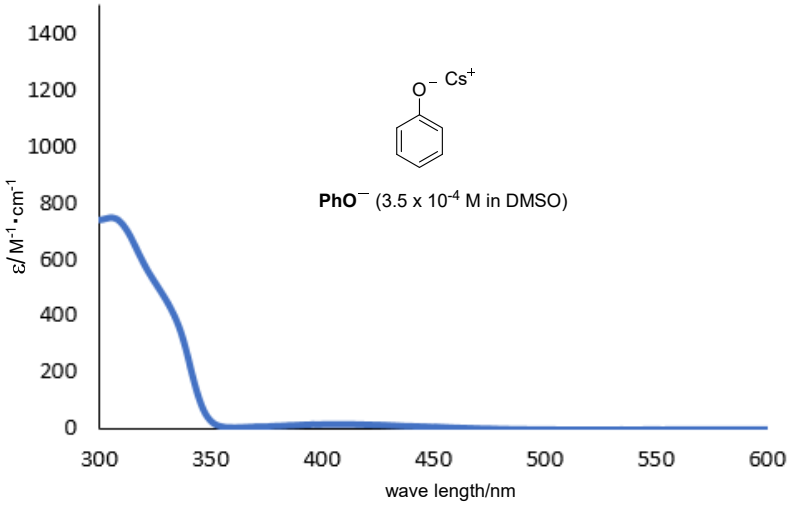
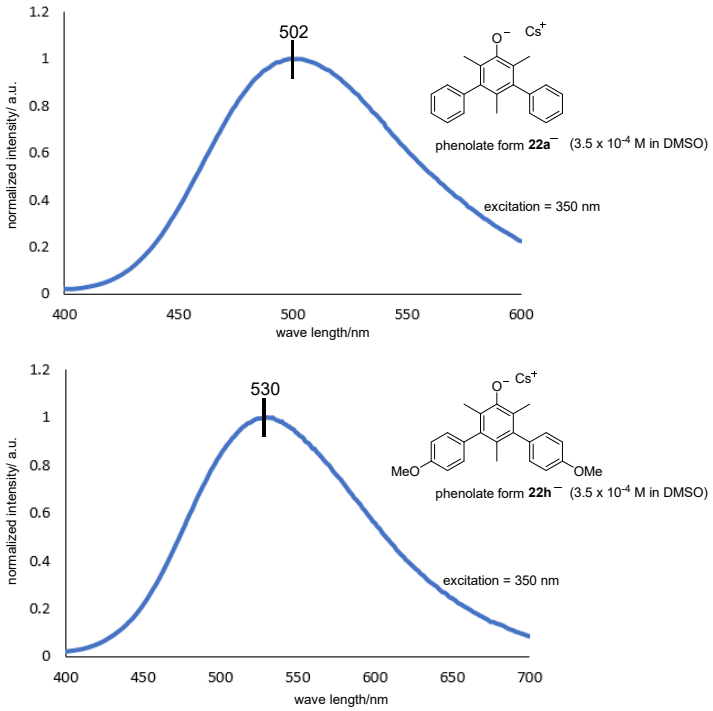


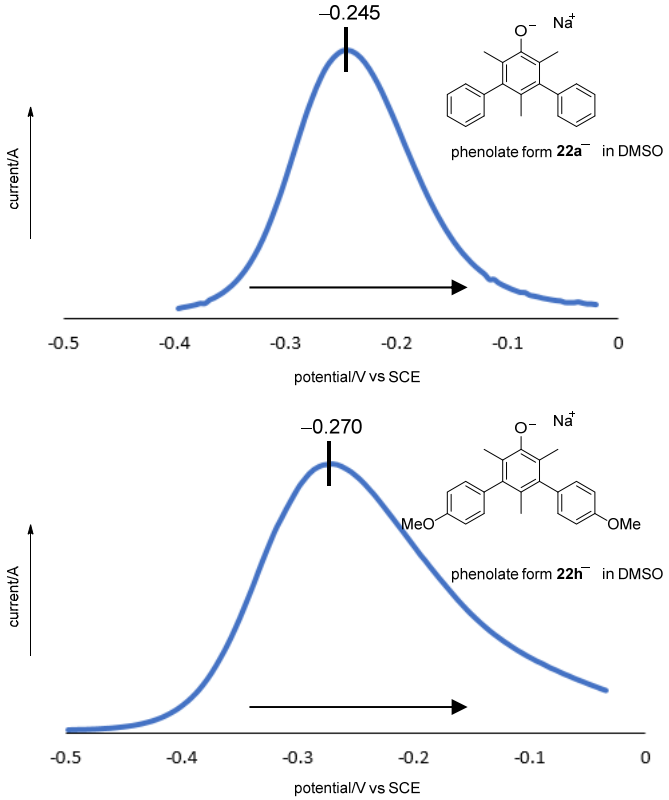
Photo Luminescence Spectroscopy

The sample solution was prepared from a phenol compound, Cs_2CO_3 (1.5 equiv), and DMSO.



Differential Pulse Voltammetry Measurement

The sample solution was prepared from a phenol compound, NaH (1.5 equiv), and DMSO.



Amplitude = 0.05 V, Pulse Width = 0.2 sec, Sample Width = 0.0167 sec, Pulse Period = 0.5 sec, Quiet Time = 2 sec, Sensitivity = 1.00 x 10^{-6} A/V

Estimation for Excited-state Oxidation Potential of Phenolates

We estimated the redox potential of excited phenolates employing the following equation according to the reported procedure (N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075):

$$E(ArO^{\bullet}/ArO^{-*}) = E(ArO^{\bullet}/ArO^{-}) - E_{0,0}$$

$E(ArO^{\bullet}/ArO^{-})$ was estimated by differential pulse voltammetry measurement.

22a^{-} : –0.245 V

22h^{-} : –0.270 V

$E_{0,0}$ was estimated from a wavelength at one-tenth of maximum luminescence intensity.

22a^{-} : 428 nm = 2.90 eV

22h^{-} : 433 nm = 2.86 eV

Therefore,

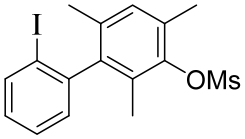
22a^{-} : $E(ArO^{\bullet}/ArO^{-*})$ = –0.245 – 2.90 = –3.145 V

22h^{-} : $E(ArO^{\bullet}/ArO^{-*})$ = –0.270 – 2.86 = –3.130 V

Products

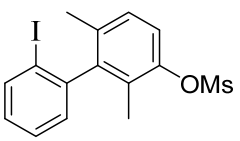
The preparation and characterization of new compounds were described below.

