Doctoral Dissertation

Development of Carbon–Carbon Bond Formation Using α-Heteroatom-Substituted Carbonyl Derivatives by a Photoredox or Lewis Acid Catalyst

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January 2018

Department of Applied Chemistry
Graduate School of Engineering
Osaka University

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(α位ヘテロ原子置換カルボニル化合物類の光レドックス触媒またはルイス酸触媒を用いた炭素－炭素結合形成反応の開発)

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Preface and Acknowledgements

The work of this thesis has been performed from 2012 to 2013 under the guidance of Prof. Akio Baba and from 2013 to 2018 under the guidance of Prof. Makoto Yasuda at Department of Applied Chemistry, Graduate School of Engineering, Osaka University. The thesis describes carbon–carbon bond formation using α-heteroatom-substituted carbonyl derivatives by a photoredox or Lewis acid catalyst.

First and foremost, I would like to express my sincerest gratitude to Professors Dr. Akio Baba and Dr. Makoto Yasuda for their precise guidances, helpful suggestions, and hearty encouragements throughout this work.

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List of Publications

1. **First *anti*-Selective Direct Michael Addition of α-Alkoxy Ketones to Enones by Cooperative Catalysis of Samarium(III) Trifluoromethanesulfonate and Tributyltin Methoxide**
   Naoto Esumi, Yoshihiro Nishimoto, Makoto Yasuda
   Eur. J. Org. Chem. **2017**, *19*, 2831–2835.

2. **Synthesis of 1,4-Dicarbonyl Compounds from Silyl Enol Ethers and Bromocarbonyls, Catalyzed by an Organic Dye under Visible-Light Irradiation with Perfect Selectivity for the Halide Moiety over the Carbonyl Group**
   Naoto Esumi, Kensuke Suzuki, Yoshihiro Nishimoto, Makoto Yasuda
   Org. Lett. **2016**, *18*, 5704–5707.

3. **Generation of α-Iminyl Radicals from α-Bromo Cyclic *N*-Sulfonylimines and Application to Coupling with Various Radical Acceptors Using a Photoredox Catalyst**
   Naoto Esumi, Kensuke Suzuki, Yoshihiro Nishimoto, Makoto Yasuda
   Chem. Eur. J. **2018**, *24*, 312–316.

Supplementary List of Publications

1. **$GaBr_3$-catalyzed Coupling between α-Iodo Esters with Alkynylstannanes under UV Irradiation**
   Itaru Suzuki, Naoto Esumi, Makoto Yasuda, and Akio Baba
   Chem Lett. **2015**, *44*, 38–40.

2. **Photoredox α-Allylation of α-Halocarbonyls with Allylboron Compounds Accelerated by Fluoride Salts under Visible Light Irradiation**
   Itaru Suzuki, Naoto Esumi, Makoto Yasuda
   Asian J. Org. Chem. **2016**, *5*, 179–182.

3. **Regio- and Stereo-controlled Allylation of Aminoallylic Stannanes with Carbonyl Compounds Mediated by Germanium Halides**
   Yoshihiro Nishimoto, Hiroshi Yunoki, Naoto Esumi, Kensuke Tsuruwa, Akio Baba, Makoto Yasuda
   Manuscript under preparation

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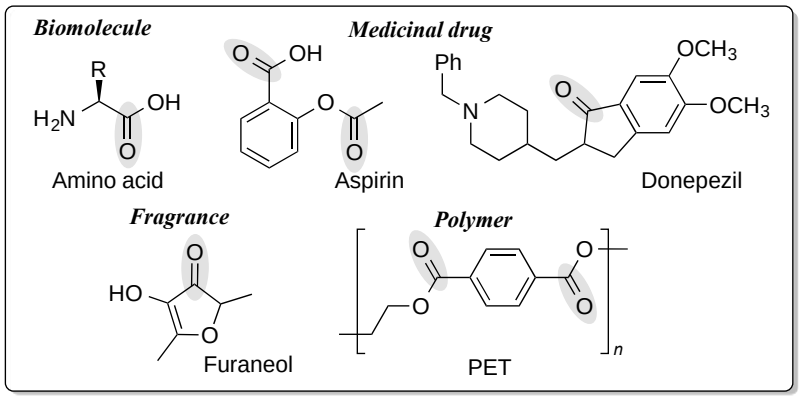
General Introduction

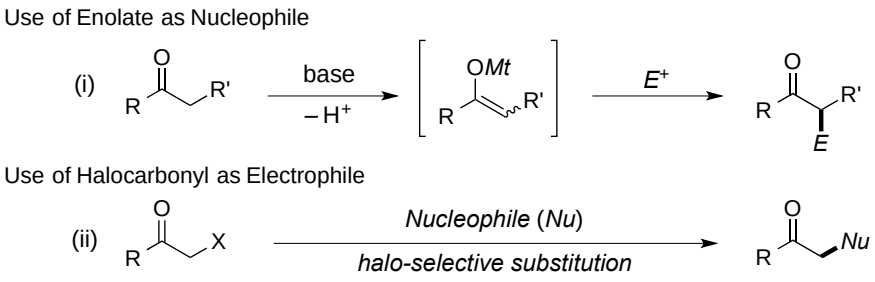
Carbonyl group is one of the most important functional groups in organic chemistry because it is common motif found in bioactive compounds, medicinal drugs, fragrances and polymers (Figure 1). Therefore, the development of introduction of carbonyl units into organic compounds is important for industry and scientific fields. In general, in the production of bulk chemicals, carbonyl compounds are synthesized by oxidation reaction[1] such as cumene process or Wacker process, and the reaction utilizing carbon monoxide[2] like Monsanto process or hydroformylation. In the synthesis of fine chemicals, various coupling reactions such as aldol reaction, Michael addition, Friedel-Crafts reaction and cross-coupling reaction using transition-metal catalysts are used to afford highly functionalized carbonyl compounds.[3]

Figure 1. Typical example of functionalized carbonyl compounds.



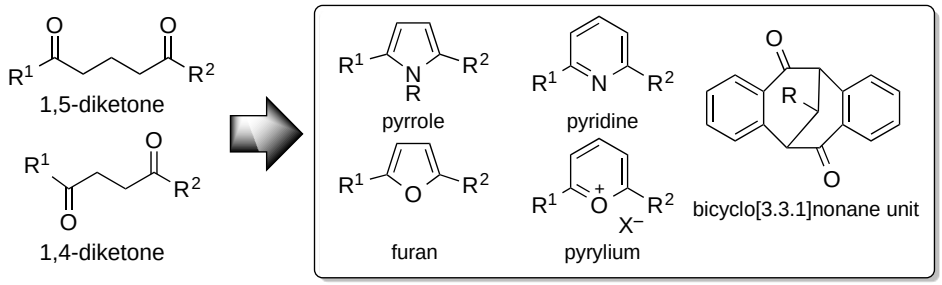
In particular, in the field of fine chemical, α-functionalization of carbonyl compounds makes one of the effective methods for the introduction of carbonyl unit into many types of organic compounds (Scheme 1). Typical reactions of α-functionalization consist of two type of reactions; i) the reaction of enolates with electrophiles, ii) the reaction of halocarbonyls with nucleophiles. Many reactions introducing carbonyl units, for example aldol reaction or Claisen condensation or Mannich reaction, are categorized into α-functionalization of carbonyl compounds.

Scheme 1. Representative α-functionalization of carbonyls.



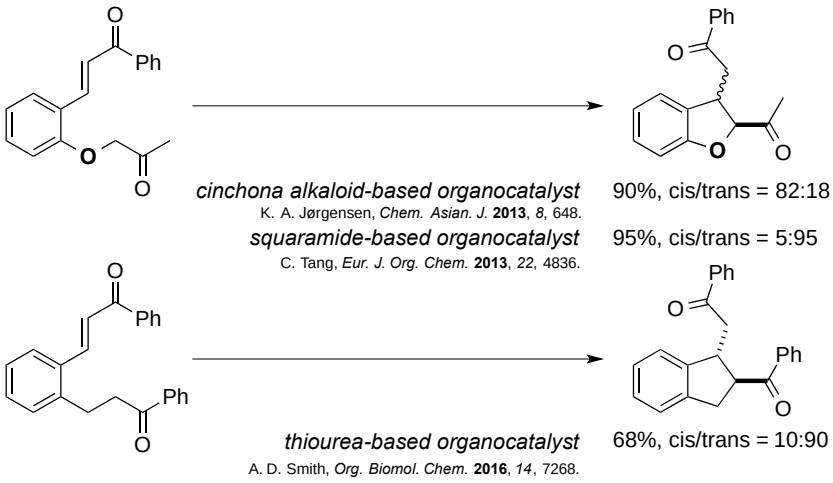
Dicarbonyl compounds, which are often synthesized by α-functionalization of carbonyl compounds, are fundamental molecules in organic chemistry. In particular, 1,5-diketones and 1,4-diketones are important compounds in organic chemistry because many bioactive compounds[4] and natural products[5] include these units and heterocyclic compounds such as pyrroles, furanes and pyridines are synthesized from 1,5-diketones or 1,4-diketones.[6] In addition, bicyclo[3.3.1]nonane unit, which works as estrogen receptors, is given from 1,5-diketones (Scheme 2).[7] Therefore, the development of the effective and economical synthetic method of 1,5-diketones and 1,4-diketones is valuable research theme.

Scheme 2. Utility of 1,4- and 1,5-diketones.



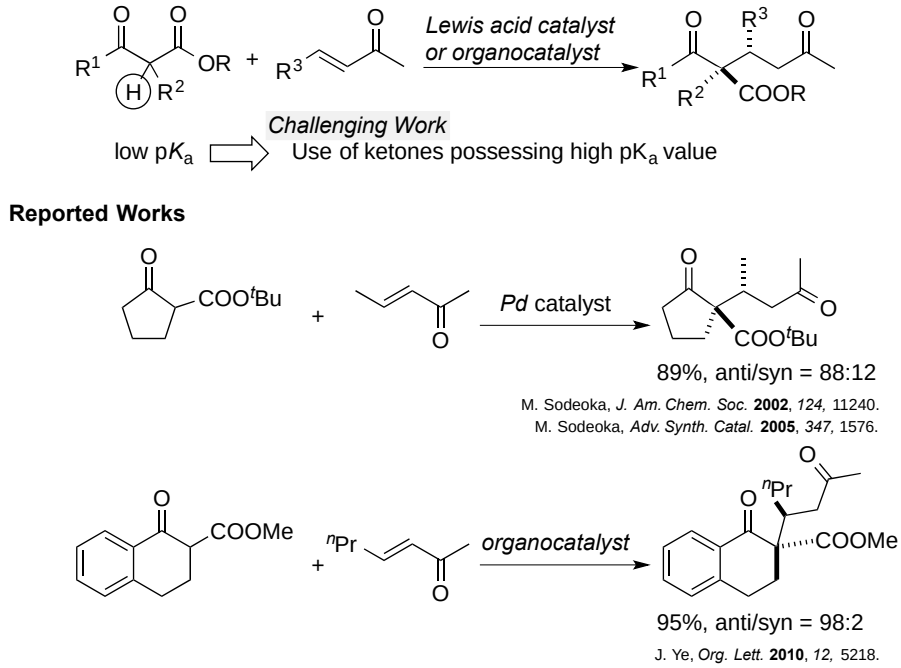
1,5-diketones are generally obtained by the Michael reaction of enolates with enones and recently some research groups have developed the direct catalytic stereoselective Michael addition for 1,5-diketones. In particular, diastereoselective reactions are highly important because the difference in stereochemistry of the molecular changes the physical and chemical properties.[8,9] Although an direct catalytic diastereoselective intramolecular Michael addition of various ketone to enone has been performed (Scheme 3),[8] in many cases of direct catalytic diastereoselective intermolecular Micheal addition, the substrate of Michael donor is limited to 1,3-dicarbonyls such as β-ketoesters, which are

Scheme 3. Direct catalytic intramolecular diastereoselective Michael additions.



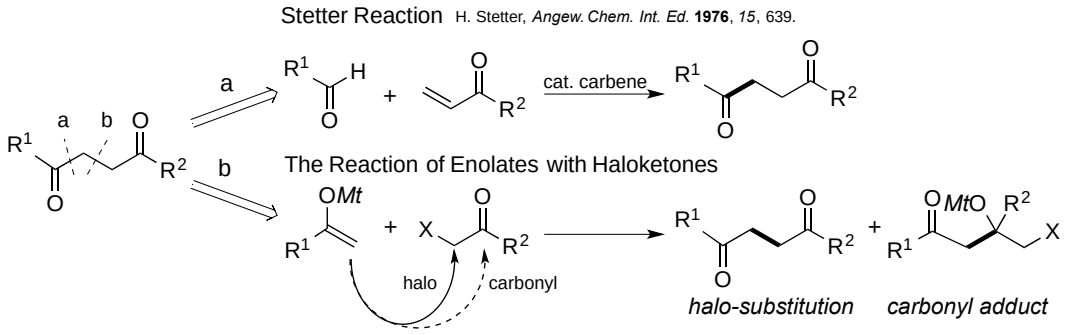
enolizable species (Scheme 4).[9] Therefore, it is needed that the expansion of generality of Michael donor for highly diastereoselective reaction and I investigated the catalytic synthesis of 1,5-diketones by using α-alkoxyketones, which are not used to the catalytic synthesis of 1,5-diketones and are difficult to generate enolate compared with 1,3-dicarbonyls because of p*K*a value.

Scheme 4. 1,5-Diketone synthesis by direct catalytic intermolecular diastereoselective Michael additions.



1,4-Diketones, which are generally synthesized by Stetter reaction,[10] would be also synthesized by the reaction of α-haloketones with enolates based on α-functionalization of carbonyl compounds. However, halo-selective substitution reactions of α-haloketones with enolates are limited because the carbonyl group of α-haloketones also undergoes 1,2-addition with enolates (Scheme 5).[11a] Recently, some research groups developed prefectly halo-selective substitution reactions of haloketones with

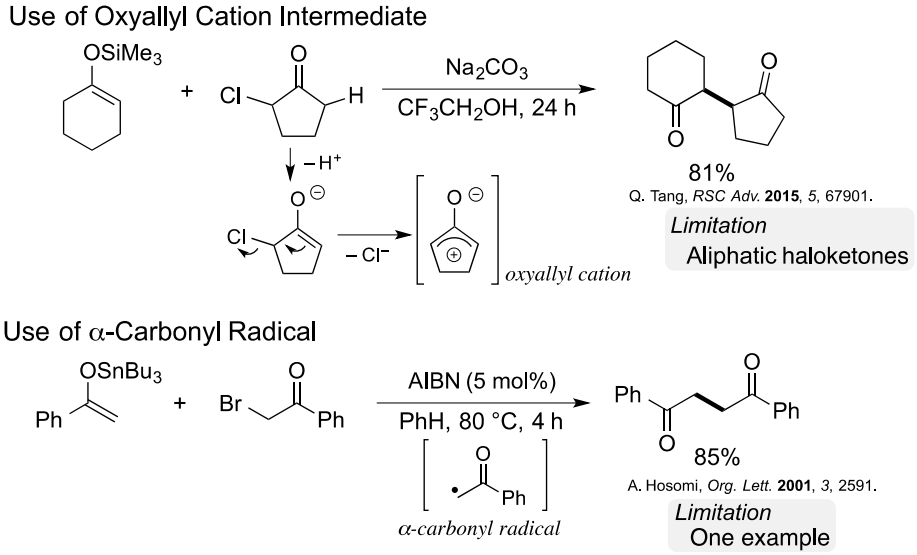
Scheme 5. General strategy for the synthesis of 1,4-diketones.