(2a) 2'-iodo-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl methanesulfonate



To a solution of (2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1a**) (0.206 mmol, 90.9 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (1.01 mmol, 97.1 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow sluggish liquid (79.6 mg, 100%).
IR: (neat) 3041 (C-H), 2858 (C-H), 1350 (-OSO_2-), 1177 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.95 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.43 (td, *J* = 7.4, 0.9 Hz, 1H), 7.13 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.08 (td, *J* = 7.4, 1.7 Hz, 1H), 7.03 (s, 1H), 3.28 (s, 3H), 2.43 (s, 3H), 1.97 (s, 3H), 1.91(s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 145.1 (s), 145.0 (s), 143.3 (s), 139.2 (d), 134.7 (s), 131.2 (s), 130.4 (d), 129.8 (s), 129.7 (d), 128.9 (d), 128.67 (d), 100.3 (s), 39.0 (q), 20.0 (q), 17.7 (q), 15.3 (q); HRMS (ESI+) Calculated ($C_{16}H_{17}O_3SINa$) 438.9835 ($[M+Na]^+$) Found: 438.9832

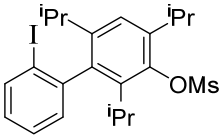
(2b) 2'-iodo-2,6-dimethyl-[1,1'-biphenyl]-3-yl methanesulfonate



To a solution of (2',6'-dimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1b**) (0.204 mmol, 86.0 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (1.15 mmol, 111 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated,

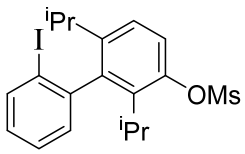
and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow sluggish liquid (62.7 mg, 77%).
IR: (neat) 3031-2937 (C-H), 1369 (-OSO_2-), 1153 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.96 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.45 (td, *J* = 8.0, 1.6 Hz, 1H), 7.30 (d, *J* = 8.6 Hz), 7.16 (d, *J* = 8.6 Hz, 1H), 7.13 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.08 (td, *J* = 8.0, 1.6 Hz, 1H), 3.18 (s, 3H), 1.954 (s, 3H), 1.948 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 146.0 (s), 145.8 (s), 144.6 (s), 139.2 (d), 135.2 (s), 129.3 (d), 129.2 (s), 129.0 (d), 128.8 (d), 128.2 (d), 121.4 (d), 99.8 (s), 37.7 (q), 20.2 (q), 14.2 (q); HRMS (ESI+) Calculated ($C_{15}H_{15}O_3SINa$) 424.96788 ($[M+Na]^+$) Found: 424.96750

(2c) 2'-iodo-2,4,6-triisopropyl-[1,1'-biphenyl]-3-yl methanesulfonate



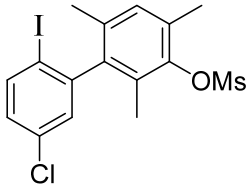
To a solution of (2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1c**) (0.192 mmol, 100.9 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (0.96 mmol, 92.1 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow solid (54.6 mg, 57%).
mp: 129-133 °C; IR: (KBr) 2959 (C-H), 2939 (C-H), 1349 (-OSO_2-), 1176 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.93 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.39 (td, *J* = 8.0, 1.4 Hz, 1H), 7.24 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.20 (s, 1H), 7.05 (td, *J* = 8.0, 1.4 Hz, 1H), 3.47 (septet, *J* = 6.4 Hz, 1H), 3.32 (s, 3H), 3.15 (septet, *J* = 8.2 Hz, 1H), 2.27 (septet, *J* = 7.0 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.21 (d, *J* = 8.2 Hz, 3H), 1.00 (d, *J* = 8.2 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 146.0 (C), 144.6 (C), 143.8 (C), 142.4 (C), 141.6 (C), 138.8 (CH,, 137.5 (C), 131.2 (CH), 128.7 (CH), 127.4 (CH), 122.2 (CH), 103.5 (C), 39.2 (CH_3), 30.1 (CH), 29.5 (CH), 28.0 (CH), 24.9 (CH_3), 23.9 (CH_3), 23.7 (CH_3), 23.2 (CH_3), 22.6 (CH_3), 21.0 (CH_3); HRMS (ESI+) Calculated ($C_{22}H_{29}O_3SINa$) 523.07519 ($[M + Na]^+$) Found: 523.07743

(2d) 2'-iodo-2,6-diisopropyl-[1,1'-biphenyl]-3-yl methanesulfonate



To a solution of (2',6'-diisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1d**) (0.202 mmol, 97.2 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (1.02 mmol, 98.2 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow sluggish liquid (76.4 mg, 79%).
IR: (neat) 2962 (C-H), 1351 (-OSO_2-), 1174 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.96 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.6 Hz, 1H), 7.41 (td, *J* = 8.0, 1.5 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.13 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.08 (td, *J* = 8.0, 1.5 Hz, 1H), 3.26 (s, 3H), 2.52 (septet, *J* = 7.0 Hz, 1H), 2.32 (septet, *J* = 7.0 Hz, 1H), 1.35 (d, *J* = 7.0 Hz, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 147.1 (C), 145.0 (C), 144.7 (C), 144.2 (C), 139.0 (CH), 136.1 (CH) 129.8 (CH), 128.9 (CH), 128.1 (CH), 124.5 (CH), 120.4 (CH), 101.0 (C), 38.9 (CH_3), 30.7 (CH), 30.5 (CH), 24.7 (CH_3), 23.2 (CH_3), 21.44 (CH_3), 21.40 (CH_3); HRMS (ESI+) Calculated ($C_{19}H_{23}O_3SINa$) 481.03048 ($[M + Na]^+$) Found: 481.03019

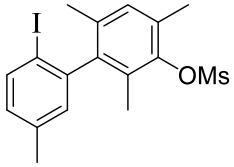
(2e) 5'-chloro-2'-iodo-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl methanesulfonate



To a solution of (5-chloro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1e**) (0.205 mmol, 97.1 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (0.95 mmol, 91.2 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a white solid (70.9 mg, 77%).

mp: 105-106 °C; IR: (KBr) 3053 (C-H), 2950 (C-H), 1351 (-OSO_2-), 1178 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.86 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 2.4 Hz, 1H), 7.06 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 (s, 1H), 3.29 (s, 3H), 2.42 (s, 3H), 1.98 (s, 3H), 1.92 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 146.6 (s), 145.0 (s), 142.0 (s), 140.2 (d), 134.9 (s), 134.4 (s), 131.7 (s), 130.6 (d), 129.7 (s), 129.6 (d), 129.2 (d), 97.6 (s), 39.0 (q), 20.0 (q), 17.6 (q), 15.3 (q); HRMS (ESI+) Calculated ($C_{16}H_{16}O_3SClINa$) 472.94456 ([M + Na]$^+$) Found: 472.94452

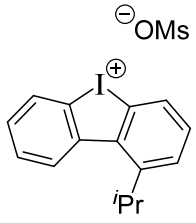
(2f) 2'-iodo-2,4,5',6-tetramethyl-[1,1'-biphenyl]-3-yl methanesulfonate



To a solution of (2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1f**) (0.196 mmol, 89.1 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (0.99 mmol, 95.1 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 2.6 cm) to give the titled compound as a yellow solid (60.4 mg, 72%).

IR: (KBr) 3050 (C-H), 2918 (C-H), 1353 (-OSO_2-), 1171 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 7.79 (d, J = 8.2 Hz, 1H), 7.02 (s, 1H), 6.95 (d, J = 2.0 Hz, 1H), 6.80 (dd, J = 8.2, 2.0 Hz, 1H), 3.28 (s, 3H), 2.42 (s, 3H), 2.32 (s, 3H), 1.97 (s, 3H), 1.91 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 145.1 (s), 144.7 (s), 143.3 (s), 138.8 (d), 138.7 (s), 134.7 (s), 131.1 (s), 130.43 (d), 130.37 (d), 129.9 (d), 129.8 (s), 96.1 (s), 39.0 (q), 21.0 (q), 20.1 (q), 17.7 (q), 15.3 (q); HRMS (ESI+) Calculated ($C_{17}H_{19}O_3SINa$) 452.99918 ([M+Na]$^+$) Found: 452.99784

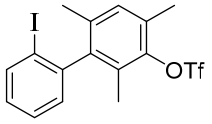
(3) 1-isopropyldibenzo[*b,d*]iodol-5-ium methanesulfonate



To a solution of (2'-isopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1g**) (0.193 mmol, 84.9 mg) in CH_2Cl_2 (5 mL) was added methane sulfonic acid (1.07 mmol, 103 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as an orange solid (65.2 mg, 77%).