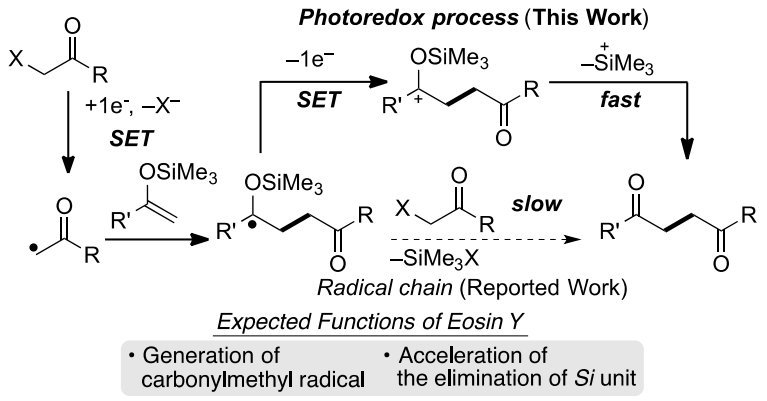
enolates to give 1,4-diketones (Scheme 6).[11b,11c] They utilized basic conditions to generate oxyallyl cations or radical initiator conditions for the accomplishment of the halo-selctive reaction, but these reactions are limited to aliphatic ketones or unsubstituted phenacyl bromide.

On the other hand, radical reactions using photoredox catalyst has much attention for the synthesis of organic compounds because of the easy generation of radical species.[12] Our group has also reported the allylation of α-halocarbonyls catalyzed by organic dye as a photoredox catalyst.[13] In this study, I applied the photoredox catalyst for the synthesis of 1,4-diketone using α-haloketones and silyl enol ethers. Photoredox catalysts would be expected for the effective generation of α-carbonyl radical by the single electron reduction and the smooth elimination of the silyl unit by the single electron oxidation of a radical adduct of the α-carbonyl radicals and silyl enol ethers to give the 1,4-diketones (Scheme 7).

Scheme 6. Reported works for the synthesis of 1,4-diketones using enolates and haloketones.

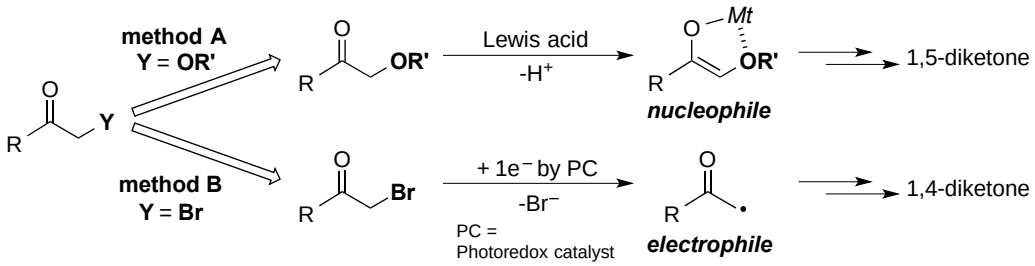


Scheme 7. Desired photoredox system for the synthesis of 1,4-diketones using haloketones and silyl enol ethers.

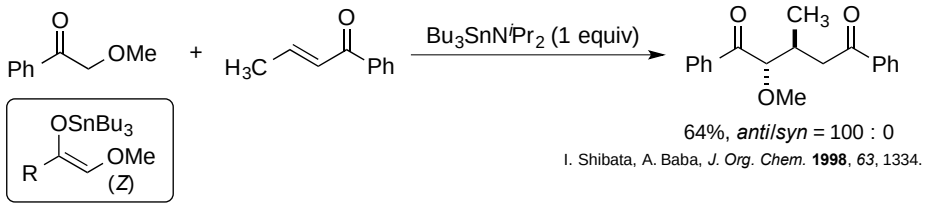


With these background in mind, I have developed a highly diastereoselective Michael addition of ketones to enones for the synthesis of 1,5-diketones and the halo-selective substitution of haloketones by enolates for the synthesis of 1,4-diketones. The key to achieve these reactions is the use of α-heteroatom substituted ketones as a nucleophile or an electrophile. In the synthesis of 1,5-diketones, by using α-alkoxyketones, which can form chelation structure with a Lewis acid,[14] I developed the direct catalytic diastereoselective Michael addition for the synthesis of 1,5-diketones via the stereo-controlled generation of enolates (Scheme 8, method A). Previously, Shibata group reported the diastereoselective Michael addition of α-alkoxyketones to enone. However, stoichiometric amount of basic additive was needed (Scheme 9).[15] In the synthesis of 1,4-diketones, I focused on α-bromoketones because it can generate α-carbonyl radicals, which act as electron-deficient radicals, by single electron reduction (Scheme 8, method B).[16] Recently, radical reactions of halocarbonyls using a photoredox catalyst such as $Ir(ppy)_3$, $Ru(bpy)_3^{2+}$ and organic dye has been developed because of efficient generations of α-carbonyl radicals under mild conditions (Scheme 10),[12] and I applied α-carbonyl radicals generated by a photoredox catalyst and a α-bromoketone to the synthesis of 1,4-diketones combinated with silyl enol ethers.

Scheme 8. Strategy of activation of α-heteroatom-substituted carbonyl compounds.



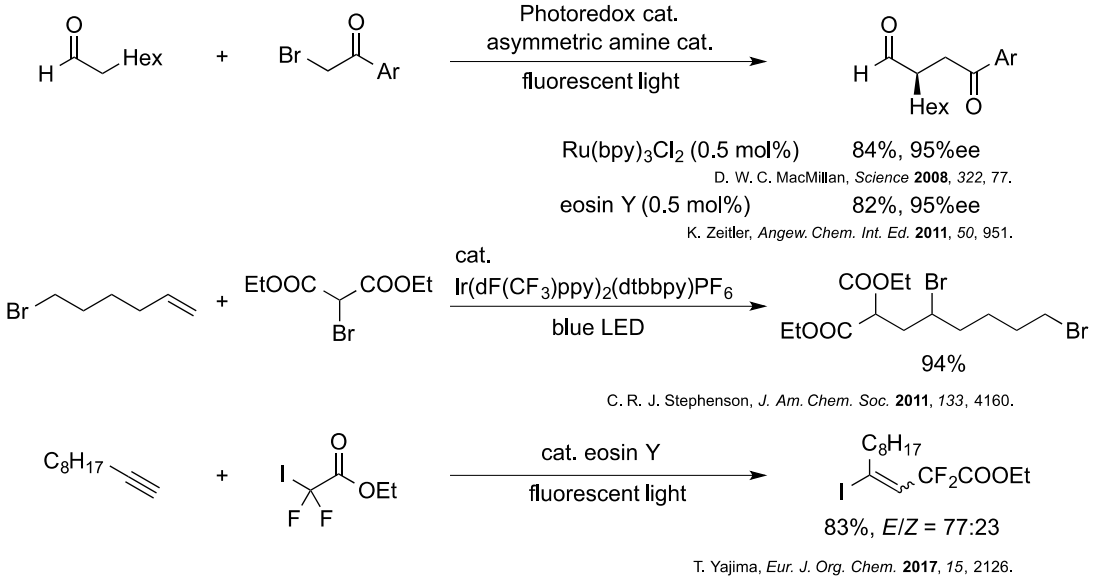
Scheme 9. Direct diastereoselective Michael addition by using stoichiometric amount of tin amide as a base.



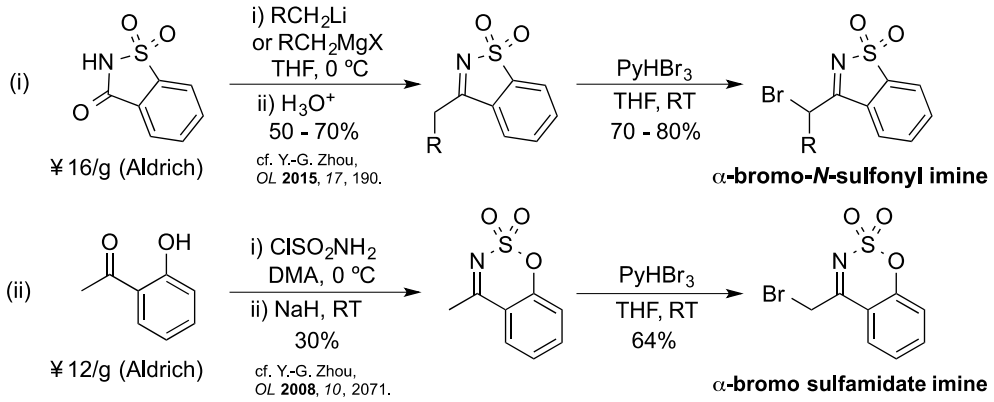
In addition, I designed and developed α-bromo-*N*-sulfonylimine derivatives[17] as new α-iminyl radical precursors based on the strategy of the generation of α-carbonyl radicals (Scheme 11) and they were used to synthesize γ-imino ketones and various radical coupling products under photoredox

catalysis conditions. In general, the reduction of haloimine is more difficult than haloketone because of the low electphilicity of imine (Scheme 12). In this study, to accelerate the reduction of bromoimines by a photoredox catalyst, I introduced a sulfonyl-unit as electron-withdrawing groups

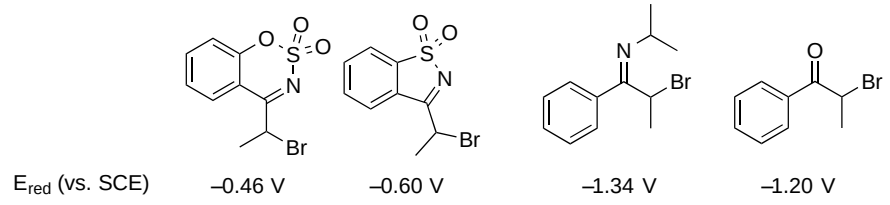
Scheme 10. Example of the radical reactions of halocarbonyls using a photoredox catalyst.



Scheme 11. Preparation of α-bromo imines.



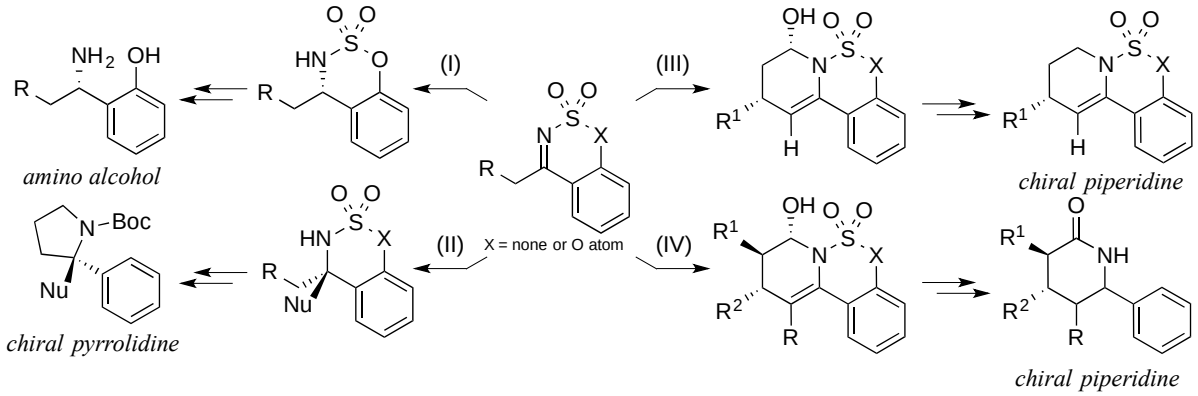
Scheme 12. Reduction potentials of haloketones and haloimines.



into the nitrogen atom of imines. Furthermore, *N*-sulfonylimine units can be easily converted into chiral amino alcohol or chiral pyrrolidine,[17] therefore the introduction of *N*-sulfonylimine units into various organic molecules are synthetically important (Scheme 13). To the best of our knowledge, this

is the first example of the generation of α-iminylradical from haloimines.

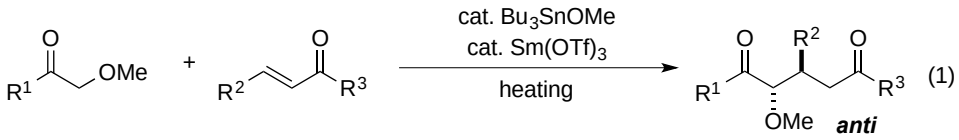
Scheme 13. Application of five- or six-membered cyclic *N*-sulfonylimines.



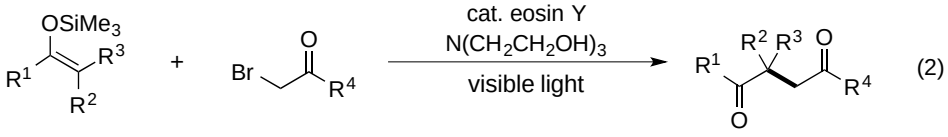
(I) Hydrogenation; Y.-G. Zhou, *Org. Lett.* **2008**, *10*, 2071.
(II) Addition; W. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7540.
(III) Michael Addition; W. Zhang, *Chem. Commun.* **2015**, *51*, 885.
(IV) Domino Reaction; W. Zhang, *Org. Lett.* **2014**, *16*, 4496.

Based on the strategy of the activation of α-heteroatom substituted ketones, I developed the synthetic methods for 1,5-diketones, 1,4-diketones and γ-imino ketones and this thesis consists of the general introduction and the following three chapters.

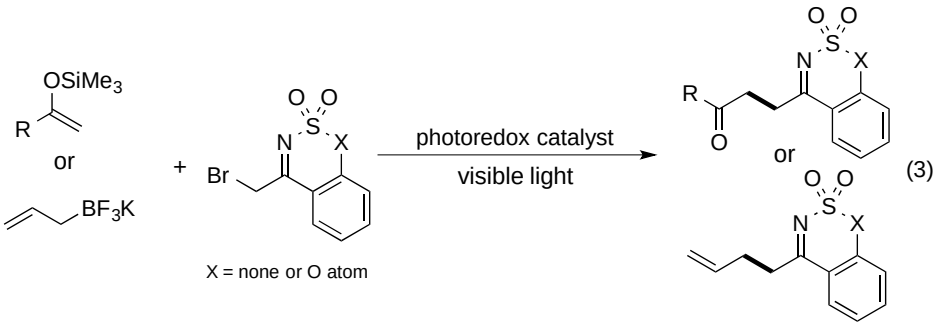
Chapter 1 deals with the *anti*-selective direct Michael addition of α-alkoxy ketones to enones by cooperative catalysis of $Sm(OTf)_3$ and Bu_3SnOMe (eq. 1). The *anti*-selectivity was achieved by the stereo-controlled genelation of tin enolate accelerated by the chelation of α-alkoxy ketones to samarium methoxide, which is generated by the transmetalation between $Sm(OTf)_3$ and Bu_3SnOMe, and the formation of eight-membered chelated transition state of tin enolate and enone.



Chapter 2 describes the synthesis of 1,4-diketones from silyl enol ethers and bromocarbonyls, catalyzed by an organic dye under visible-light irradiation (eq. 2). The combination of eosin Y and triethanolamine effectively produced α-carbonyl radical from α-haloketones and the use of silyl enol ether that has low nucleophilicity is important for the halo-selective reaction.



Chapter 3 provides the generation of α-iminyl radicals from α-bromo cyclic *N*-sulfonylimines and application to coupling with various radical acceptors using a photoredox catalyst (eq. 3). The key for this radical generation was the incorporation of a sulfonyl group into an imine moiety, which facilitated a single-electron reduction by a photoredox catalyst and stabilized the α-iminyl radical.



References and Notes

(1) (a) K. Bowden, I. M. Heilbron, E. R. H. Jones, B. C. L. Weedon, *J. Chem. Soc.* **1946**, 39. (b) E. J. Eisenbraun, *Org. Synth.* **1965**, *45*, 28. (c) R. Jira, *Angew. Chem. Int. Ed.* **2009**, *48*, 9034.

(2) (a) D. Evans, J. A. Osborn, G. Wilkinson, *J. Chem. Soc. A* **1968**, 3133. (b) B. Cornils, W. A. Herrmann, M. Rasch, *Angew. Chem. Int. Ed.* **1994**, *33*, 2144. (d) J. H. Jones, *Platinum Metals Rev.* **2000**, *44*, 94.