mp: 35-36 °C; IR: (KBr) 2966 (C-H), 1166 (-OSO_2-) cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$): 8.76 (d, J = 7.9 Hz, 1H), 8.57 (d, J = 7.7 Hz, 1H), 8.32 (d, J = 7.9 Hz, 1H), 7.74-7.70 (m, 2H), 7.57 (t, J = 7.9 Hz, 1H), 7.49 (t, J = 7.7 Hz, 1H), 3.98 (septet J = 6.8 Hz, 1H), 3.08 (s, 3H), 1.46 (d, J = 6.8 Hz, 6H); ^{13}C NMR: (100 MHz, $CDCl_3$): 150.4 (s), 142.7 (s), 138.6 (s), 132.2 (d), 130.2 (d), 130.0 (d, overlapping), 129.8 (d), 129.6 (d), 128.2 (d), 122.4 (s), 120.6 (s), 40.1 (q), 29.9 (d), 23.4 (q); HRMS: (ESI+) Calculated ($C_{15}H_{14}I$) 321.01347 ([M - OMs]$^+$) Found: 321.01248

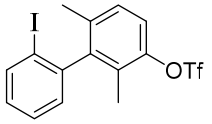
(4a) 2'-iodo-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of (2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1a**) (0.191 mmol, 84.2 mg) in CH_2Cl_2 (5 mL) was added trimethylsilyl trifluoromethanesulfonate (0.995 mmol, 212 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5, column length 10 cm, diameter 2.6 cm) to give the clear liquid (78.9 mg, 88%).

IR: (neat) 3050 (C-H), 2973 (C-H), 1380 (-OSO_2-), 1140 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.96 (d, J = 7.8 Hz, 1H), 7.44 (td, J = 7.8, 0.8 Hz, 1H), 7.12 (dd, J = 7.8, 0.8 Hz, 1H), 7.10-7.06 (m, 2H) 2.42 (s, 3H), 1.97 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.1 (s), 144.4 (s), 143.8 (s), 139.3 (d), 136.0 (s), 130.9 (d), 130.6 (s), 129.6 (d), 129.5 (s), 129.1 (d), 128.8 (d), 118.6 (s, q, $J_{C\text{-}F}$ = 535 Hz), 100.0 (s), 20.1 (q), 17.2 (q), 14.9 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -73.0 (s, 3F, CF_3); HRMS (EI) Calculated ($C_{16}H_{14}F_3O_3SI$) 469.9660 ([M]$^+$) Found: 469.9667

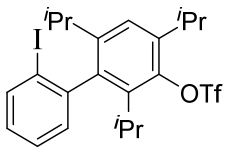
(4b) 3-(2-iodophenyl)-2,4-dimethylphenyl trifluoromethanesulfonate



To a solution of (2',6'-dimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1b**) (0.209 mmol, 89.1 mg) in CH_2Cl_2 (5 mL) was added Me_3SiOTf (1.09 mmol, 242 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a colorless sluggish liquid (70.0 mg, 74%).

IR: (neat) 3052 (C-H), 2926 (C-H), 1421 (-OSO_2-), 1217 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.97 (dd, J = 7.8, 1.0 Hz, 1H), 7.46 (td, J = 7.8, 1.0 Hz, 1H), 7.21-7.17 (m, 2H), 7.14-7.08 (m, 2H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 146.8 (s), 146.1 (s), 144.1 (s), 139.4 (d), 136.4 (s), 129.3 (d), 129.2 (d), 129.0 (s), 128.8 (d), 128.5 (d), 120.5 (d), 118.6 (s, q, J = 322 Hz), 99.5 (s), 20.3 (q), 14.1 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -74.3 (s, 3F, CF_3); HRMS (FAB+) Calculated ($C_{15}H_{12}F_3O_3SI$) 455.9504 ([M]$^+$) Found: 455.9501

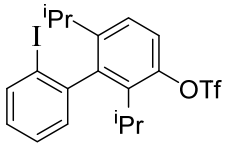
(4c) 2'-iodo-2,4,6-triisopropyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of (2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1c**) (0.200 mmol, 105 mg) in CH_2Cl_2 (5 mL) was added Me_3SiOTf (1.04 mmol, 231 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a white solid (55.8 mg, 51%).

mp: 76-78 °C; IR (KBr): 2966 (C-H), 1397 (-OSO_2-), 1219 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.93 (dd, J = 7.8, 1.2 Hz, 1H), 7.39 (td, J = 7.8, 1.2 Hz, 1H), 7.26-7.24 (m, 2H), 7.07 (td, J = 7.8, 1.2 Hz, 1H), 3.39 (septet, J = 7.0 Hz, 1H), 3.23 (septet, J = 7.6 Hz, 1H), 2.29 (septet, J = 7.0 Hz, 1H), 1.30-1.28 (m, 6H), 1.25 (d, J = 7.0 Hz, 3H), 1.15 (d, J = 7.6 Hz, 3H), 0.96 (d, J = 7.6 Hz, 3H), 0.93 (d, J = 7.0 Hz, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 147.7 (C), 144.0 (C), 142.8 (C), 142.0 (C, two signals are overlapping), 138.9 (CH), 137.8 (C), 131.4 (CH), 129.0 (CH), 127.4 (CH), 122.7 (CH), 118.7 (s, q, $J_{C\text{-}F}$ = 322 Hz), 103.6 (C), 30.0 (CH), 29.0 (CH), 27.6 (CH), 24.9 (CH_3), 23.8 (CH_3), 23.5 (CH_3), 23.0 (CH_3), 22.8 (CH_3), 20.7 (CH_3); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -73.5 (s, 3F, CF_3); HRMS (ESI+) Calculated ($C_{22}H_{26}O_3F_3SINa$) 577.04916 ([M + Na]$^+$) Found: 577.04836

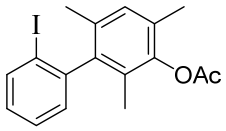
(4d) 2'-iodo-2,6-diisopropyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of (2',6'-diisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1d**) (0.198 mmol, 95.3 mg) in CH_2Cl_2 (5 mL) was added Me_3SiOTf (1.06 mmol, 235.1 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) to give the titled compound as a colorless sluggish liquid (82.5 mg, 83%).

IR: (neat) 2965 (C-H), 1143 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.97 (d, J = 7.8 Hz, 1H), 7.43 (td, J = 7.8, 0.8 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 7.28 (d, J = 9.2 Hz, 1H), 7.13-7.07 (m, 2H), 2.57 (septet, J = 7.2 Hz, 1H), 2.34 (septet, J = 7.0 Hz, 1H), 1.36 (d, J = 7.2 Hz, 3H), 1.23 (d, J = 7.0 Hz, 3H), 1.14 (d, J = 7.2 Hz, 3H), 0.97 (d, J = 7.0 Hz, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 147.4 (s), 146.6 (s), 144.5 (s), 144.3 (s), 139.1 (d), 136.9 (d), 129.7 (d), 129.1 (d), 128.1 (d), 124.9 (d), 120.8 (d), 118.4 (s, q, J = 322 Hz), 100.8 (s), 30.63 (d), 30.60 (d), 24.7 (q), 23.1 (q), 21.2 (q), 20.9 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -73.2 (s, 3F, CF_3); HRMS (EI) Calculated ($C_{19}H_{20}O_3F_3SI$) 512.0130 ($[M]^+$) Found: 512.0119

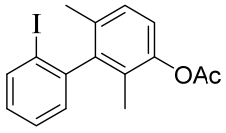
(5a) 2'-iodo-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl acetate



To a solution of (2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1a**) (0.208 mmol, 91.8 mg) in CH_2Cl_2 (5 mL) was added acetic acid (4.20 mmol, 252 mg) and BF_3•OEt_2 (0.434 mmol, 61.2 mg). The mixture was stirred at 0 °C for 6 h and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5, column length 10 cm, diameter 2.6 cm) to give the titled compound as a colorless sluggish liquid (29.3 mg, 39%).

IR: (neat) 2924 (C-H), 1746 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.95 (d, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.15 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 7.01 (s, 1H), 2.35 (s, 3H), 2.19 (s, 3H), 1.91 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.0 (s), 146.2 (s), 145.3 (s), 142.7 (d), 139.0 (s), 133.3 (s), 129.8 (d), 129.6 (d), 129.3 (s), 128.7 (d), 128.5 (d), 128.0 (s), 100.6 (s), 20.5 (q), 20.0 (q), 16.4 (q), 13.8 (q); HRMS (ESI+) Calculated ($C_{17}H_{17}O_2INa$) 403.01654 ($[M+Na]^+$) Found: 403.01605

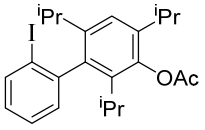
(5b) 2'-iodo-2,6-dimethyl-[1,1'-biphenyl]-3-yl acetate



To a solution of (2',6'-dimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1b**) (0.198 mmol, 84.3 mg) in CH_2Cl_2 (5 mL) was added acetic acid (1.02 mmol, 61.2 mg) and BF_3•OEt_2 (0.419 mmol, 59.2 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 2.6 cm) to give the titled compound as a colorless sluggish liquid (28.2 mg, 39%).

IR: (neat) 3045 (C-H), 2923 (C-H), 1714 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.95 (dd, J = 7.8, 1.2 Hz, 1H), 7.30 (td, J = 7.8, 1.2 Hz, 1H), 7.17-7.12 (m, 2H), 7.06 (td, J = 7.8, 1.2 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H), 2.33 (s, 3H), 1.94 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.5 (s), 147.4 (s), 145.13 (s), 145.10 (s), 139.2 (d), 133.6 (s), 129.5 (d), 128.8 (d), 128.6 (d), 128.1 (s), 127.9 (d), 121.2 (d), 100.1 (s), 20.9 (q), 20.2 (q), 13.6 (q); HRMS (ESI+) Calculated ($C_{16}H_{15}O_2INa$) 389.00089 ($[M + Na]^+$) Found: 388.99908

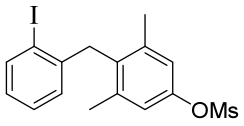
(5c) 2'-iodo-2,4,6-triisopropyl-[1,1'-biphenyl]-3-yl acetate



To a solution of (2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1c**) (0.205 mmol, 107.3 mg) in CH_2Cl_2 (5 mL) was added BF_3•OEt_2 (0.438 mmol, 62.2 mg) and AcOH (4.17 mmol, 251 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (only hexane, column length 10 cm, diameter 2.6 cm) and recycle GPC ($CHCl_3$) to give the titled compound as a white solid (24.0 mg, 26%).

mp: 130-131 °C; IR: (KBr) 2961 (C-H), 1753 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.94 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.7 Hz, 1H), 7.15 (m, 2H), 7.04 (dd, J = 7.7, 1.6 Hz, 1H), 2.81 (septet, J = 6.8 Hz, 1H), 2.48 (septet, J = 7.0 Hz, 1H), 2.35 (s, 3H), 2.31 (septet, J = 7.0 Hz, 1H), 1.33-1.21 (m, 12H), 0.96-0.95 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 170.1 (C), 145.7 (C), 144.9 (C), 144.0 (C), 140.9 (C), 138.8 (CH), 135.8 (C), 130.2 (CH), 129.9 (C), 128.4 (CH), 127.9 (CH), 121.3 (CH), 101.8 (C), 30.8 (CH), 30.6 (CH), 27.4 (CH), 24.9 (CH_3), 24.4 (CH_3), 23.4 (CH_3), 22.5 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 21.2 (CH_3); HRMS (ESI+) Calculated ($C_{23}H_{29}O_2INa$) 487.11044 ($[M + Na]^+$) Found: 487.11033

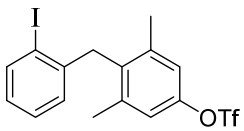
(7a) 4-(2-iodobenzyl)-3,5-dimethylphenyl methanesulfonate



To a solution of {2-(2,6-dimethylbenzyl)phenyl}-λ^3-iodanediyl diacetate (**6**) (0.203 mmol, 89.5 mg) in CH_2Cl_2 (5 mL) was added methanesulfonic acid (1.05 mmol, 101 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a pale yellow solid (69.1 mg, 82%).

mp: 95-96 °C; IR: (KBr) 3034 (C-H), 2913 (C-H), 1362 (-OSO_2-), 1171 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.89 (d, J = 7.6 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.02 (s, 2H), 6.91 (t, J = 7.6 Hz, 1H), 6.47 (d, J = 7.6 Hz, 1H), 3.95 (s, 2H), 3.18 (s, 3H), 2.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 147.4 (s), 140.9 (s), 139.6 (s), 139.3 (d), 135.9 (s), 128.5 (d), 128.0 (d), 127.4 (d), 121.2 (d), 101.7 (s), 40.9 (t), 37.4 (q), 20.2 (q); HRMS: (ESI+) Calculated ($C_{16}H_{17}O_3SINa$) 438.98353 ($[M+Na]^+$) Found: 438.98283

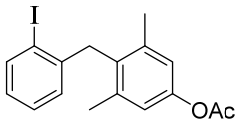
(7b) 4-(2-iodobenzyl)-3,5-dimethylphenyl trifluoromethanesulfonate



To a solution of {2-(2,6-dimethylbenzyl)phenyl}-λ^3-iodanediyl diacetate (**6**) (0.205 mmol, 90.1 mg) in CH_2Cl_2 (5 mL) was added Me_3SiOTf (0.98 mmol, 218 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layer was dried over Na_2SO_4. The solvent was evaporated, and the residue was purified by column chromatography (hexane/ethyl acetate = 90:10, column length 20 cm, diameter 2.6 cm) to give the titled compound a white solid (0.085 g, 89%).

mp: 72-74 °C; IR: (KBr) 3069-2859 (C-H), 1422 (-OSO_2-), 1138 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.89 (d, J = 7.0 Hz, 1H), 7.15 (t, J =7.0 Hz, 1H), 7.00 (s, 2H), 6.91 (t, J = 7.0 Hz, 1H), 6.43 (d, J = 7.0 Hz, 1H), 3.96 (s, 2H) 2.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 147.8 (s), 140.6 (s), 140.0 (s), 139.4 (d), 137.1 (s) 128.5 (d), 128.1 (d), 127.2 (d), 118.7 (s, q, $^1J_{C\text{-}F}$ = 322 Hz), 120.4 (d), 101.6 (s), 40.9 (t), 20.2 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -73.1 (s, 3F, CF_3); HRMS: (EI) Calculated ($C_{16}H_{14}F_3IO_3S$) 469.9660 ($[M]^+$) Found: 469.9670