(3) (a) J. K. Groves, *Chem. Soc. Rev.* **1972**, *1*, 73. (b) B. M. Trost, C. S. Brindle, *Chem. Soc. Rev.* **2010**, *39*, 1600. (c) T. Tokoroyama, *Eur. J. Org. Chem.* **2010**, *10*, 2009.

(4) (a) C. Avonto, O. T.-Scafati, F. Pollastro, A. Minassi, V. D. Marzo, L. D. Petrocellis, G. Appendino, *Angew. Chem. Int. Ed.* **2011**, *50*, 467. (b) M. J. Uddin, B. C. Crews, K. Ghebreselasie, L. J. Marnett, *Bioconjugate Chem.* **2013**, *24*, 712. (c) E. Y. Schmidt, I. A. Bidusenko, N. I. Protsuk, I. A. Ushakov, B. A. Trofimov, *Eur. J. Org. Chem.* **2013**, *12*, 2453.

(5) (a) A. Kawamura, M. Kita, H. Kigoshi, *Angew. Chem. Int. Ed.* **2015**, *54*, 7073. (b) Y. Enomoto, K. Shiomi, M. Hayashi, R. Masuma, T. Kawakubo, K. Tomosawa, Y. Iwai, S. Omura, *J. Antibiot.* **1996**, *49*, 50.

(6) (a) C. Paal, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2756. (b) L. Knorr, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2863. (c) V. Amarnath, D. C. Anthony, K. Amarnath, W. M. Valentine, L. A. Wetterau, D. G. Graham, *J. Org. Chem.* **1991**, *56*, 6924. (d) Z. Kaleta, B. T. Makowski, T. Soos, R. Dembinski, *Org. Lett.* **2006**, *8*, 1625.

(7) (a) R. S. Muthyala, K. E. Carlson, J. A. Katzenellenbogen, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4485. (b) J. Ju, L. Zhang, R. Hua, *Tetrahedron Lett.* **2014**, *55*, 3374.

(8) (a) J. Christensen, Ł. Alberecht, K. A. Jørgensen, *Chem. Asian J.* **2013**, *8*, 648. (b) Y. Liu, A. Lu, K. Hu, Y. Wang, H. Song, Z. Zhou, C. Tang, *Eur. J. Org. Chem.* **2013**, 4836. (c) D. J. B. Antúnez, M. D. Greenhalgh, C. Fallan, A. M. Z. Slawin, A. D. Smith, *Org. Biomol. Chem*., **2016**, *14*, 7268.

(9) (a) Y. Hamashima, D. Hotta, M. Sodeoka, *J. Am. Chem. Soc*. **2002**, *124*, 11240. (b) Y. Hamashima, D. Hotta, N. Umebayashi, Y. Tsuchiya, T. Suzuki, M. Sodeoka, *Adv. Synth. Catal.* **2005**, *347*, 1576. (d) J. Yang, W. Li, Z. Jin, X. Liang, J. Ye, *Org. Lett.* **2010**, *12*, 5218. (e) N. R. Cichowicz, W. Kaplan, Y. Khomutnyk, B. Bhattarai, Z. Sun, P. Nagorny, *J. Am. Chem. Soc*. **2015**, *137*, 14341.

(10) (a) H. Stetter, *Angew. Chem. Int. Ed.* **1976**, *15*, 639. (b) S. R. Yetra, A. Patra, A. T. Biju, *Synthesis* **2015**, *47*, 1357. (c) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511. (d) A. T. Biju, N. Kuhl, F. Glorius, *ACC. Chem. Res.* **2011**, *44*, 1182. (e) S. Esposti, D. Dondi, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2007**, *46*, 2531.

(11) (a) M. Yasuda, T. Oh-hata, I. Shibata, A. Baba, H. Matsuda, *J. Chem. Soc., Perkin Trans. 1* **1993**, 859. (b) J. Luo, Q. Jiang, H. Chen, Q. Tang, *RSC Adv*. **2015**, *5*, 67901. (c) K. Miura, N. Fujisawa, H. Saito, D. Wang, A. Hosomi, *Org. Lett.* **2001**, *3*, 2591.

(12) (a) D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77. (b) M. Neumann, S. Füldner, B. König, K. Zeitler, *Angew. Chem. Int. Ed.* **2011**, *50*, 951. (c) J. D. Nguyen, J. W. Tucker, M. D. Konieczнska, C. R. J. Stephenson, *J. Am. Chem. Soc*. **2011**, *133*, 4160. (d) T. Yajima, M. Ikegami, *Eur. J. Org. Chem.* **2017**, *15*, 2126.

(13) I. Suzuki, N. Esumi, M. Yasuda, *Asian J. Org. Chem.* **2016**, *5*, 179.

(14) (a) D. J. Cram, F. A. A. Elhafez, *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) D. J. Cram, K. R. Kopecky, *J. Am. Chem. Soc.* **1959**, *81*, 2748. (c) G. R. Stanton, G. Koz, P. J. Walsh, *J. Am. Chem. Soc.* **2011**, *133*, 7969. (d) X. Fan, P. J. Walsh, *Acc. Chem. Res.* **2017**, *50*, 2389.

(15) I. Shibata, K. Yasuda, Y. Tanaka, M. Yasuda, A. Baba, *J. Org. Chem*. **1998**, *63*, 1334.

(16) (a) T. Migita, K. Nagai, M. Kosugi, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2480. (b) K. Takami, S. Usugi, H. Yorimitsu, K. Oshima, *Synthesis* **2005**, *5*, 824.

(17) (a) Y.-Q. Wang, C.-B. Yu, D.-W. Wang, X.-B. Wang, Y.-G. Zhou, *Org. Lett.* **2008**, *10*, 2071. (b) B. Song, C-B. Yu, W.-X. Huang, M.-W. Chen, Y.-G. Zhou, *Org. Lett.* **2015**, *17*, 190 (c) G. Yang, W. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7540. (d) Q. An, J. Shen, N. Butt, D. Liu, Y. Liu, W. Zhang, *Org. Lett.* **2014**, *16*, 4496. (e) Q. An, J. Li, J. Shen, N. Butt, D. Liu, Y. Liu, W. Zhang, *Chem. Commun.* **2015**, *51*, 885.

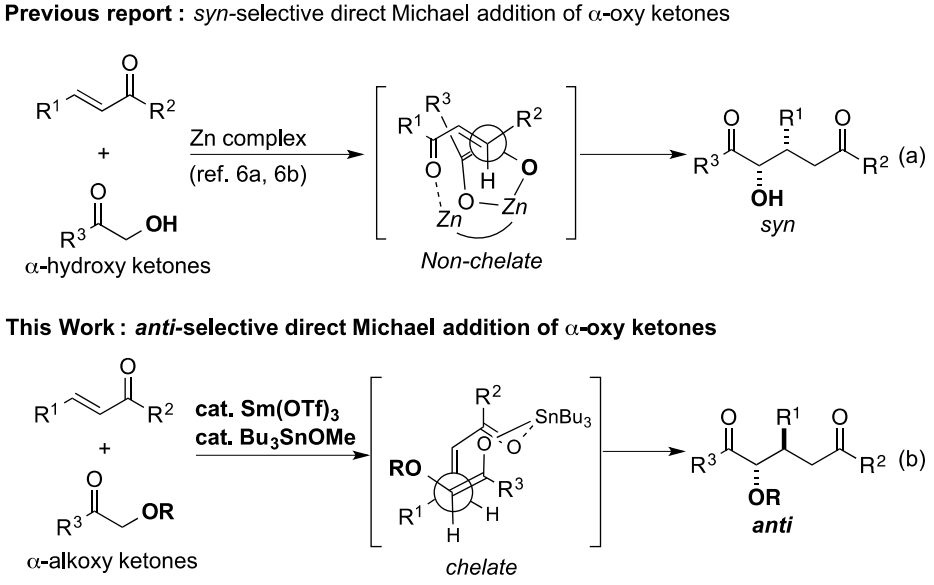
Chapter 1

anti-Selective Direct Michael Addition of α-Alkoxyketones to Enones by Cooperative Catalysis of $Sm(OTf)_3$ and Bu_3SnOMe

1-1. Introduction

The diastereoselective Michael addition reaction is a powerful and versatile tool in organic synthesis.[1, 2] In particular, much effort has been extended to develop the reaction of enolates as nucleophiles with α,β-unsaturated carbonyl compounds, which is one of the most useful methods for the construction of 1,5-dicarbonyl units.[3] Especially, the ability to directly use carbonyl compounds as nucleophiles is desired for atom- and step-economical reactions. α-Functionalized ketones are applied to various direct catalytic diastereoselective Michael reactions with enones to provide functionalzed 1,5-dicarbonyl compounds. In many cases, however, the functional groups that can be used at the α-position of the carbonyl group has been limited to electron-withdrawing groups because of the ease of enolization.[4] Therefore, demands to extend the diversity of available functional groups have increased. In particular, the application of α-oxycarbonyl compounds such as α-hydroxy- and α-alkoxyketones to yield 2-oxy-1,5-dicarbonyl compounds, which are important building blocks for bioactive compounds,[5] remains a challenging issue. Previous reports have described the *syn*-selective direct catalytic 1,4-addition of α-hydroxyketones to enones catalyzed by dinuclear Zn complexes (Scheme 1a).[6] A catalytic reaction system that could selectively give an *anti*-product, however, has

Scheme 1. Catalytic diastereoselective Michael additions by the α-oxy ketones to enones.

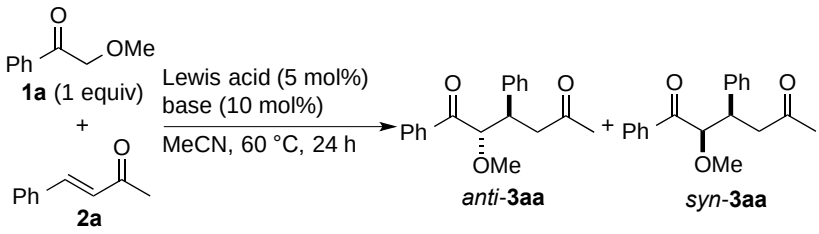


never been reported.[7] Therefore, a methodology for the control of diastereoselectivity is needed, especially for the production of an *anti*-form. In the present study, I present the first highly *anti*-selective direct catalytic Michael addition of α-alkoxyketones to α,β-unsaturated ketones via the combination of a catalytic amount of $Sm(OTf)_3$ and Bu_3SnOMe (Scheme 1b).[8,9] In this reaction system, control of both the geometry of generated metal enolates and the chelated transition state via the combination of catalysts achieved high *anti*-selectivity.

1-2. Results and Discussion

The optimization of the reaction conditions of a Michael addition of benzylideneacetone (**1a**) with α-methoxyacetophenone (**2a**) was conducted in the presence of various types of Lewis acids and basic additives (Table 1). The combination of $Sm(OTf)_3$ as a Lewis acid and Bu_3SnOMe as a base[10] afforded the product **3aa** in high yield and high diastereoselectivity (88% yield, *anti*/*syn* = 93:7) (entry 1). Using other lanthanide triflate catalysts such as $La(OTf)_3$, $Yb(OTf)_3$, and $Sc(OTf)_3$ gave the product **3aa** in lower yields (entries 2–4), but some main group metal and transition metal catalysts

Table 1. Optimization of reaction conditions of the *anti*-selective Michael addition.[a]



entry	Lewis acid	base	yield (%)[b]	(*anti*/*syn*)[c]
1	$Sm(OTf)_3$	Bu_3SnOMe	88(84)[d]	(93:7)
2	$La(OTf)_3$	Bu_3SnOMe	79	(90:10)
3	$Yb(OTf)_3$	Bu_3SnOMe	42	(94:6)
4	$Sc(OTf)_3$	Bu_3SnOMe	50	(89:11)
5	$In(OTf)_3$	Bu_3SnOMe	<5	nd
6	$Sn(OTf)_2$	Bu_3SnOMe	0	nd
7	$Zn(OTf)_2$	Bu_3SnOMe	7	nd
8	AgOTf	Bu_3SnOMe	<5	nd
9	$Cu(OTf)_2$	Bu_3SnOMe	<5	nd
10	none	Bu_3SnOMe	0	nd
11	$Sm(OTf)_3$	none	11	(85:15)
12	$Sm(OTf)_3$	$^iPr_2NEt$	61	(75:25)
13	$Sm(OTf)_3$	NaOMe	73	(78:22)
14	$Sm(OTf)_3$	NaO^tBu	70	(83:17)

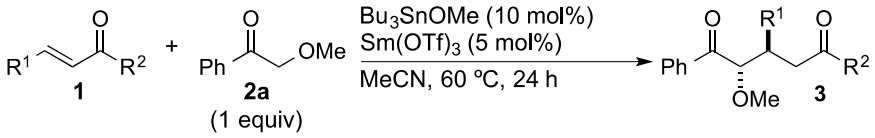
[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), Lewis acid (0.050 mmol), basic additives (0.10 mmol), MeCN (1.0 mL), 60 °C, 24 h. [b] Determined by ^1H NMR analysis using 1,1,2,2-tetrachloroethane as the internal standard. [c] Determined by ^1H NMR analysis of the crude products. [d] Isolated yield.

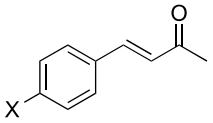
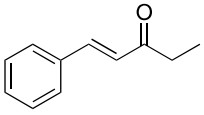
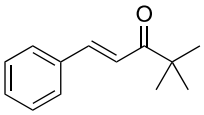
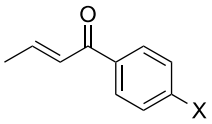
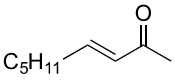
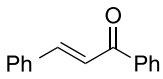
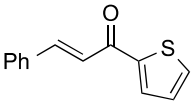
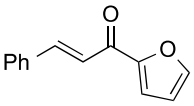
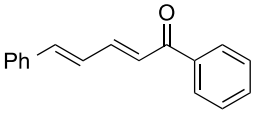
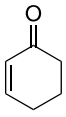
were not effective (entries 5–9). The addition reaction was significantly suppressed in the absence of either $Sm(OTf)_3$ or Bu_3SnOMe (entries 10 and 11). When other basic additives such as an amine or sodium alkoxide were used, the reactions resulted in only moderate yields and moderate diastereoselectivities (entries 12–14). These results clearly show that the combination of $Sm(OTf)_3$ and Bu_3SnOMe contributed to both high yield and high diastereoselectivity.

With the optimized reaction conditions in hand (Table 1, entry 1), various enones **1** were applied to the reaction of α-methoxyacetophenone (**2a**), as shown in Table 2. β-Aryl substituted enones **1a**–**1e** furnished the corresponding products in high yields and high *anti*-selectivity (entries 1–5).[11] The sterically hindered enone **1f** was also applicable to afford the product **3fa** (entry 6). Excellent yields were obtained in the reactions of aromatic enones bearing electron-withdrawing and electron-donating groups **1g**–**1i** (entries 7–9). It is noteworthy that aliphatic enone **1j** was also applied to this reaction system to give **3ja** in high yield and high selectivity (entry 10). Chalcone derivatives **1k** and **1l** furnished the corresponding products **3ka** and **3la**, respectively, in a high yield with a high level of diastereoselectivity (entries 11 and 12). The heteroaryl-substituted enones **1m** and **1n** were smoothly converted to the corresponding Michael addition products **3ma** and **3na**, respectively (entries 13 and 14). The reaction of highly conjugated enone **1o** also proceeded to provide the corresponding 1,4-addition product **3oa** (entry 15). Unfortunately, the reaction of cyclic enone **1p** resulted in a very low yield (entry 16).

Next, the reactions of various α-alkoxyketones **2** with benzylideneacetone (**1a**) were investigated, as shown in Table 3. In the reactions of *o*-, *m*-, and *p*-methylated α-methoxyacetophenones **2b**–**2d**, the position of Me group on the aryl ring of methoxyacetophenones had little effect on either yield or diastereoselectivity (entries 1–3). Naphthyl substituted ketone **2e** provided high yield and high *anti*-selectivity (entry 4). Although the yield of **3af** was low, aliphatic methoxyketone **2f** was also applicable to this reaction system (entry 5). The reaction of isopropoxy ketone **2g**, which has the greater steric hindrance of an alkoxy group, afforded the corresponding product **3ag** with high diasteoselectivity, although the yield was moderate (entry 6).