(7c) 4-(2-iodobenzyl)-3,5-dimethylphenyl acetate

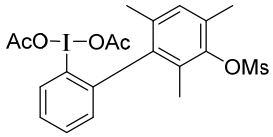


To a solution of {2-(2,6-dimethylbenzyl)phenyl}-λ^3-iodanediyl diacetate (**6**) (0.191 mmol, 84.1 mg) in CH_2Cl_2 (5 mL) was added BF_3•OEt_2 (0.432 mmol, 61.3 mg) and AcOH (1.02 mmol, 61.3 mg). The mixture was stirred at room temperature for 6 h and then quenched by water (5 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 10 cm, diameter 2.6 cm) to give the titled compound as a pale yellow solid (42.8 mg, 57%).

mp: 86-87 °C; IR: (KBr) 2919 (C-H), 1755 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.88 (dd, J = 7.8, 1.4 Hz, 1H), 7.13 (td, J = 7.8, 1.4 Hz, 1H), 6.89 (td, J = 7.8, 1.4 Hz, 2H), 6.87 (s, 2H), 6.53 (dd, J = 7.8, 1.4 Hz, 1H), 3.93 (s, 2H), 2.30 (s, 3H), 2.16 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.8 (s), 148.9 (s), 141.4 (s), 139.2 (d), 138.8 (s), 134.1 (s), 128.4 (d, C-10), 127.9 (d), 127.7 (d), 120.9 (d), 101.7 (s), 40.9 (t), 21.2 (q), 20.1 (q); HRMS (ESI+) Calculated ($C_{17}H_{17}O_2INa$) 403.01654 ([M+Na]$^+$) Found: 403.01631

Synthesis of 3,5-diaryl-phenols via mesyloxylation and trifluoromethanesulfonyloxylation (Scheme 5)

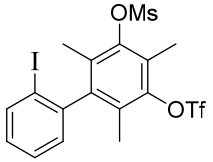
(19a) (2',4',6'-trimethyl-3'-((methylsulfonyl)oxy)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl methanesulfonate (**2a**) (1.29 g, 2.09 mmol) and 9% peracetic acid (13 mL). The reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as a white solid (1.01 g, 91%).

mp: 113-114 °C; IR: (KBr) 3006 (C-H), 2928 (C-H), 1644 (C=O), 1349 (O=S=O), 1177 (O=S=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8.40 (d, J = 7.6 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.50-7.45 (m, 2H), 7.02 (s, 1H), 3.30 (s, 3H), 2.42 (s, 3H), 2.06 (s, 3H), 2.01 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (s), 145.0 (s), 143.8 (s), 140.0 (s), 138.1 (d), 135.4 (s), 132.9 (d), 132.1 (s), 131.2 (s), 130.9 (d), 130.5 (d), 129.9 (d), 126.2 (s), 39.1 (q), 20.2 (q), 20.1 (q), 17.6 (q), 15.8 (q); HRMS (ESI+) Calculated ($C_{20}H_{23}O_7SINa$) 557.01014 ([M + Na]$^+$) Found: 557.01111

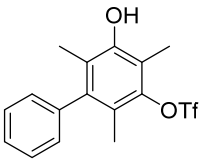
(20a) 2'-iodo-2,4,6-trimethyl-5-((methylsulfonyl)oxy)-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of (2',4',6'-trimethyl-3'-((methylsulfonyl)oxy)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**19a**) (1.88 mmol, 1.01 g) in CH_2Cl_2 (50 mL) was added trifluoromethanesulfonic acid (9.87 mmol, 1.48 g). The mixture was stirred at room temperature for 6 h and then quenched by water (20 mL). The mixture was extracted with chloroform (3 x 10 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by by silica gel column chromatography (hexane/ethyl acetate = 80:20, column length 10 cm, diameter 26 mm silica gel) and recycle GPC ($CHCl_3$) to give the titled compound as a colorless sluggish liquid (0.499 g, 48%).

IR: (neat) 3033 (C-H), 2941 (C-H), 1362 (-OSO_2-), 1141 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.97 (dd, J = 8.0, 1.2 Hz, 1H), 7.47 (td, J = 8.0, 1.2 Hz, 1H), 7.16 (dd, J = 8.0, 1.2 Hz, 1H), 7.11 (td, J = 8.0, 1.2 Hz, 1H), 3.32 (s, 3H), 2.49 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.2 (s), 144.8 (s), 144.5 (s), 143.4 (s), 139.4 (d), 131.2 (s), 129.55 (d), 129.51 (d), 129.3 (s), 128.9 (d), 126.5 (s), 118.5 (s, q, $J_{C\text{-}F}$ = 322 Hz), 99.6 (s), 39.2 (q), 15.6 (q), 15.1 (q), 12.8 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -76.3 (s, 3F, CF_3); HRMS: (ESI+) Calculated ($C_{17}H_{16}F_3O_6S_2INa$) 586.92773 ([M + Na]$^+$) Found: 586.92591

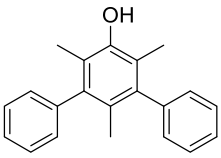
(21a) 5-hydroxy-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of 2'-iodo-2,4,6-trimethyl-5-((methylsulfonyl)oxy)-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (**20a**) (0.263 g, 0.466 mmol) in THF (2 mL) was added ^{n}BuLi (0.37 mL of a 2.6 M solution in *n*-hexane, 0.96 mmol) at -78 °C. The mixture was stirred for 1 hour at -78 °C and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5, column length 10 cm, diameter 2.6 cm) to give the titled compound as a pale yellow liquid (0.139 g, 84%).

IR: (neat) 3581 (OH), 2938 (C-H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.44 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 2H), 4.81 (s, 1H), 2.32 (s, 3H), 1.96 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 150.9 (s), 145.0 (s), 141.8 (s), 139.6 (s), 129.1 (d), 128.6 (d), 127.3 (d), 121.9 (s), 121.5 (s), 118.6 (s, q, $J_{C\text{-}F}$ = 321 Hz), 116.5 (s), 14.9 (q), 13.7 (q), 10.6 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -73.9 (s, 3F, CF_3); HRMS (FAB+) Calculated ($C_{16}H_{15}F_3O_4S$) 360.0643 ([M]$^+$) Found: 360.0635

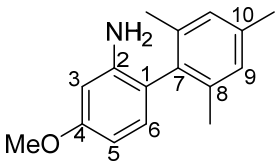
(22a) 2',4',6'-trimethyl-[1,1':3',1''-terphenyl]-5'-ol



To the flame-dried three-necked flask was added phenylboronic acid (0.041 g, 0.33 mmol), K_2CO_3 (0.070 g, 0.50 mmol), LiCl (0.022 g, 0.50 mmol), and $Pd(PPh_3)_4$ (0.019 g, 0.017 mmol) were then dissolved in 2.5 mL of toluene and 1 mL of H_2O. 5-Hydroxy-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (**21a**) (0.060 g, 0.17 mmol) was added, and the resulting mixture was heated to 95 ˚C for 16 hours. After cooling, the solution was diluted with 3 mL of saturated aqueous NH_4Cl. The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 2.6 cm) to give the titled compound as a white solid (0.018 g, 38%).

mp: 104-106 °C; IR: (KBr) 3579 (OH), 3021 (C-H), 2931 (C-H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.42 (t, 4H), 7.34 (d, 2H), 7.17 (d, 4H), 4.67 (s, 1H), 1.98 (s, 6H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 149.8 (s), 141.5 (s), 140.5 (s), 129.4 (d), 128.3 (d), 126.5 (d), 126.0 (s), 120.4 (s), 18.8 (q), 13.7 (q); HRMS (FAB+) Calculated ($C_{21}H_{20}O$) 288.1514 ([M]$^+$) Found: 288.1515