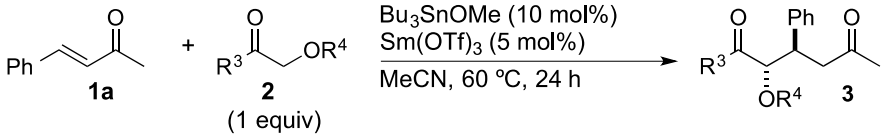
Table 2. Substrate scope of enones **1**.[a]

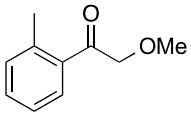
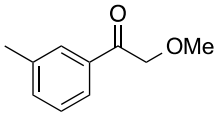
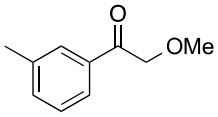
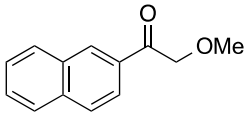
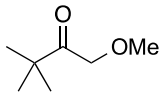
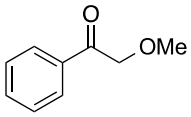


Entry	1		Product	Yield[b]	(*anti*/*syn*)
1		X = H	**3aa**	84%	93:7
2		Cl	**3ba**	83%	92:8
3		Me	**3ca**	83%	93:7
4		OMe	**3da**	76%	91:9
5			**3ea**	70%	94:6
6[d]			**3fa**	80%	95:5
7		X = H	**3ga**	84%	93:7
8		Cl	**3ha**	91%	94:6
9		OMe	**3ia**	85%	95:5
10[e]			**3ja**	75%	93:7
11[f]		X = H	**3ka**	89%	91:9
12[f]		OMe	**3la**	87%	92:8
13[f]			**3ma**	89%	96:4
14[f]			**3na**	89%	95:5
15[d,f]			**3oa**	79%	95:5
16			**3pa**	trace	nd

[a] Reaction conditions: **1** (1.0 mmol), **2a** (1.0 mmol), Bu_3SnOMe (0.10 mmol), $Sm(OTf)_3$ (0.050 mmol), MeCN (1.0 mL), 60 °C, 24 h. [b] Isolated products. [c] Determined by ^1H NMR analysis of the crude products. [d] $Sm(OTf)_3$ (10 mol %) was used. [e] THF was used instead of MeCN. [f] The reaction was performed at 40 °C.

Table 3. Substrate scope of alkoxyketones **2**.[a]



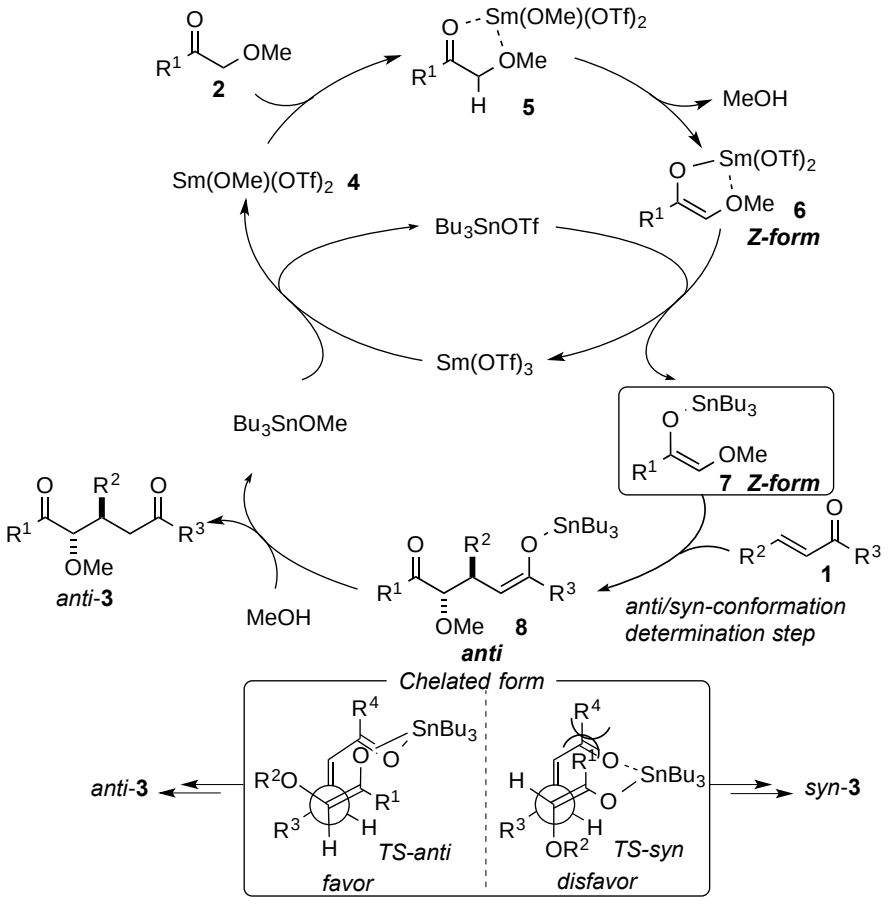
Entry	2	Product	Yield	(*anti*/*syn*)
1[d]		**3ab**	82%	96:4
2		**3ac**	79%	93:7
3		**3ad**	74%	94:6
4[d]		**3ae**	81%	93:7
5		**3af**	24%	94:6
6		**3ag**	30%	92:8

[a] Reaction conditions: **1a** (1.0 mmol), **2** (1.0 mmol), Bu_3SnOMe (0.10 mmol), $Sm(OTf)_3$ (0.050 mmol), MeCN (1.0 mL), 60 °C, 24 h. [b] Isolated products. [c] Determined by ^1H NMR analysis of the crude products. [d] The reaction was performed at 50 °C.

A plausible reaction mechanism is shown in Scheme 2. First, the transmetalation between Bu_3SnOMe and $Sm(OTf)_3$ proceeds to give the samarium methoxide **4** and Bu_3SnOTf.[12] Samarium methoxide **4** is coordinated by alkoxyketone **2** to form the chelate complex **5**, which increases the acidity of the α-proton.[13] Then, a proton abstraction of the methoxy group on the samarium atom effectively affords the samarium enolate species **6** in *Z*-form, because of the chelation effect. In the transmetallation between Bu_3SnOTf and **6**, (*Z*)-tin enolate **7** is formed,[14] and the reaction of **7** with (*E*)-enone **1** affords the corresponding Michael adduct **8** in *anti*-selectivity through the chelated transition state, **TS-*anti***. [15,16,17] The *syn* product is suppressed by the steric repulsion between enone **1** and R^1 in **TS-*syn***. Finally, the protonation of **8** by MeOH yields the product *anti*-**3**, and Bu_3SnOMe is

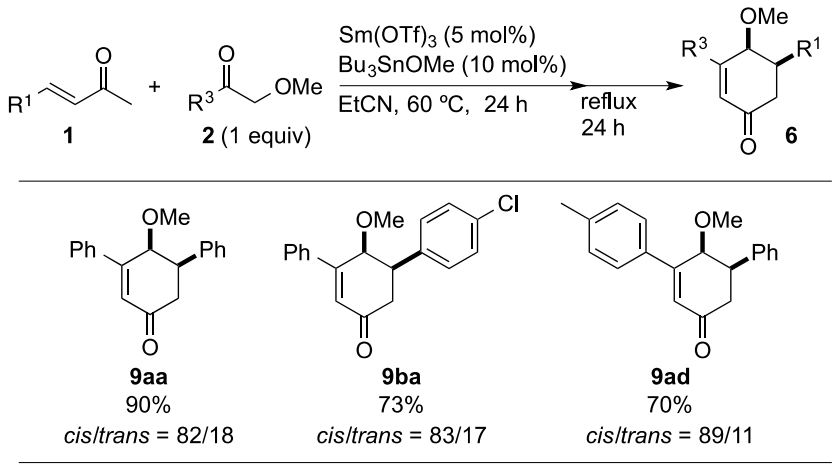
regenerated. The cooperative $Sm(OTf)_3/Bu_3SnOMe$ system includes two important points that allow the realization of a selective reaction for the *anti*-form, **3**: 1) samarium triflate can have a higher coordination number to give the chelated *Z*-form **6**; and, 2) the chelated transition state ***TS-anti*** includes highly coordinated tin enolates, which is favorable.

Scheme 2. Plausible reaction mechanism of the *anti*-selective Michael addition of alkoxyketone **2** with enone **1**.



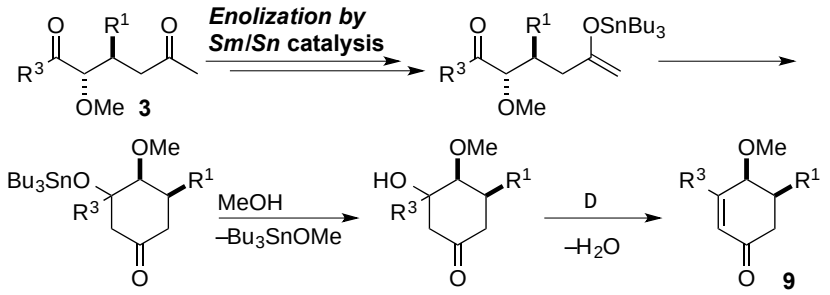
During the course of the present study, I found that a direct Michael addition followed by heating at high temperature gave cyclic enones (Scheme 3).[2j, 18] The reaction of enone **1a** with methoxyketone **2a** was conducted under the optimized catalyst system in propionitrile for 24 h, and then the reaction mixture was heated to reflux (ca.115 °C) to afford a *cis*-isomer of cyclic enone **9ba** in a 90% yield.[19, 20] Reaction using either enone **1b** or α-methoxyketone **2d** also gave the corresponding *cis*-isomers **9ba** and **9ad**, respectively, in high yields with high diastereoselectivity.

Scheme 3. Michael/aldol cyclization reaction of enone **1** with alkoxyketone **2**.



A possible reaction mechanism is shown in Scheme 4. The acetyl moiety of Michael adduct **3** is converted into a tin enolate unit by $Sm(OTf)_3/Bu_3SnOMe$. Subsequently, an intramolecular aldol reaction and a dehydration reaction proceed to give the corresponding *cis*-isomer of a cyclic enone.

Scheme 4. Possible mechanism of cyclization reaction of Michael adduct **3**.



1-3. Conclusion

I have developed the first *anti*-selective direct Michael addition reaction of α-alkoxyketones to enones using $Bu_3SnOMe/Sm(OTf)_3$ cooperative catalysis. This reaction is applicable to various types of enones to afford 1,5-dicarbonyl compounds with a high level of *anti*-selectivity. Moreover, the direct Michael addition/intramolecular aldol condensation sequence effectively provided a variety of cyclic enones.

1-4. Experimental Section

General

New compounds were characterized by ^{1}H, ^{13}C, DEPT, COSY, HMQC, HMBC, IR, MS, HRMS. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL AL-400 spectrometer (JEOL, Tokyo, Japan) in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data are reported as follows: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in hertz, and integration. IR spectra were recorded as thin films. Mass spectrometry (MS) and High resolution mass spectrometry (HRMS) was performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University. Medium-pressure column chromatography was carried out on a YAMAZEN Flash Purification System, which is equipped with a 254 nm UV detector. All reactions were carried out in dry solvents under nitrogen atmosphere. Bulb-to-bulb distillation (Kugelrohr) was accomplished at the oven temperatures and pressures indicated. NMR Yields were determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Materials

Dehydrated solvents, including acetonitrile, hexane, diethyl ether (ether), tetrahydrofuran (THF), dichloromethane, 1,4-dioxane, chloroform, toluene, acetone, ethyl acetate, methanol (MeOH), and ethanol (EtOH), were purchased (Wako Pure Chemical Industries) and used as obtained. Enones **1a**, **1b**, **1c**, **1j**, **1k**, **1l**, **1m**, **1p** were also purchased from commercial sources (Sigma-Aldrich). The other enones **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1n**, **1o** were synthesized based on the literature procedure.[21] Alkoxyketone **2a** was purchased from commercial sources (Sigma-Aldrich). The other alkoxyketone **2b, 2d, 2f, 2g** were synthesized based on the literature procedure.[22] The catalysts and bases in Table 1 were purchased from commercial sources (Sigma-Aldrich). The purchased Bu_3SnOMe was used after purification by distillation.

Metrical data for the solid state structures are available from Cambridge Crystallographic Data Centre: CCDC 1536136 (**3ea**), 1536139 (**9ba**)

Experimental Procedure in Optimization of Reaction Conditions (Table 1).

To a suspended solution of Lewis acid (0.050 mmol) in acetonitrile (1.0 mL), enone **1** (1.0 mmol), α-alkoxyketone **2** (1.0 mmol), and base (0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried over $MgSO_4$, and evaporation of volatiles gave the crude product, which was analyzed by ^{1}H NMR spectroscopy to decide diastereomeric ratio and product yield.

Experimental Procedure in the Michael addition (Table 2 and Table 3).

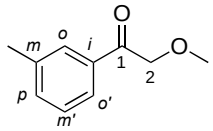
To a suspended solution of $Sm(OTf)_3$ (0.050 mmol) in acetonitrile (1.0 mL), enone **1** (1.0 mmol), α-alkoxyketone **2** (1.0 mmol), and Bu_3SnOMe (0.10 mmol) was added. The reaction mixture was stirred for 24 h at 40-60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried over $MgSO_4$, and evaporation of volatiles gave the crude product, which was analyzed by ^1H NMR spectroscopy to decide diastereomeric ratio. The crude product was purified by silica gel column chromatography to give the product.

Experimental Procedure in the domino Michael/aldol reaction (Scheme 3).

To a suspended solution of $Sm(OTf)_3$ (0.050 mmol) in acetonitrile (1.0 mL), enone **1** (1.0 mmol), α-alkoxyketone **2** (1.0 mmol), and Bu_3SnOMe (0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, then it was heated to 115 °C for 24 h. After the reaction, it was quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried over $MgSO_4$, and evaporation of volatiles gave the crude product, which was analyzed by ^1H NMR spectroscopy to decide diastereomeric ratio. The crude product was purified by silica gel column chromatography to give the product.

Synthesis of Substrates

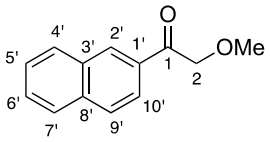
Preparation of 2-methoxy-1-(*m*-tolyl)ethan-1-one (2c)



To a THF solution (100 mL) of magnesium (1.79 g, 73.7 mmol), 1-bromo-3-methylbenzene (12.7 g, 74.3 mmol) was dropwise added at 40 °C, and the mixture was stirred with warming to 70 °C for 3 h. To the solution of the Grignard reagent, a THF solution (30 mL) of 2-methoxy-1-acetonitrile (4.24 g, 59.7 mmol) was added, which was then stirred for 2 h. The reaction was quenched with 1M-HCl aq, and the mixture was extracted with AcOEt, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified via silica gel column chromatography (hexane : AcOEt = 9 : 1) to give the product as a yellow liquid (6.83 g, 70% yield). ^1H NMR: (400 MHz, $CDCl_3$) 7.74 (s, 1H, *o*), 7.71 (d, J = 8.0 Hz, 1H, *o'*), 7.40-7.33 (m, 2H, *p* and *m'*), 4.71 (s, 2H, 2-H), 3.51 (s, 3H, OMe), 2.41 (s, 3H, *m*-CH_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 196.1 (s, C-1), 138.4 (s), 134.7 (s), 134.2 (d), 128.4 (d), 127.7 (d), 124.8 (d), 75.1 (t, C-2), 59.3 (q, OMe), 21.2 (d, C-3) MS: (EI, 70 eV) *m*/*z* 164 (M^+, 0.4), 134 (17),

119 (100), 91 (53) HRMS: (EI, 70 eV) calcd for ($C_{10}H_{12}O_2$) 164.0837 (M^+) found *m*/*z* 164.0837 Analysis: $C_{10}H_{12}O_2$ (164.20) Calcd: C, 73.15; H, 7.37 Found: C, 73.33; H, 7.54

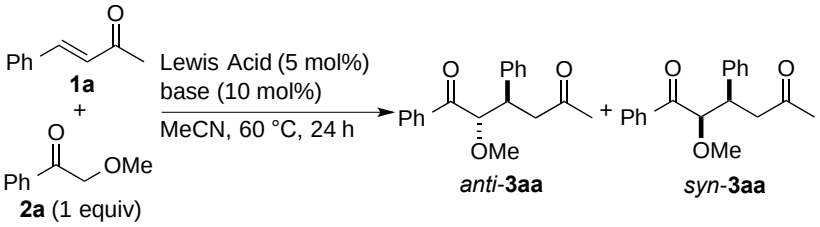
Preparation of 2-methoxy-1-(naphthalen-2-yl)ethan-1-one (2e)



To a THF solution (80 mL) of magnesium (1.75 g, 72.0 mmol), 2-bromonaphthalene (15.0 g, 72.4 mmol) was dropwise added at 40 °C, and the mixture was stirred with warming to 70 °C for 2 h. To the solution of the Grignard reagent, a THF solution (30 mL) of 2-methoxy-1-acetonitrile (4.26 g, 60.0 mmol) was added, which was then stirred for 2 h at room temperature. The reaction was quenched with 1M-HCl aq, and the mixture was extracted with Et_2O, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified via silica gel column chromatography (hexane : AcOEt = 9 : 1) to give 2-methoxy-1-phenylethanone as a yellow solid (7.58 g, 63% yield). IR: (neat) 1689 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.44 (s, 1H, 2'-H), 7.99-7.85 (m, 4H), 7.60 (t, *J* = 6.8 Hz, 1H), 7.55 (t, *J* = 6.8 Hz, 1H), 4.83 (s, 2H, 2-H), 3.55 (s, 3H, OMe) ^{13}C NMR: (100 MHz, $CDCl_3$) 196.0 (s, C-1), 135.7 (s), 132.3 (s), 132.0 (s), 129.5 (d), 129.4 (d), 128.6 (d), 128.5 (d), 127.7 (d), 126.8 (d), 123.3 (d), 75.3 (t, C-2), 59.4 (q, OMe) MS: (EI, 70 eV) *m*/*z* 200 (M^+, 15), 156 (11), 155 (100), 127 (55) HRMS: (EI, 70 eV) calcd for ($C_{13}H_{12}O_2$) 200.0837 (M^+) found *m*/*z* 200.0839 Analysis: $C_{13}H_{12}O_2$ (200.24) Calcd: C, 77.98; H, 6.04 Found: C, 77.92; H, 5.93

Optimization of Reaction Conditions.

Table 4. Optimization of reaction conditions of the *anti*-selective Michael addition.



Entry	Lewis acid	basic additives	Yield (%)[b]	*anti*/*syn*[c]
1	$ZnBr_2$	Bu_3SnOMe	0	Nd
2	$Zn(OTf)_2$	Bu_3SnOMe	7	75:25
3	$Yb(OTf)_3$	Bu_3SnOMe	42	94:6
4	$Sc(OTf)_3$	Bu_3SnOMe	50	89:11
5	$La(OTf)_3$	Bu_3SnOMe	79	90:10
6	**$Sm(OTf)_3$**	**Bu_3SnOMe**	**88(84)[d]**	**93:7**
7	$Y(OTf)_3$	Bu_3SnOMe	<5	Nd
8	$In(OTf)_3$	Bu_3SnOMe	<5	Nd
9	$Cu(OTf)_2$	Bu_3SnOMe	<5	Nd
10	AgOTf	Bu_3SnOMe	<5	Nd
11	$Sn(OTf)_2$	Bu_3SnOMe	0	Nd

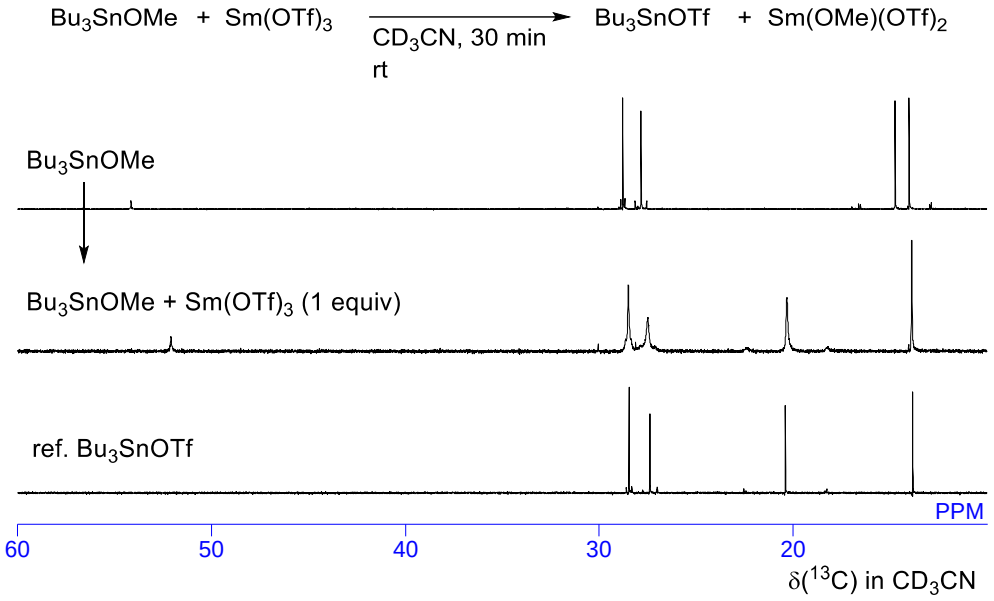
12	$Sm(OTf)_3$	none	11	85:15
13	none	Bu_3SnOMe	0	Nd
14	$Sm(OTf)_3$	*i*Pr_2NEt	61	75:25
15	$Sm(OTf)_3$	NaOMe	73	78:22
16	$Sm(OTf)_3$	NaO*t*-Bu	70	83:17

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), Lewis acid (0.050 mmol), basic additives (0.10 mmol), MeCN (1.0 mL), 60 °C, 24 h. [b] Determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as the internal standard. [c] Determined by ^{1}H NMR analysis of the crude products. [d] Isolated yield.

Investigation of Reaction Mechanism

1) NMR Study

1-1) Transmetalation between Bu_3SnOMe and $Sm(OTf)_3$ in CD_3CN

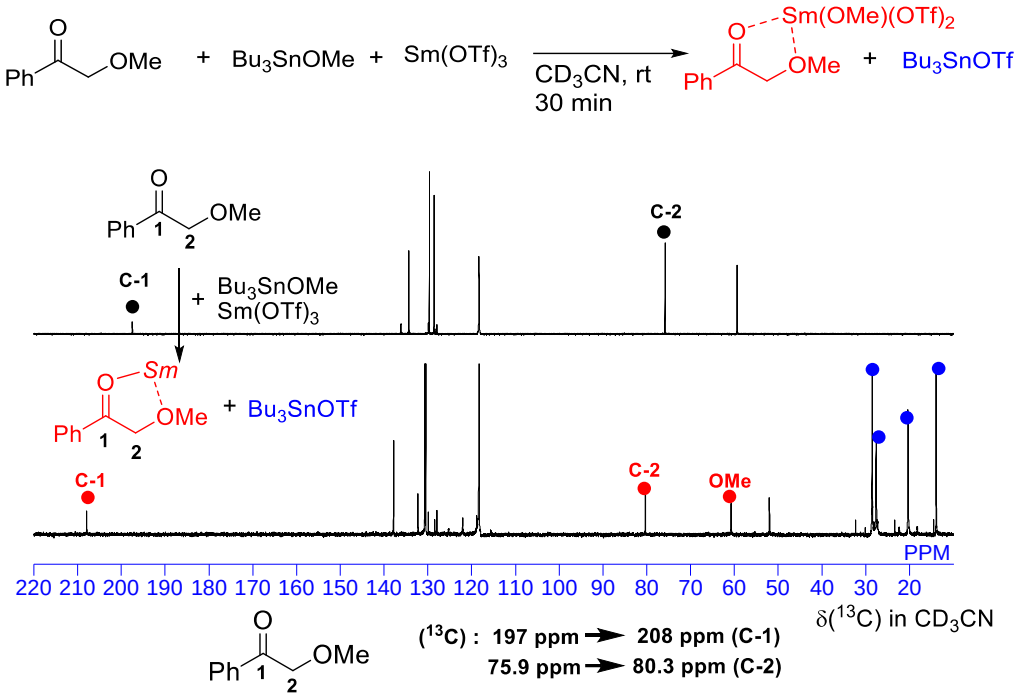


Transmetalation between Bu_3SnOMe and $Sm(OTf)_3$ smoothly proceeded to provide Bu_3SnOTf and samarium methoxide.

1-2) Interaction between alkoxyketone and Bu_3SnOTf

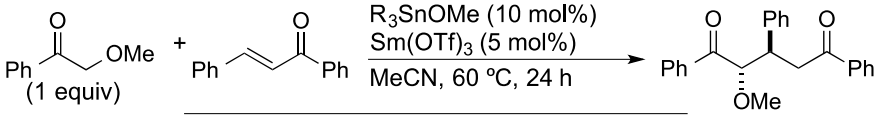
Bu_3SnOTf was not coordinated by the alkoxyketone.

1-3) Chelation of alkoxyketone by Samarium Methoxide in CD_3CN



Alkoxyketone was coordinated by samarium methoxide generated by the transmetalation between Bu_3SnOMe and $Sm(OTf)_3$ because Bu_3SnOTf was not coordinated by the alkoxyketone.

2) Effect of alkyl moiety of tin alkoxide on the *anti*/*syn* ratio

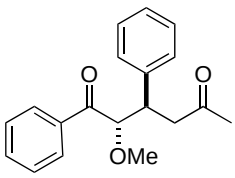


entry	R_3SnOMe	yield (%)	(*anti*/*syn*)
1	Bu_3SnOMe	84	93:7
2	Me_3SnOMe	75	77:23

These results showed the substituent on the Sn atom strongly affected the diastereoselectivity and suggested that the tin enolate generated in *situ* acted as a reactive species of Michael addition step.

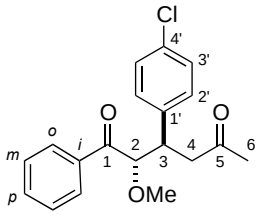
Product Data

(2*S,3*R**)-1,3-diphenyl-2-methoxy-1,5-hexanedione (*anti*-3aa)**



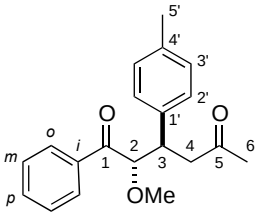
To a suspended solution of $Sm(OTf)_3$ (0.049 mmol, 0.029 g) in acetonitrile (1.0 mL), 4-phenylbut-3-en-2-one **1** (1.0 mmol, 0.149 g), α-methoxyacetophenone **2** (1 mmol, 0.1525 g), and Bu_3SnOMe (0.11 mmol, 0.035 g) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 7 : 93. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.252 g, 84% yield, *syn/anti* = 4 : 96). The analytical data agreed with the previous report.[7a]

(2*S,3*R**)-3-(4-chlorophenyl)-2-methoxy-1-phenylhexane-1,5-dione (*anti*-3ba)**



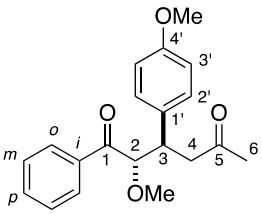
To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), 4-(*p*-chlorophenyl)-3-buten-2-one (0.180 g, 0.99 mmol), α-methoxyacetophenone (0.154 g, 1.0 mmol), and Bu_3SnOMe (0.036 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 8 : 92. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.272 g, 83% yield, *syn/anti* = 6 : 94). IR: (neat) 1716, 1689 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.92 (d, J = 7.2 Hz, 2H, *o*), 7.59 (t, J = 7.2 Hz, 1H, *p*), 7.46 (t, J = 7.2 Hz, 2H, *m*), 7.22 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 8.8 Hz, 2H), 4.57 (d, J = 4.8 Hz, 1H, 2-H), 3.74 (dt, J = 8.8, 4.8 Hz, 1H, 3-H), 3.34 (s, 3H, OMe), 3.05 (dd, J = 17.6, 4.8 Hz, 1H, 4-H^A), 2.87 (dd, J = 17.6, 8.8 Hz, 1H, 4-H^B), 2.05 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.3 (s, C-5), 198.8 (s, C-1), 140.0 (s, C-1'), 135.3 (s, C-*i*), 133.6 (d, C-*p*), 132.8 (s, C-4'), 129.5 (d, C-2'), 128.7 (d), 128.6 (d), 128.4 (d), 87.1 (d, C-2), 58.2 (q, OMe), 44.3 (t, C-4), 42.6 (d, C-3), 30.4 (q, C-6) MS: (CI, 70 eV) *m*/*z* 333 (M + 3, 33), 332 (20), 331 (M + 1, 100), 225 (M^+ - PhCO, 17), 181 (24), 151 (23) HRMS: (CI, 70 eV) calcd for ($C_{19}H_{20}ClO_3$) 331.1101 (M + 1) found *m*/*z* 331.1104

(2*S,3*R**)-2-Methoxy-1-phenyl-3-(*p*-tolyl)-1,5-hexadione (*anti*-3ca)**



To a suspended solution of $Sm(OTf)_3$ (0.031 g, 0.052 mmol) in acetonitrile (1.0 mL), 4-(*p*-tolyl)-3-buten-2-one (0.159 g, 0.99 mmol), α-methoxyacetophenone (0.152 g, 1.0 mmol), and Bu_3SnOMe (0.032 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (3 x 10 mL). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 7 : 93. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.256 g, 83% yield, *syn/anti* = 6 : 94). IR: (neat) 1712, 1685 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.93 (d, *J* = 7.2 Hz, 2H, *o*), 7.56 (t, *J* = 7.2 Hz, 1H, *p*), 7.43 (t, *J* = 7.2 Hz, 2H, *m*), 7.11 (d, *J* = 8.0 Hz, 2H, 2'-H x 2), 7.04 (d, *J* = 8.0 Hz, 2H, 3'-H x 2), 4.57 (d, *J* = 5.6 Hz, 1H, 2-H), 3.74 (dt, *J* = 8.0, 5.6 Hz, 1H, 3-H), 3.34 (s, 3H, OMe), 3.04 (dd, *J* = 17.6, 5.6 Hz, 1H, 4-H^A), 2.87 (dd, *J* = 17.6, 8.0 Hz, 1H, 4-H^B), 2.27 (s, 3H, 4'-Me), 2.04 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.8 (s, C-5), 199.2 (s, C-1), 137.8 (s), 136.6 (s), 135.4 (s, C-*i*), 133.3 (d, C-*p*), 129.2 (d, C-3'), 128.6 (d), 128.5 (d), 128.0 (d, C-2'), 87.8 (d, C-2), 58.2 (q, OMe), 44.7 (t, C-4), 43.0 (d, C-3), 30.4 (q, C-6), 21.0 (q, 4-Me) MS: (CI, 70 eV) *m*/*z* 312 (22), 311 (M + 1, 100) HRMS: (CI, 70 eV) calcd for ($C_{20}H_{23}O_3$) 311.1647 (M + 1) found *m*/*z* 311.1648

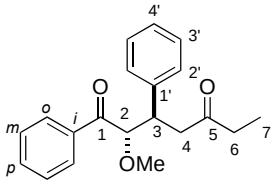
(2*S,3*R**)-2-methoxy-3-(4-methoxyphenyl)-1-phenylhexane-1,5-dione (*anti*-3da)**