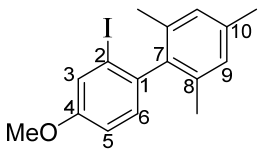
(S7) 4-methoxy-2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine



This manipulation was carried out according to the reported method (T. G. Driver *et al*., *J. Org. Chem.* **2009**, *74*, 3225.). To the flame-dried three-necked flask was added 2,4,6-trimethylphenylboronic acid (3.32 g, 20.2 mmol), K_2CO_3 (8.68 g, 62.8 mmol), and $Pd(PPh_3)_4$ (1.72 g, 1.49 mmol) were then dissolved in 74 mL of toluene, 50 mL of H_2O, and 24 mL of EtOH. 2-bromo-5-methoxyaniline (3.11 mg, 15.4 mmol) and was added, and the resulting mixture was heated to 95 ˚C for 16 hours. After cooling, the solution was diluted with 30 mL of saturated aqueous NH_4Cl. The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 20 cm, diameter 2.6 cm) to give the titled compound as an orange solid 2.16 g, 59%).

mp: 80-82 °C; IR: (neat) 3380 (NH_2), 2950 (C-H), 1202 (C-O-C) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 6.96 (s, 2H), 6.81 (d, J = 8.4 Hz, 1H), 6.40 (dd, J = 8.4, 2.6 Hz, 1H), 6.40 (d, J = 2.6 Hz, 1H), 3.81 (s, 3H), 3.41 (s, 2H), 2.32 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.7 (s), 144.6 (s), 137.6 (s), 136.9 (s), 134.6 (s), 130.7 (d), 128.3 (d), 119.1 (s), 103.9 (d), 100.5 (d), 55.1 (q), 21.1 (q), 20.2 (q); HRMS (DART+) Calculated ($C_{16}H_{20}NO$) 242.15394 ([M + H]$^+$) Found: 242.15422

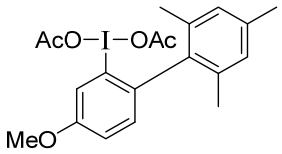
(S8) 2'-iodo-4'-methoxy-2,4,6-trimethyl-1,1'-biphenyl



This manipulation was carried out according to the reported method (*Eur. J. Org. Chem.* **2019**, 696). 4-Methoxy-2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine (**S7**) (12.3 mmol, 2.96 g) was added to a solution of *p*-TsOH•H_2O (37.4 mmol, 7.12 g) in MeCN (53 mL). The resulting precipitate was cooled to 0 °C and a solution of $NaNO_2$ (33.5 mmol, 2.31 g) and KI (38.4 mmol, 6.37 g) in H_2O (62 mL) was added gradually. The reaction mixture was stirred for 3 hours at room temperature and then quenched by water (30 mL) and $NaHCO_3$ aq. The mixture was extracted with ethyl acetate (3 x 10 mL). The collected organic layers were washed with aqueous Na_2SO_3, and dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 20 cm, diameter 2.6 cm) to give the titled compound as a colorless liquid (2.14 g, 50%).

IR: (neat) 2963 (C-H), 2917 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.48 (d, J = 2.7 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 6.96 (dd, J = 8.5, 2.7 Hz, 1H), 6.94 (s, 2H), 3.83 (s, 3H), 2.34 (s, 3H), 1.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 158.4 (s), 140.1 (s), 138.1 (s), 137.2 (s), 136.1 (s), 129.8 (d), 128.0 (s), 123.7 (d), 114.8 (d), 100.7 (s), 55.4 (q), 21.2 (q), 20.4 (q); HRMS (EI) Calculated ($C_{16}H_{17}OI$) 352.0324 ($[M]^+$) Found: 352.0318

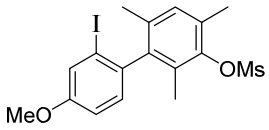
(1h) (4-methoxy-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-4'-methoxy-2,4,6-trimethyl-1,1'-biphenyl (**S8**) (2.09g, 5.85 mmol) and 9% peracetic acid (21 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as an orange solid (2.16 g, 79%).

mp: 75-77 °C; IR: (KBr) 2923 (C-H), 1650 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.90 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 7.22 (dd, J = 8.6, 2.4 Hz, 1H), 6.90 (s, 2H), 3.92 (s, 3H), 2.33 (s, 3H), 2.02 (s, 6H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.4 (s, *C*OCH_3), 159.0 (s), 138.2 (s), 137.4 (s), 136.8 (s), 136.7 (s), 131.2 (d), 128.1 (d), 126.4 (s), 122.6 (d), 119.0 (d), 55.7 (q), 21.1 (q), 20.4 (q), 20.2 (q); HRMS (ESI+) Calculated ($C_{20}H_{23}O_5NaI$) 493.04824 ($[M + Na]^+$) Found: 493.04839

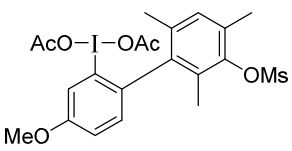
(2h) 3-(2-iodo-4-methoxyphenyl)-2,4,6-trimethylphenyl methanesulfonate



To a solution of (4-methoxy-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**1h**) (3.97 mmol, 1.89 g) in CH_2Cl_2 (80 mL) was added methanesulfonic acid (20.6 mmol, 1.98 g). The mixture was stirred at room temperature for 6 h and then quenched by water (20 mL). The mixture was extracted with chloroform (3 x 10 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 85:15, column length 10 cm, diameter 2.6 cm) to give the titled compound as an orange sluggish liquid (0.897 g, 51%).

IR: (neat) 3006 (C-H), 2937 (C-H), 1360 (-OSO_2-), 1178 (-OSO_2-) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.48 (d, J = 2.0 Hz, 1H), 7.02-6.96 (m, 3H), 3.84 (s, 3H), 3.28 (s, 3H), 2.42 (s, 3H), 1.98 (s, 3H), 1.92 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 158.7 (s), 145.0 (s), 142.9 (s), 137.1 (s), 135.3 (s), 131.1 (s), 130.35 (s), 130.27 (d), 129.8 (d), 124.0 (d), 114.8 (d), 100.2 (s), 55.5 (q), 39.0 (q), 20.1 (q), 17.7 (q), 15.3 (q); HRMS (ESI+) Calculated ($C_{17}H_{19}O_4SINa$) 468.99409 ($[M+Na]^+$) Found: 468.99310

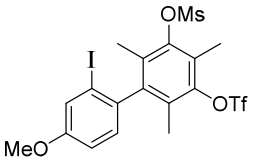
(19h) (4-methoxy-2',4',6'-trimethyl-3'-((methylsulfonyl)oxy)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate



To the flame-dried flask was added 2'-iodo-4'-methoxy-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl methanesulfonate (**2h**) (2.00 mmol 0.893 g) and 9% peracetic acid (7 mL). The reaction mixture was stirred at room temperature over 12 h. The solvent was evaporated, and the sluggish liquid was washed with hexane briefly to give the product as an orange solid (1.02 g, 91%).

mp: 60-61 °C; IR: (KBr) 3010 (C-H), 2938 (C-H), 1649 (C=O), 1361 (-OSO_2-), 1178 (-OSO_2-) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.91 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.5 Hz, 1H), 7.23 (dd, J = 8.5, 2.4 Hz, 1H), 7.00 (s, 1H), 3.93 (s, 3H), 3.29 (s, 3H), 2.41 (s, 3H), 2.07 (s, 3H), 2.01 (s, 3H), 1.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.4 (s), 159.4 (s), 145.0 (s), 139.8 (s), 136.0 (s), 135.6 (s), 132.0 (s), 131.7 (s), 131.2 (d), 130.4 (d), 126.0 (s), 122.8 (d), 119.1 (d), 55.8 (q), 39.1 (q), 20.3 (q), 20.2 (q), 17.6 (q), 15.8 (q); HRMS (ESI+) Calculated ($C_{21}H_{25}O_8SINa$) 587.02070 ([M + Na]$^+$) Found: 587.02126