To a suspended solution of $Sm(OTf)_3$ (0.029 g, 0.049 mmol) in acetonitrile (1 mL), 4-(4-methoxyphenyl)but-3-en-2-one (0.173 g, 0.98 mmol), α-methoxyacetophenone (0.158 g, 1.05 mmol), and Bu_3SnOMe (0.035 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the

crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 9 : 91. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a yellow viscous liquid (0.245 g, 76% yield, *syn/anti* = 7 : 93). IR: (neat) 1720, 1682 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.93 (d, *J* = 7.2 Hz, 2H, *o*), 7.56 (t, *J* = 7.2 Hz, 1H, *p*), 7.44 (t, *J* = 7.2 Hz, 2H, *m*), 7.14 (d, *J* = 8.8 Hz, 2H, 2'-H), 6.77 (d, *J* = 8.8 Hz, 2H, 3'-H), 4.55 (d, *J* = 5.8 Hz, 1H, 2-H), 3.75 (s, 3H, 4'-OMe), 3.77-3.69 (m, 1H, 3-H), 3.35 (s, 3H, OMe), 3.04 (dd, *J* = 16.8, 5.3 Hz, 1H, 4-H^A), 2.86 (dd, *J* = 16.8, 8.7 Hz, 1H, 4-H^B), 2.04 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.8 (s, C-5), 199.3 (s, C-1), 158.5 (s, C-4'), 135.5 (s, C-*i*), 133.4 (d, C-*p*), 132.8 (s, C-1'), 129.1 (d, C-2'), 128.6 (d), 128.5 (d), 113.9 (d), 87.8 (d, C-2), 58.2 (q, 2-OMe), 55.1 (q, 4'-OMe), 44.9 (t, C-4), 42.7 (d, C-3), 30.4 (q, C-6) MS: (EI, 70 eV) *m*/*z* 326 (M^+, 5), 294 (11), 221 (M - PhCO, 48), 179 (17), 178 (12), 177 (100), 150 (47), 147 (84), 135 (14), 105 (PhCO, 21), 91 (10), 77 (24), 43 (MeCO, 98) HRMS: (EI, 70 eV) calcd for ($C_{20}H_{22}O_4$) 326.1518 (M^+) found *m*/*z* 326.1516

(2*S,3*R**)-2-methoxy-1,3-diphenylheptane-1,5-dione (*anti*-3ea)**



To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-1-phenylpent-1-en-3-one (0.160 g, 1.0 mmol), α-methoxyacetophenone (0.152 g, 1.0 mmol), and Bu_3SnOMe (0.032 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 6 : 94. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.216 g, 70% yield, *syn/anti* = 4 : 96). IR: (neat) 1704, 1678 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.92 (d, *J* = 7.2 Hz, 2H, *o*), 7.55 (t, *J* = 7.2 Hz, 1H, *p*), 7.43 (t, *J* = 7.2 Hz, 2H, *m*), 7.27-7.15 (m, 5H), 4.63 (d, *J* = 5.6 Hz, 1H, 2-H), 3.80 (dt, *J* = 8.0, 5.6 Hz, 1H, 3-H), 3.34 (s, 3H, OMe), 3.02 (dd, *J* = 17.6, 5.6 Hz, 1H, 4-H^A), 2.89 (dd, *J* = 17.6, 8.0 Hz, 1H, 4-H^B), 2.39 (dq, *J* = 17.6, 7.2 Hz, 1H, 6-H^A), 2.26 (dq, *J* = 17.6, 7.2 Hz, 1H, 6-H^B), 0.92 (t, *J* = 7.2 Hz, 3H, 7-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 209.2 (s, C-5), 199.1 (s, C-1), 141.0 (s, C-1'), 135.4 (s, C-*i*), 133.3 (d, C-*p*), 128.5 (d), 128.4 (d), 128.0 (d), 127.0 (d, C-4'), 87.4 (d, C-2), 58.1 (q, OMe), 43.3 (d, C-3), 43.2 (t, C-4), 36.3 (t, C-6), 7.44 (q, C-7) MS: (EI, 70 eV) *m*/*z* 310 (M^+, 0.2), 206 (14), 205 (M^+-PhCO, 100), 150 (12), 117 (85), 77 (17), 57 (66) HRMS: (EI, 70 eV) calcd for ($C_{20}H_{22}O_3$)

310.1569 (M^+) found *m/z* 310.1570

The preparation of the single crystal to measure X-ray diffraction; The CH_2Cl_2/Hexane solution of the product was allowed to stand still and then single crystal was obtained as a colorless solid after wash with hexane. After the measurement of X-ray crystallography, it was confirmed by NMR spectroscopy that the colorless solid was the *anti* product (*anti/syn* > 99:1).

X-ray data M = 310.39 colorless monoclinic $P2_1/c$ (#14) a = 15.256(2) Å b = 5.7496(3) Å c = 19.778(1) Å α = 90° β = 105.906(6)° γ = 90° V = 1668.4(3) $Å^3$ Z = 4 D_{calcd} = 1.236 g/cm^3 T = -150 °C R_1 (wR_2) = 0.0989 (0.2314)

Figure 1-1. Molecular structures of *anti*-**3ea**.

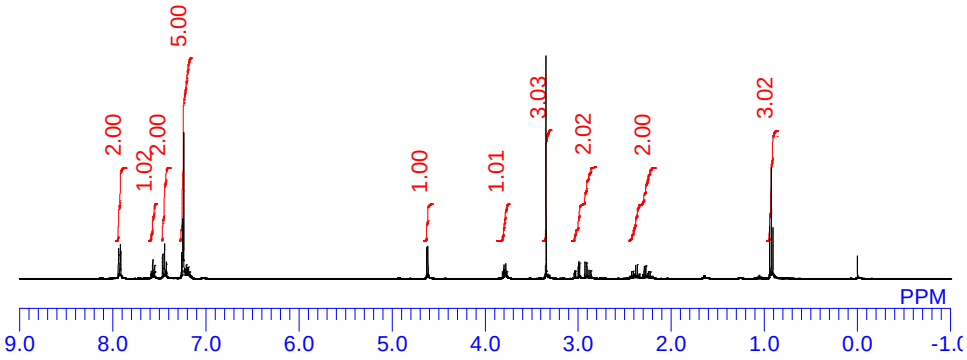
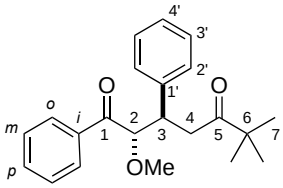


Figure 1-2. NMR spectrum of *anti*-**3ea** after recrystallization.

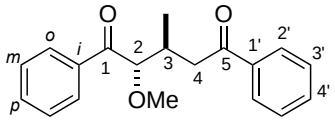
(2*S,3*R**)-2-methoxy-6,6-dimethyl-1,3-diphenylheptane-1,5-dione (*anti*-3fa)**



To a suspended solution of $Sm(OTf)_3$ (0.060 g, 0.10 mmol) in acetonitrile (1.0 mL), (*E*)-4,4-dimethyl-1-phenylpent-1-en-3-one (0.184 g, 0.98 mmol), α-methoxyacetophenone (0.156 g,

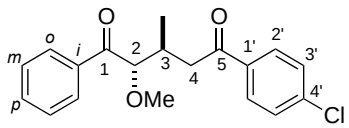
1.0 mmol), and Bu_3SnOMe (0.060 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 5 : 95. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.266 g, 80% yield, *syn/anti* = 3 : 97). IR: (neat) 1693 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.94 (d, J = 7.2 Hz, 2H, *o*), 7.56 (t, J = 7.2 Hz, 1H, *p*), 7.44 (t, J = 7.2 Hz, 2H, *m*), 7.26-7.14 (m, 5H, 3-Ph), 4.74 (d, J = 4.8 Hz, 1H, 2-H), 3.81 (dt, J = 9.0, 4.8 Hz, 1H, 3-H), 3.35 (s, 3H, 2-OMe), 3.09 (dd, J = 18.0, 9.0 Hz, 1H, 4-H^A), 2.94 (dd, J = 18.0, 4.8 Hz, 1H, 4-H^B), 0.98 (s, 9H, 7-H_3 and 6-Me_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 213.5 (s, C-5), 199.1 (s, C-1), 141.6 (s, C-1'), 135.4 (s, C-*i*), 133.4 (d, C-*p*), 128.6 (d), 128.5 (d), 128.4 (d), 128.2 (d), 126.9 (d, C-4'), 87.5 (d, C-2), 58.2 (q, OMe), 44.0 (s, C-6), 43.1 (d, C-3), 37.7 (t, C-4), 26.0 (q, C-7 and 6-Me_2) MS: (EI, 70 eV) *m*/*z* 338 (M^+, 0.7), 233 (M-PhCO, 100), 150 (11), 147 (16), 117 (13), 105 (24), 85 (tBuCO, 31), 77 (Ph, 15), 57 (85) HRMS: (EI, 70 eV) calcd for ($C_{22}H_{26}O_3$) 338.1882 (M^+) found *m*/*z* 338.1885

(2*S,3*S**)-1,5-Diphenyl-2-methoxy-3-methyl-1,5-pentanedione (*anti*-3ga)**



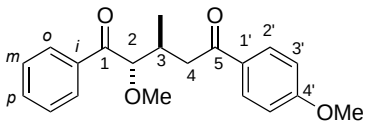
To a suspended solution of $Sm(OTf)_3$ (0.049 mmol, 0.029 g) in acetonitrile (1.0 mL), (*E*)-1-phenylbut-2-en-1-one (0.97 mmol, 0.142 g), α-methoxyacetophenone (1.0 mmol, 0.151 g), and Bu_3SnOMe (0.10 mmol, 0.032 g) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 4 : 96. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.242 g, 84% yield, *syn/anti* = 4 : 96). The analytical data agreed with the previous report.[7a]

(2*S,3*S**)-5-(4-chlorophenyl)-2-methoxy-3-methyl-1-phenylpentane-1,5-dione (*anti*-3ha)**



To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), 1-(4-chlorophenyl)-2-buten-1-one (0.174 g, 0.96 mmol), α-methoxyacetophenone (0.153 g, 1.0 mmol), and Bu_3SnOMe (0.030 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 6 : 94. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.290 g, 91% yield, *syn/anti* = 2 : 98). IR: (neat) 1685, 1589 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 8.07 (d, *J* = 7.2 Hz, 2H, *o*), 7.87 (d, *J* = 8.8 Hz, 2H, 2'-H_2), 7.59 (t, *J* = 7.2 Hz, 1H, *p*), 7.47 (t, *J* = 7.2 Hz, 2H, *m*), 7.40 (d, *J* = 8.8 Hz, 2H, 3'-H x 2), 4.35 (d, *J* = 5.6 Hz, 1H, 2-H), 3.34 (s, 3H, OMe), 3.24-3.16 (m, 1H, 4-H^A), 2.90-2.80 (m, 1H, 4-H^B), 2.86-2.78 (m, 1H, 3-H), 1.07 (d, *J* = 6.8 Hz, 3H, 3-Me) ^{13}C NMR: (100 MHz, $CDCl_3$) 200.0 (s, C-1), 197.9 (s, C-5), 139.2 (s), 135.4 (s), 135.2 (s), 133.5 (d, C-*p*), 129.4 (d, C-2'), 128.69 (d), 128.66 (d), 128.57 (d), 88.8 (d, C-2), 58.2 (q, OMe), 40.6 (t, C-4), 32.8 (d, C-3), 17.3 (q, 3-Me) MS: (CI, 70 eV) *m*/*z* 333 (M + 3, 34), 332 (M + 2, 21), 331 (M + 1, 100), 227 (12), 225 (M^+ – PhCO, 38), 139 (11) HRMS: (CI, 70 eV) calcd for ($C_{19}H_{20}ClO_3$) 331.1101 (M + 1) found *m*/*z* 331.1096

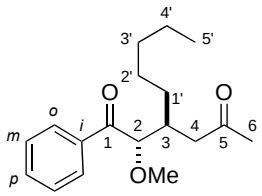
(2*S,3*S**)-2-methoxy-5-(4-methoxyphenyl)-3-methyl-1-phenylpentane-1,5-dione (*anti*-3ia)**



To a suspended solution of $Sm(OTf)_3$ (0.033 g, 0.055 mmol) in acetonitrile (1.0 mL), (*E*)-1-(4-methoxyphenyl)but-2-en-1-one (0.176 g, 1.0 mmol), α-methoxyacetophenone (0.154 g, 1.00 mmol), and Bu_3SnOMe (0.033 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 5 : 95. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.277 g, 85% yield, *syn/anti* = 4 : 96). IR: (neat) 1674, 1592 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 8.08 (d, *J* = 8.0 Hz, 2H, *o*), 7.92 (d, *J* = 8.0 Hz, 2H, 2'-H x 2), 7.58 (t, *J* = 8.0 Hz, 1H, *p*), 7.47 (t, *J* = 8.0 Hz, 2H, *m*), 6.91 (d, *J* = 8.0 Hz, 2H, 3'-H x 2), 4.36 (d, *J* = 5.6 Hz, 1H, 2-H), 3.85 (s, 3H, 4'-OMe), 3.37 (s, 3H, 2-OMe), 3.22-3.11 (m, 1H, 4-H^A), 2.91-2.81 (m, 1H, 4-H^B), 2.87-2.76 (m, 1H, 3-H), 1.05 (d, *J* = 6.4 Hz, 3H, 3-Me) ^{13}C NMR: (100 MHz, $CDCl_3$) 200.2 (s, C-1), 197.7 (s, C-5), 163.3 (s, C-4'), 135.3 (s, C-*i*), 133.5 (d, C-*p*), 130.3

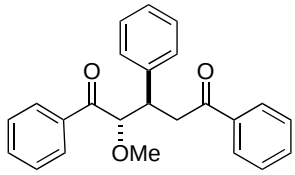
(d, C-2'), 130.2 (s, C-1'), 128.7 (d), 128.6 (d), 113.5 (d, C-3'), 89.0 (d, C-2), 58.3 (q, 2-OMe), 55.4 (q, 4'-OMe), 40.2 (t, C-4), 32.9 (d, C-3), 17.3 (q, C-3) MS: (EI, 70 eV) *m*/*z* 326 (M^+, 2), 254 (12), 222 (11), 221 (M^+– PhCO, 81), 189 (21), 161 (28), 135 (100), 105 (19) HRMS: (EI, 70 eV) calcd for ($C_{20}H_{22}O_4$) 326.1518 (M^+) found *m*/*z* 326.1521

(2*S,3*S**)-2-methoxy-3-pentyl-1-phenylhexane-1,5-dione (*anti*-3ja)**



To a suspended solution of $Sm(OTf)_3$ (0.031 g, 0.052 mmol) in THF (1.0 mL), (*E*)-non-3-en-2-one (0.140 g, 1.0 mmol), α-methoxyacetophenone (0.150 g, 1.0 mmol), and Bu_3SnOMe (0.032 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (3 x 10 mL). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product (85% yield). ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 7 : 93. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless liquid (0.218 g, 75% yield, *syn/anti* = 6 : 94). IR: (neat) 1709, 1678 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.99 (d, *J* = 7.2 Hz, 2H, *o*), 7.59 (t, *J* = 7.2 Hz, 1H, *p*), 7.48 (t, *J* = 7.2 Hz, 2H, *m*), 4.55 (d, *J* = 4.4 Hz, 1H, 2-H), 3.34 (s, 3H, OMe), 2.60 (dd, *J* = 17.6, 6.4 Hz, 1H, 4-H^A), 2.54 (sext, *J* = 6.4 Hz, 1H, 3-H), 2.40 (dd, *J* = 17.6, 6.4 Hz, 1H, 4-H^B), 1.52-1.20 (m, 8H, 1'-H_2, 2'-H_2, 3'-H_2 and 4'-H_2), 0.88 (t, *J* = 6.8 Hz, 3H, 5'-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 207.7 (s, C-5), 200.2 (s, C-1), 135.5 (s, C-*i*), 133.4 (d, C-*p*), 128.7 (d), 128.4 (d), 85.3 (d, C-2), 58.2 (q, OMe), 43.4 (t, C-4), 36.8 (d, C-3), 31.7 (t), 31.6 (t), 30.4 (q, C-6), 26.7 (t), 22.5 (t), 14.0 (q, C-5') MS: (EI, 70 eV) *m*/*z* 290 (M^+, 0.2), 185 (M - PhCO, 100), 153 (10), 105 (15), 95 (25), 77 (12), 69 (21), 55 (12), 44 (38) HRMS: (EI, 70 eV) calcd for ($C_{18}H_{26}O_3$) 290.1882 (M^+) found *m*/*z* 290.1884

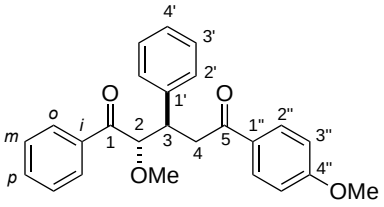
(2*S,3*R**)-2-methoxy-1,3,5-triphenylpentane-1,5-dione (*anti*-3ka)**



To a suspended solution of $Sm(OTf)_3$ (0.050 mmol, 0.030 g) in acetonitrile (1.0 mL), (*E*)-chalcone (0.99 mmol, 0.207 g), α-methoxyacetophenone (1.1 mmol, 0.160 g), and Bu_3SnOMe (0.097 mmol,

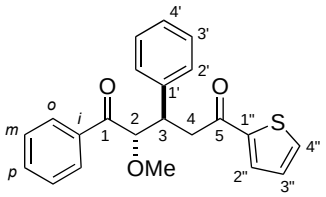
0.0311 g) was added. The reaction mixture was stirred for 24 h at 40 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 9 : 91. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.318 g, 89% yield, *syn/anti* = 5 : 95). The analytical data agreed with the previous report.[7a]

(2*S,3*R**)-2-methoxy-5-(4-methoxyphenyl)-1,3-diphenylpentane-1,5-dione (*anti*-3la)**



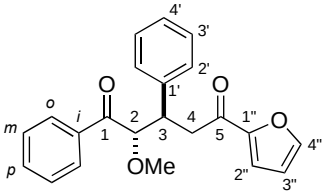
To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), 4'-methoxychalcone (0.237 g, 0.99 mmol), α-methoxyacetophenone (0.159 g, 1.1 mmol), and Bu_3SnOMe (0.033 g, 0.55 mmol) was added. The reaction mixture was stirred for 24 h at 40 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 8 : 92. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a yellow viscous liquid (0.337 g, 87% yield, *syn/anti* = 4 : 96). IR: (neat) 1678, 1597 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.96 (d, *J* = 7.2 Hz, 2H, *o*), 7.88 (d, *J* = 8.8 Hz, 2H, 2"-H x 2), 7.56 (t, *J* = 7.2 Hz, 1H, *p*), 7.44 (t, *J* = 7.2 Hz, 2H, *m*), 7.32 (d, *J* = 7.2 Hz, 2H, 2'-H x 2), 7.23 (t, *J* = 7.2 Hz, 2H, 3'-H x 2), 7.16 (t, *J* = 7.2 Hz, 2H, 4'-H x 2), 6.86 (d, *J* = 8.8 Hz, 2H, 3"-H x 2), 4.74 (d, *J* = 4.8 Hz, 1H, 2-H), 3.99 (ddd, *J* = 7.2, 5.6, 4.8 Hz, 1H, 3-H), 3.81 (s, 3H, 4"-OMe), 3.56-3.42 (m, 2H, 4-H_2), 3.36 (s, 3H, 2-OMe) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.2 (s, C-1), 196.4 (s, C-5), 163.2 (s, C-4"), 141.4 (s, C-1'), 135.4 (s, C-*i*), 133.4 (d, C-*p*), 130.2 (d, C-2"), 130.0 (s, C-1"), 128.6 (d), 128.5 (d), 128.4 (d), 128.2 (d), 126.9 (d, C-4'), 113.5 (d, C-3"), 87.6 (d, C-2), 58.2 (q, 2-OMe), 55.3 (q, 4"-OMe), 43.5 (d, C-3), 38.9 (t, C-4) MS: (EI, 70 eV) *m*/*z* 388 (M, 0.3), 283 (M − PhCO, 47), 135 (100), 77 (11) HRMS: (EI, 70 eV) calcd for ($C_{25}H_{24}O_4$) 388.1676 found *m*/*z* 388.1675

(2*S,3*R**)-2-methoxy-1,3-diphenyl-5-(thiophen-2-yl)pentane-1,5-dione (*anti*-3ma)**



To a suspended solution of $Sm(OTf)_3$ (0.031 g, 0.052 mmol) in acetonitrile (1.0 mL), (*E*)-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-one (0.214 g, 1.0 mmol), α-methoxyacetophenone (0.151 g, 1.0 mmol), and Bu_3SnOMe (0.032 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 40 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (3 x 10 mL). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 4 : 96. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.322 g, 89% yield, *syn/anti* = 1 : 99). IR: (neat) 1682, 1658 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.96 (d, *J* = 7.2 Hz, 2H, *o*), 7.70 (dd, *J* = 4.0, 1.2 Hz, 2H, 2"-H), 7.60-7.52 (m, 2H), 7.44 (t, *J* = 7.2, 7.2 Hz, 2H, *m*), 7.31 (d, *J* = 7.2 Hz, 2H, 2'-H x 2), 7.23 (t, *J* = 7.2 Hz, 2H, 3'-H x 2), 7.18 (d, *J* = 7.2 Hz, 2H, 4'-H), 7.06 (t, *J* = 4.0 Hz, 2H, 3"-H), 4.73 (d, *J* = 5.6 Hz, 1H, 2-H), 3.97 (dt, *J* = 7.6, 5.6 Hz, 1H, 3-H), 3.49-3.45 (m, 2H, 4-H_2), 3.36 (s, 3H, OMe) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.0 (s, C-1), 190.8 (s, C-5), 144.2 (s, C-1"), 140.9 (s, C-1'), 135.3 (s, C-*i*), 133.42 (d), 133.39 (d), 131.8 (d), 128.6 (d), 128.5 (d), 128.2 (d), 127.9 (d), 127.1 (d), 87.5 (d, C-2), 58.2 (q, OMe), 43.6 (d, C-3), 40.2 (t, C-4) MS: (CI, 70 eV) *m*/*z* 366 (M + 2, 24), 365 (M + 1, 100) HRMS: (CI, 70 eV) calcd for ($C_{22}H_{21}O_3S$) 365.1211 (M + 1) found *m*/*z* 365.1210

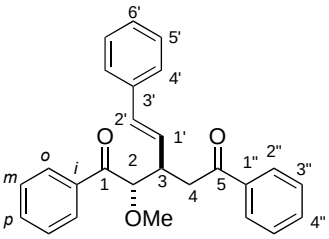
(2*S,3*R**)-5-(furan-2-yl)-2-methoxy-1,3-diphenylpentane-1,5-dione (*anti*-3na)**



To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-1-(furan-2-yl)-3-phenylprop-2-en-1-one (0.198 g, 1.0 mmol), α-methoxyacetophenone (0.157 g, 1.05 mmol), and Bu_3SnOMe (0.032 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 40 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (3 x 10 mL). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 5 : 95. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20,

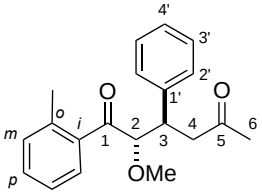
column length; 11 cm] to give the product as a colorless viscous liquid (0.310 g, 89% yield, *syn/anti* = 1 : 99). IR: (neat) 1678 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.96 (d, *J* = 7.8 Hz, 2H, *o*), 7.57 (t, *J* = 7.8 Hz, 1H, *p*), 7.52-7.51 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 2H, *m*), 7.31-7.15 (m, 5H, 3-Ph), 7.13 (d, *J* = 4.0 Hz, 1H), 6.47 (dd, *J* = 4.0, 2.0 Hz, 1H, 3"-H_2), 4.69 (d, *J* = 5.2 Hz, 1H, 2-H), 3.96 (dt, *J* = 7.2, 5.2 Hz, 1H, 3-H), 3.42-3.36 (m, 2H, 4-H), 3.35 (s, 3H, OMe) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.1 (s, C-1), 187.1 (s, C-5), 152.7 (s, C-1"), 146.1 (d, C-4"), 140.7 (s, C-1'), 135.4 (s, C-*i*), 133.4 (d, C-*p*), 128.64 (d), 128.58 (d), 128.5 (d), 128.2 (d), 127.1 (d), 116.9 (d, C-2"), 112.1 (d, C-3"), 87.9 (d, C-2), 58.3 (q, OMe), 43.4 (d, C-3), 39.5 (t, C-4) MS: (CI, 70 eV) *m*/*z* 350 (M + 2, 23), 349 (M + 1, 100) HRMS: (CI, 70 eV) calcd for ($C_{22}H_{21}O_4$) 349.1440 (M + 1) found *m*/*z* 349.1438

(2*S,3*R**)-2-methoxy-1,5-diphenyl-3-((*E*)-styryl)pentane-1,5-dione (*anti*-3oa)**



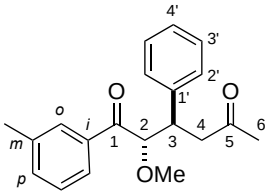
To a suspended solution of $Sm(OTf)_3$ (0.060 g, 0.10 mmol) in acetonitrile (1.0 mL), 1,5-diphenylpenta-2,4-dien-1-one (0.232 g, 0.99 mmol), α-methoxyacetophenone (0.152 g, 1.0 mmol), and Bu_3SnOMe (0.034 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 40 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 5 : 95. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.303 g, 79% yield, *syn/anti* = 5 : 95). IR: (neat) 1682, 1597 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.05 (d, *J* = 8.0 Hz, 2H, *o*), 7.92 (d, *J* = 7.2 Hz, 2H, 2"-H x 2), 7.58-7.39 (m, 6H), 7.24-7.13 (m, 5H), 6.41 (d, *J* = 15.5 Hz, 1H, 2'-H), 6.20 (dd, *J* = 15.5, 9.2 Hz, 1H, 1'-H), 4.69 (d, *J* = 5.8 Hz, 1H, 2-H), 3.61-3.52 (m, 1H, 3-H), 3.40 (s, 3H, OMe), 3.40-3.28 (m, 2H, 4-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.4 (s, C-1), 198.2 (s, C-5), 137.0 (s), 136.7 (s), 135.6 (s), 133.4 (d), 132.9 (d), 132.3 (d), 128.7, 128.5, 128.4, 128.4, 128.3, 127.9, 127.3 (d), 126.2 (d), 86.6 (d, C-2), 58.2 (q, 2-OMe), 41.9 (d, C-3), 38.9 (t, C-4) MS: (EI, 70 eV) *m*/*z* 384 (M^+, 0.1), 352 (22), 105 (PhCO, 100), 77 (19) HRMS: (EI, 70 eV) calcd for ($C_{26}H_{24}O_3$) 384.1725 (M^+) found *m*/*z* 384.1723

(2*S,3*R**)-2-methoxy-3-phenyl-1-(*o*-tolyl)hexane-1,5-dione (*anti*-3ab)**



To a suspended solution of $Sm(OTf)_3$ (0.031 g, 0.052 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.147 g, 1.01 mmol), 2-methoxy-1-(*o*-tolyl)ethan-1-one (0.168 g, 1.0 mmol), and Bu_3SnOMe (0.036 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 50 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 4 : 96. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.255 g, 82% yield, *syn/anti* = 1 : 99). IR: (neat) 1716, 1689 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.68 (d, *J* = 7.6 Hz, 2H, *o'*), 7.34 (t, *J* = 7.6 Hz, 1H, *p*), 7.25-7.10 (m, 7H, *m*, *m'* and Ph), 4.50 (d, *J* = 5.2 Hz, 1H, 2-H), 3.61 (dt, *J* = 8.8, 5.2 Hz 1H, 3-H), 3.40 (s, 3H, OMe), 3.01 (dd, *J* = 17.8, 5.2 Hz, 1H, 4-H^A), 2.89 (dd, *J* = 17.8, 8.8 Hz, 1H, 4-H^B), 2.19 (s, 3H, *o*-CH_3), 2.03 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.6 (s, C-5), 202.3 (s, C-1), 140.5 (s, C-1'), 138.8 (s), 136.2 (s), 131.8 (d), 131.4 (d), 128.3 (d), 128.1 (d), 128.0 (d), 126.9 (d), 125.4 (d), 88.3 (d, C-2), 58.1 (q, 2-OMe), 45.0 (t, C-4), 42.9 (d, C-3), 30.3 (q, C-6), 20.5 (q, Ar-*C*H_3) MS: (CI, 70 eV) *m*/*z* 312 (M + 2, 21), 311 (M + 1, 100), 191 (M – PhCO, 13) HRMS: (CI, 70 eV) calcd for ($C_{20}H_{23}O_3$) 311.1647 (M + 1) found *m*/*z* 311.1645

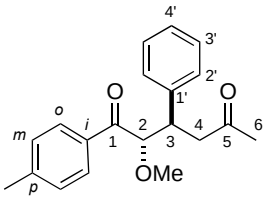
(2*S,3*R**)-2-methoxy-3-phenyl-1-(*m*-tolyl)hexane-1,5-dione (*anti*-3ac)**



To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.147 g, 1.0 mmol), 2-methoxy-1-(*m*-tolyl)ethan-1-one (0.169 g, 1.0 mmol), and Bu_3SnOMe (0.035 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 7 : 93. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column

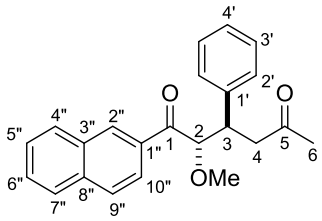
length; 11 cm] to give the product as a colorless viscous liquid (0.246 g, 79% yield, *syn/anti* = 2 : 98). IR: (neat) 1716, 1689 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.75-7.69 (m, 2H, *o* and *o'*), 7.38 (d, *J* = 7.8 Hz, 1H, *p*), 7.32 (t, *J* = 7.2 Hz, 1H, *m'*), 7.27-7.13 (m, 5H, Ph), 4.63 (d, *J* = 5.6 Hz, 1H, 2-H), 3.75 (dt, *J* = 8.8, 5.6 Hz 1H, 3-H), 3.34 (s, 3H, OMe), 3.05 (dd, *J* = 17.4, 5.6 Hz, 1H, 4-H^A), 2.92 (dd, *J* = 17.4, 8.8 Hz, 1H, 4-H^B), 2.39 (s, 1H, Ar-CH_3), 2.04 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.6 (s, C-5), 199.3 (s, C-1), 141.1 (s, C-1'), 138.4 (s), 135.4 (s), 134.2 (d, C-*p*), 128.9 (d), 128.5 (d), 128.4 (d), 128.0 (d), 127.0 (d), 125.6 (d), 87.1 (d, C-2), 58.1 (q, 2-OMe), 44.3 (t, C-4), 43.2 (d, C-3), 30.4 (q, C-6), 21.3 (q, Ar-*C*H_3) MS: (CI, 70 eV) *m*/*z* 312 (M + 2, 22), 311 (M + 1, 100) HRMS: (CI, 70 eV) calcd for ($C_{20}H_{23}O_3$) 311.1647 (M + 1) found *m*/*z* 311.1649