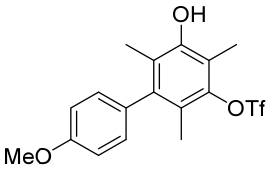
(20h) 2'-iodo-4'-methoxy-2,4,6-trimethyl-5-((methylsulfonyl)oxy)-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of (4-methoxy-2',4',6'-trimethyl-3'-((methylsulfonyl)oxy)-[1,1'-biphenyl]-2-yl)-λ^3-iodanediyl diacetate (**19h**) (1.81 mmol, 1.02 g) in CH_2Cl_2 (45 mL) was added Me_3SiOTf (9.49 mmol, 2.11 g). The mixture was stirred at room temperature for 6 h and then quenched by water (20 mL). The mixture was extracted with chloroform (3 x 5 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by by silica gel column chromatography (hexane/ethyl acetate = 80:20, column length 10 cm, diameter 26 mm silica gel) and recycle GPC ($CHCl_3$) to give the titled compound as a brown sluggish liquid (0.512 g, 48%).

IR: (neat) 3022 (C–H), 2942 (C–H), 1358 (-OSO_2-), 1139 (-OSO_2-) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.49 (d, J = 2.0 Hz, 1H), 7.05-6.99 (m, 2H), 3.85 (s, 3H), 3.32 (s, 3H), 2.48 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$): 159.2 (s), 145.1 (s), 144.7 (s), 144.2 (s), 135.5 (s), 131.7 (s), 129.79 (s), 129.75 (d), 126.3 (s), 124.3 (d), 118.5 (s, q, $J_{C\text{-}F}$ = 321 Hz), 115.0 (d), 99.6 (s), 55.5 (q), 39.1 (q), 15.6 (q), 15.1 (q), 12.8 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -72.1 (s, 3F, CF_3); HRMS (ESI+) Calculated ($C_{18}H_{18}F_3O_7S_2INa$) 616.93829 ([M + Na]$^+$) Found: 616.93797

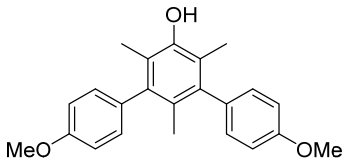
(21h) 5-hydroxy-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate



To a solution of 2'-iodo-4'-methoxy-2,4,6-trimethyl-5-((methylsulfonyl)oxy)-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (**20h**) (0.239 g, 0.447 mmol) in THF (2 mL) was added ^{n}BuLi (0.35 mL of a 2.6 M solution in *n*-hexane, 0.894 mmol) at -78 °C. The mixture was stirred for 1 hour at -78 °C and then quenched by water (3 mL). The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 80:20, column length 10 cm, diameter 2.6 cm) to give the titled compound as a pale yellow liquid (0.106 g, 61%).

IR: (neat) 3578 (OH), 2939 (C-H), 1138 (-OSO_2-) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.01 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 4.88 (s, 1H), 3.86 (s, 3H), 2.31 (s, 3H), 1.97 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 158.6 (s), 150.8 (s), 144.9 (s), 141.5 (s), 131.7 (s), 130.2 (d), 122.3 (s), 121.9 (s), 118.5 (s, q, $J_{C\text{-}F}$ = 322 Hz), 116.3 (s), 113.9 (d), 55.2 (q), 15.0 (q), 13.8 (q), 10.6 (q); ^{19}F NMR (372 MHz, $CDCl_3$, external standard: TFA in D_2O): -72.3 (s, 3F, CF_3); HRMS: (FAB+) Calculated ($C_{17}H_{17}F_3O_5S$) 390.0749 ([M]$^+$) Found: 390.0747

(22h) 4,4''-dimethoxy-2',4',6'-trimethyl-[1,1':3',1''-terphenyl]-5'-ol



To the flame-dried three-necked flask was added 4-methoxyphenylboronic acid (0.063 g, 0.42 mmol), K_2CO_3 (0.091 g, 0.66 mmol), LiCl (0.030 g, 0.71 mmol), and $Pd(PPh_3)_4$ (0.026 g, 0.023 mmol) were then dissolved in 2.8 mL of toluene and 1.2 mL of H_2O. 5-Hydroxy-4'-methoxy-2,4,6-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (**21h**) (0.081 g, 0.21 mmol) was added, and the resulting mixture was heated to 95 ˚C for 16 hours. After cooling, the solution was diluted with 3 mL of saturated aqueous NH_4Cl. The mixture was extracted with chloroform (3 x 3 mL). The collected organic layers were dried over Na_2SO_4. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90:10, column length 10 cm, diameter 2.6 cm) and recycle GPC ($CHCl_3$) to give the titled compound as a white solid (0.022 g, 31%).
mp: 128-129 °C; IR: (KBr) 3456 (OH), 2935 (C-H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.08 (d, J = 8.8 Hz, 4H), 6.96 (d, J = 8.8 Hz, 4H), 4.65 (s, 1H), 3.85 (s, 6H), 1.99 (s, 6H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 158.1 (s), 149.8 (s), 140.1 (s), 133.8 (s), 130.4 (d), 126.9 (s), 120.8 (s), 113.7 (d), 55.2 (q), 18.9 (q), 13.7 (q); HRMS: (ESI+) Calculated ($C_{23}H_{25}O_3$) 349.17982 ($[M + Na]^+$) Found: 349.17988

3-5. Reference

[1] a) S. A. Baechler, M. Fehr, M. Habermeyer, A. Hofmann, K. H. Merz, H. H. Fiebig, D. Marko, G. Eisenbrand, *Bioorg. Med. Chem.* **2013**, *21*, 814. b) J. Wencel-Delord, A. Panossian, F. R. Leroux, F. Colobert, *Chem. Soc. Rev.* **2016**, *44*, 3418.

[2] a) P. Wu, T. E. Nielsen, M. H. Clausen, *Drug Discov. Today* **2016**, *21*, 5. b) S. Yuan, J. Chang, BKhalid, M. A. Zahid, H. Ali, Y. S. Kim, S. Khan, *BMC Neurosci.* **2018**, *19*, 74.

[3] a) D. C. Patel, Z. S. Breitbach, R. M. Woods, Y. Lim, A. Wang, F. W. Foss Jr., D. W. Armstraong, *J. Org. Chem.* **2016**, *81*, 1295. b) J.-H. Tay, A. J. Arguelles, P. Nagorny, *Org. Lett.* **2015**, *17*, 3774. c) T. Uemura, X. Zhang, K. Matsumura, N. Sayo, H. Kumobayashi, T. Ohta, K. Nozaki, H. Takaya, *J. Org. Chem.* **1996**, *61*, 5510.

[4] A review of C–H functionalization of diaryl compounds: J. Wang, C.-F. Liu, Q. Zheng, G.-W. Rao, *Eur. J. Org. Chem.* **2020**, 3737.

[5] a) Iodine Catalysis in Organic Synthesis (Eds.: K. Ishihara, K. Muñiz), Wiley-VCH, Weinheim, **2022**. b) PATAI's Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds (Eds.: B. Olofsson, I. Marek, Z. Rappoport) Wiley-Blackwell, **2019**. c) A. Yoshimura, V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328. d) T. Wirth, Hypervalent Iodine Chemistry (Topics in Current Chemistry, 373), Springer, **2016**.

[6] a) P. A. Evans, T. A. Brandt, *J. Org. Chem.* **1997**, *62*, 5321. b) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai, S. Oka, *J. Am. Chem. Soc.* **1994**, *116*, 3684. c) H. Liu, X. Wang, Y. Gu, *Org. Biomol. Chem.* **2011**, *9*, 1614. d) S. Wang, Z. Ni, Y. Wang, Y. Pang, Y. Pan, *Tetrahedron* **2014**, *70*, 6879. e) M. M. Konnick, B. G. Hashiguchi, D. Devarajan, N. C. Boaz, T. B. Gunnoe, J. T. Groves, N. Gunsalus, D. H. Ess, R. A. Periana, *Angew. Chem. Int. Ed.* **2014**, *53*, 10490. f) S. Maiti, T. Alam, P. Mal, *Asian J. Org. Chem.* **2018**, *7*, 715.

[7] a) H. Liu, Y. Xie, Y. Gu, *Tetrahedron Lett.* **2011**, *52*, 4324. b) A. Pialat, B. Liégault, M. Taillefer, *Org. Lett.* **2013**, *15*, 1764. c) S. C. Fosu, C. M. Hambira, A. D. Chen, J. R. Fuchs, D. A. Nagib, *Chem* **2019**, *5*, 417. d) T. Liang, X. He, D. Ji, H. Wu, Y. Xu, Y. Li, Z. Wang, Y. Xu, Q. Zhu, *Eur. J. Org. Chem.* **2019**, 2513.

[8] G. F. Koser, S. Telua, K. K. Laali, *Tetrahedron Lett.* **2006**, *47*, 7011.

[9] a) K. Hata, H. Hamamoto, Y. Shiozaki, S. B. Cammerer, Y. Kita, *Tetrahedron* **2007**, *63*, 4052.

[10] a) M. Ochiai, T. Ito, Y. Takaoka, Y. Masaki, *J. Am. Chem. Soc.* **1991**, *113*, 1319. b) S. Izquierdo, S. Bouvet, Y. Wu, S. Molina, A. Shafir, *Chem. Eur. J.* **2018**, *24*, 15517. c) W. W. Chen, A. Cunillera, D. Chen, S. Lethu, A. López de Moragas, J. Zhu, M. Solá, A. B. Cuenca, A. Shafir, *Angew. Chem. Int. Ed*. **2020**, *59*, 20201. A review, d) W. W. Chen, A. B. Cuenca, A. Shafir, *Angew. Chem. Int. Ed.* **2020**, *59*, 16294. A review, e) A Shafir, *Tetrahedron Lett.* **2016**, *57*, 2673.

[11] A review, V. V. Grushin, *Chem. Soc. Rev.* **2000**, *29*, 315.

[12] K. Kraszewski, I, Tomczyk, A. Drabinska, K. Bienkowski, R. Solarska, M. Kalek, *Chem. Eur. J.* **2020**, *26*, 11584.

[13] S. Izquierdo, S. Essafi, I. der Rosal, P. Vidossich, R. Pleixats, A. Vallribera, G. Ujaque, A. Lledós, A. Shafir, *J. Am. Chem. Soc.* **2016**, *138*, 12747.
[14] *ortho*-, *meta*-, and *para*-Xylenes all gave ESR spectra centered at $g = 2.0033 \pm 0.0003$. M. Tabata, A. Lund, *Z. Naturforsch.* **1983**, *38a*, 428.
[15] G. F. Koser, R. H. Wettach, *J. Org. Chem.* **1976**, *41*, 3609.
[16] Recent selected reports: a) K. Liang, Q. Liu, L. Shen, X. Li, D. Wei, L. Zheng, C. Xia, *Chem. Sci.* **2020**, *11*, 6996. b) C. Liu, N. Shen, R. Shang, *Nat. Commun.* **2022**, *13*, 354. c) N. Shen, R. Li, C. Liu, X. Shen, W. Guan, R. Shang, *ACS Catal.* **2022**, *12*, 2788.
[17] A review; M. Schmalzbauer, M. Marcon, B. König, *Angew. Chem. Int. Ed.* **2021**, *60*, 6270.
[18] See the Chapter 3-4 for absorption spectra and an estimation of the excited-state redox potential of phenolate forms **22a** and **22h**.

Conclusion

In this study, the modifications of carbon frameworks on hypervalent iodines for controlling reactivity have been developed. The controlling of reactivity by noncovalent interactions in ion pairs, a synergistic substituent effect and a neighboring effect allowed the novel oxidative functionalization.

In chapter 1, it was discovered that the noncovalent interaction between the sulfonyloxy group and the cationic nitrogen-containing heterocyclic moiety substituted in the hypervalent iodines caused specific regioselectivity in the sulfonyloxylactonization of 2-vinyl benzoic acids. Hypervalent iodines bearing an imidazolium moiety exhibited 5-*exo* cyclization selectivity in contrast to 6-*endo* selectivity shown by simple $PhI(OAc)_2$. ^1H NMR spectroscopy established ArI(OTs)OX as the intermediate. DFT studies clarified the trapping of the sulfonyloxy group by the imidazolium moiety via noncovalent interactions such as cation-π and cation-oxygen interactions, which allowed a significant change in regioselectivity.

In chapter 2, the 1-fluoro-1-sulfonyloxylation of styrenes with RSO_3H and Bu_4NBF_4 mediated by *o*-{2,4-$(CF_3)_2C_6H_3$}- and *p*-NO_2-substituted $ArI(OAc)_2$ was achieved. Regression analysis of the substituents suggested the importance of the electron-withdrawing effect and bulkiness in facilitating 1-fluoro-1-sulfonyloxylation. A feasible one-pot synthesis of fluorine-containing building blocks and the synthesis of the fluoroalkylene-tethered bioactive compound were demonstrated.

In chapter 3, iodane-mediated proximal aryl C–H sulfonyloxylation and acetoxylation on 2-iodo-1,1′-biphenyl and 1-benzyl-2-iodobenzene structures were achieved. MsOH, Me_3SiOTf, or BF_3 mediates the elimination of AcO^- from λ^3-iodanediyl diacetates to generate cationic I(III) species. An ESR study supported the key step where intramolecular electron transfer between the cationic I(III) and proximal aryl moieties provides an iodanyl radical intermediate with a radical cationic Ar moiety. The sequential process of two sulfonyloxylations allowed access to 3,5-diaryl-2,4,6-trimethylphenols that functioned as efficient photoredox catalysts in the coupling between an aryl chloride and *N*-methylpyrrole.

Knowledge obtained from Chapter 1 is that the noncovalent attractive forces in ion pairs on hypervalent iodines change the reaction route upon oxidative cyclization. This strategy will be applicable to other cyclization systems. Chapter 2 provided important knowledge that a regression analysis methodology can be applicable in hypervalent iodine chemistry. The strategy of 1,1-heterodifunctionalization via the substituent effect of hypervalent iodines, as revealed by regression analysis, will be further developed in the future. In chapter 3, the intramolecular electron transfer methodology allows the direct functionalization of biaryls which is distinct from the synthesis of 2,2'-difunctionalized biaryls via cyclic diaryliodonium salts. Moreover, this method will enlarge the strategy of iodane-mediated C–H functionalizations.

The knowledge provides us strategies to design the controlling reactivity by modification of carbon frameworks on hypervalent iodines for oxidative functionalization. The insights obtained from the present study have a great contribution to the methodology for the tuning of organic hypervalent iodines.