(2*S,3*R**)-2-methoxy-3-phenyl-1-(*p*-tolyl)hexane-1,5-dione (*anti*-3ad)**



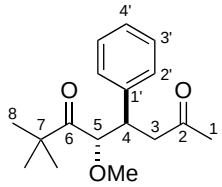
To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.145 g, 1.0 mmol), 2-methoxy-1-(*p*-tolyl)ethan-1-one (0.164 g, 1.00 mmol), and Bu_3SnOMe (0.030 g, 0.096 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 6 : 94. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80 : 20, column length; 11 cm] to give the product as a white solid (0.227 g, 74% yield, *syn/anti* = 1 : 99). IR: (neat) 1716, 1673 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.84 (d, *J* = 8.0 Hz, 2H, *o*), 7.32-7.17 (m, 7H), 4.60 (d, *J* = 5.6 Hz, 1H, 2-H), 3.76 (dt, *J* = 8.4, 5.6 Hz, 1H, 3-H), 3.33 (s, 3H, OMe), 3.06 (dd, *J* = 17.4, 5.6 Hz, 1H, 4-H^A), 2.91 (dd, *J* = 17.4, 8.4 Hz, 1H, 4-H^B), 2.41 (s, 3H, *p*-CH_3), 2.04 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.7 (s, C-5), 198.7 (s, C-1), 144.4 (s, C-*p*), 141.2 (s, C-1'), 132.9 (s, C-*i*), 129.3 (d), 128.6 (d), 128.5 (d), 128.1 (d), 127.1 (d), 87.3 (d, C-2), 58.2 (q, 2-OMe), 44.5 (t, C-4), 43.4 (d, C-3), 30.4 (q, C-6), 21.7 (q, *p*-CH_3) MS: (EI, 70 eV) *m*/*z* 310 (M^+, 0.2), 191 (100), 119 (19), 117 (90), 91 (16), 43 (22) HRMS: (EI, 70 eV) calcd for ($C_{20}H_{22}O_3$) 310.1569 (M^+) found *m*/*z* 310.1563

(2*S,3*R**)-2-methoxy-1-(naphthalen-2-yl)-3-phenylhexane-1,5-dione (*anti*-3ae)**



To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.146 g, 1.0 mmol), 2-methoxy-1-(naphthalen-2-yl)ethan-1-one (0.201 g, 1.0 mmol), and Bu_3SnOMe (0.0326 g, 0.10 mmol) was added. The reaction mixture was stirred for 24 h at 50 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried by $MgSO_4$, and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the ratio of *syn/anti* was 7 : 93. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.280 g, 81% yield, *syn/anti* = 1 : 99). IR: (neat) 1712, 1682 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.50 (s, 1H, 10'-H), 7.96-7.93 (m, 2H), 7.87-7.84 (m, 2H), 7.60-7.54 (m, 2H), 7.29-7.14 (m, 5H, Ph), 4.73 (d, *J* = 5.2 Hz, 1H, 2-H), 3.87 (dt, *J* = 8.4, 5.2 Hz, 1H, 3-H), 3.39 (s, 3H, OMe), 3.14 (dd, *J* = 17.6, 5.2 Hz, 1H, 4-H^A), 2.93 (dd, *J* = 17.6, 8.0 Hz, 1H, 4-H^B), 2.06 (s, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.6 (s, C-5), 199.1 (s, C-1), 140.9 (s, C-1"), 135.6 (s), 132.7 (s), 132.3 (s), 130.4 (d), 129.7 (d), 128.7 (d), 128.5 (d), 128.5 (d), 128.2 (d), 127.7 (d), 127.1 (d), 126.7 (d), 124.1 (d), 87.7 (d, C-2), 58.2 (q, 2-OMe), 44.7 (t, C-4), 43.6 (d, C-3), 30.4 (q, C-6) MS: (EI, 70 eV) *m*/*z* 346 (M^+, 0.3), 192 (13), 191 (M - ArCO, 100), 155 (19), 134 (15), 127 (23), 117 (75), 43 (22) HRMS: (EI, 70 eV) calcd for ($C_{23}H_{22}O_3$) 346.1569 (M^+) found *m*/*z* 346.1573

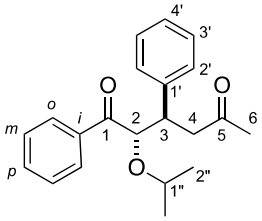
(4*R,5*S**)-5-methoxy-7,7-dimethyl-4-phenyloctane-2,6-dione (*anti*-3af)**



To a suspended solution of $Sm(OTf)_3$ (0.029 g, 0.049 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.145 g, 1.0 mmol), 1-methoxy-3,3-dimethylbutan-2-one (0.138 g, 1.1 mmol), and Bu_3SnOMe (0.035 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the

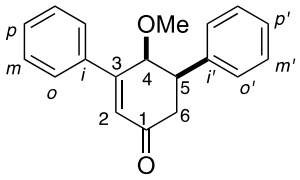
crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 6 : 94. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.067 g, 24% yield, *syn/anti* = 5 : 95). IR: (neat) 1705 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.41-7.19 (m, 5H, Ph), 4.29 (d, *J* = 3.2 Hz, 1H, 5-H), 3.68 (ddd, *J* = 7.2, 4.8, 3.2 Hz, 1H, 4-H), 3.21-3.13 (m, 4H, OMe and 3-H^A), 2.79 (dd, *J* = 18.0, 7.2 Hz, 1H, 3-H^B), 2.05 (s, 3H, 1-H_3), 1.14 (s, 9H, 8-H_3 and 7-Me x 2) ^{13}C NMR: (100 MHz, $CDCl_3$) 213.9 (s, C-6), 207.0 (s, C-2), 142.2 (s, C-1'), 128.4 (d), 128.3 (d), 126.9 (d, C-4'), 83.0 (d, C-5), 57.4 (q, OMe), 43.7 (s, C-7), 43.0 (t, C-3), 41.2 (d, C-4), 30.3 (q, C-1), 26.1 (q, C-8 and 7-Me x 2) MS: (CI, 70 eV) *m*/*z* 278 (M + 2, 18), 277 (M + 1, 100), 245 (14), 191 (M - ^{t}BuCO, 14), 147 (22) HRMS: (CI, 70 eV) calcd for ($C_{17}H_{25}O_3$) 277.1804 (M + 1) found *m*/*z* 277.1804

(2*S,3*R**)-2-isopropoxy-1,3-diphenylhexane-1,5-dione (*anti*-3ag)**



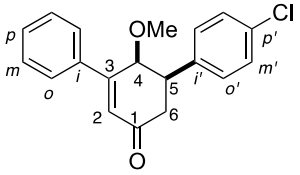
To a suspended solution of $Sm(OTf)_3$ (0.030 g, 0.050 mmol) in acetonitrile (1.0 mL), (*E*)-4-phenylbut-3-en-2-one (0.147 g, 1.1 mmol), 2-isopropoxy-1-phenylethan-1-one (0.179 g, 1.0 mmol), and Bu_3SnOMe (0.031 g, 0.097 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^{1}H NMR analysis of the crude products indicated the ratio of *syn/anti* was 8 : 92. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a yellow viscous liquid (0.131 g, 30% yield, *syn/anti* = 1 : 99). IR: (neat) 1716, 1689 (C=O) cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.96 (d, *J* = 8.0 Hz, 2H, *o*), 7.55 (t, *J* = 8.0 Hz, 1H, *p*), 7.43 (t, *J* = 8.0 Hz, 2H, *m*), 7.24-7.14 (m, 5H, 3-Ph), 4.65 (d, *J* = 6.8 Hz, 1H, 2-H), 3.75 (dt, *J* = 8.4, 5.2 Hz, 1H, 3-H), 3.51 (septet, *J* = 6.0 Hz, 1H, 1"-H), 3.10 (dd, *J* = 18.0, 5.2 Hz, 1H, 4-H^A), 2.91 (dd, *J* = 18.0, 8.4 Hz, 1H, 4-H^B), 2.06 (s, 3H, 6-H_3), 1.13 (d, *J* = 6.0 Hz, 3H, 2"-H_3), 1.09 (d, *J* = 6.0 Hz, 3H, 2"-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.9 (s, C-5), 200.2 (s, C-1), 140.4 (s, C-1'), 135.4 (s, C-*i*), 133.2 (d, C-*p*), 128.7 (d), 128.5 (d), 128.4 (d), 128.2 (d), 127.1 (d), 84.5 (d, C-2), 72.4 (d, C-1"), 45.0 (t, C-4), 43.9 (d, C-3), 30.4 (q, C-6), 22.8 (q, C-2"), 21.3 (q, C-2") MS: (CI, 70 eV) *m*/*z* 326 (M + 2, 22), 325 (M + 1, 100), 219 (M - PhCO, 12) HRMS: (CI, 70 eV) calcd for ($C_{21}H_{25}O_3$) 325.1804 (M + 1) found *m*/*z* 325.1801

***cis*-4-methoxy-3,5-diphenylcyclohex-2-en-1-one (*cis*-9aa)**



To a suspended solution of $Sm(OTf)_3$ (0.029 g, 0.049 mmol) in propionitrile (1.0 mL), 4-phenylbut-3-en-2-one (0.147 g, 1.0 mmol), α-methoxyacetophenone (0.152 g, 1.0 mmol), and Bu_3SnOMe (0.034 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then the mixture was stirred for 24 h at 115 °C. The reaction mixture was quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the diastereomeric ratio was 18 : 82. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.252 g, 90% yield, *cis*/*trans* > 99:1). IR: (neat) 1678 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.63-7.55 (m, 2H), 7.47-7.25 (m, 8H), 6.36 (s, 1H, 2-H), 4.50 (d, J = 3.6 Hz, 1H, 4-H), 3.53 (dt, J = 13.0, 3.6 Hz 1H, 5-H), 3.32 (dd, J = 16.8, 13.0 Hz, 1H, 6-H^A), 2.94 (s, 3H, OMe), 2.61 (dd, J = 16.8, 3.6 Hz, 1H, 6-H^B) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.8 (s, C-1), 157.6 (s, C-*i*), 140.5 (s, C-*i'*), 138.1 (s, C-3), 130.0 (d), 128.9 (d), 128.5 (d), 128.1 (d), 127.2 (d), 126.6 (d), 126.2 (d), 78.6 (d, C-4), 60.2 (q, 2-OMe), 45.1 (d, C-5), 36.7 (t, C-6) MS: (EI, 70 eV) *m*/*z* 278 (M^+, 16), 175 (12), 174 (100), 159 (20), 103 (19) HRMS: (EI, 70 eV) calcd for ($C_{19}H_{18}O_2$) 278.1307 (M^+) found *m*/*z* 278.1304

***cis*-4-methoxy-5-(*p*-chlorophenyl)-3-phenylcyclohex-2-en-1-one (*cis*-9ba)**



To a suspended solution of $Sm(OTf)_3$ (0.031 g, 0.051 mmol) in propionitrile (1.0 mL), 4-(4-chlorophenyl)but-3-en-2-one (0.181 g, 1.0 mmol), α-methoxyacetophenone (0.161 g, 1.1 mmol), and Bu_3SnOMe (0.036 g, 0.11 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then the mixture was stirred for 24 h at 115 °C. The reaction mixture was quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the crude products indicated the diastereomeric ratio was 17 : 83. The crude product was purified by

column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a colorless viscous liquid (0.229 g, 73% yield, *cis*/*trans* > 99:1). IR: (neat) 1666 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.60-7.55 (m, 2H), 7.48-7.43 (m, 3H), 7.38-7.33 (m, 4H), 6.35 (s, 1H, 2-H), 4.46 (d, J = 3.6 Hz, 1H, 4-H), 3.50 (dt, J = 13.2, 3.6 Hz, 1H, 5-H), 3.25 (dd, J = 16.4, 13.2 Hz, 1H, 6-H^A), 2.97 (s, 3H, OMe), 2.57 (dd, J = 16.4, 3.6 Hz, 1H, 6-H^B) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.3 (s, C-1), 157.5 (s, C-*i*), 139.1 (s), 138.0 (s, C-3), 133.1 (s), 130.1 (d), 129.4 (d), 129.0 (d), 128.7 (d), 126.6 (d), 126.2 (d), 78.2 (d, C-4), 60.1 (q, 2-OMe), 44.6 (d, C-5), 37.1 (t, C-6) MS: (EI, 70 eV) *m*/*z* 314 (M + 2, 3)312 (M^+, 9), 175 (12), 174 (100), 159 (19), 103 (17) HRMS: (EI, 70 eV) calcd for ($C_{19}H_{17}ClO_2$) 312.0917 (M^+) found *m*/*z* 312.0916

The preparation of the single crystal to measure X-ray diffraction; The CH_2Cl_2/Hexane solution of the product was allowed to stand still and then single crystal was obtained as a colorless solid. After the measurement of X-ray crystallography, it was confirmed by NMR spectroscopy that the colorless solid was the *cis* product.

X-ray data M = 312.80 colorless monoclinic $P2_1/c$ (#14) a = 7.0808(2) Å b = 14.9756(3) Å c = 14.8655(3) Å α = 90° β = 104.618(2)° γ = 90° V = 1525.29(6) $Å^3$ Z = 4 D_{calcd} = 1.362 g/cm^3 T = -150 °C R_1 (wR_2) = 0.0553 (0.0801)

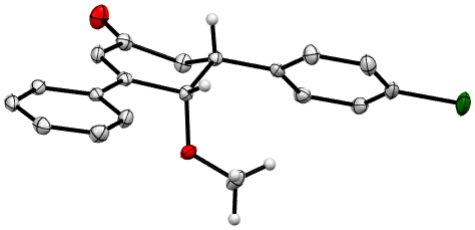
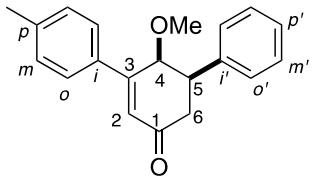


Figure 2. Molecular structures of *cis*-**9ba**.

***cis*-4-methoxy-5-phenyl-3-(*p*-tolyl)cyclohex-2-en-1-one (*cis*-9ad)**



To a suspended solution of $Sm(OTf)_3$ (0.029 g, 0.049 mmol) in propionitrile (1.0 mL), 4-phenylbut-3-en-2-one (0.145 g, 0.099 mmol), 2-methoxy-1-(*p*-tolyl)ethan-1-one (0.171 g, 1.0 mmol), and Bu_3SnOMe (0.039 g, 0.12 mmol) was added. The reaction mixture was stirred for 24 h at 60 °C, and then the mixture was stirred for 24 h at 115 °C. The reaction mixture was quenched by NH_4F aq (10%, 10 mL). The mixture was extracted with diethyl ether (10 mL x 3). The collected organic layers were dried ($MgSO_4$), and evaporation of volatiles gave the crude product. ^1H NMR analysis of the

crude products indicated the diastereomeric ratio was 11 : 89. The crude product was purified by column chromatography [solvent; hexane/ethyl acetate = 80/20, column length; 11 cm] to give the product as a yellow solid (0.179 g, 70% yield, *cis*/*trans* > 99:1). IR: (neat) 1651 (C=O) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.49 (d, *J* = 8.0 Hz, 2H), 7.43-7.37 (m, 4H), 7.35-7.29 (m, 1H), 7.26-7.21 (m, 2H), 6.35 (s, 1H, 2-H), 4.50 (d, *J* = 3.6 Hz, 1H, 4-H), 3.51 (dt, *J* = 13.4, 3.6 Hz, 3H, 5-H), 3.30 (dd, *J* = 16.4, 13.4 Hz, 1H, 6-H^A), 2.94 (s, 3H, OMe), 2.60 (dd, *J* = 16.4, 3.6 Hz, 1H, 6-H^B), 2.39 (s, 3H, CH_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 199.9 (s, C-1), 157.5 (s, C-*i*), 140.7 (s), 140.5 (s), 135.0 (s, C-3), 129.7 (d), 128.5 (d), 128.1 (d), 127.2 (d), 126.6 (d), 125.4 (d, C-2), 78.4 (d, C-4), 60.1 (q, OMe), 45.1 (d, C-5), 37.0 (t, C-6), 21.3 (q, CH_3) MS: (EI, 70 eV) *m*/*z* 292 (M^+, 22), 189 (15), 188 (100), 173 (26), 145 (13), 117 (20), 115 (12) HRMS: (EI, 70 eV) calcd for ($C_{20}H_{20}O_2$) 292.1463 (M^+) found *m*/*z* 292.1461

1-5. References

(1) P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon, Oxford, **1992**.

(2) For selected reviews, see: (a) J. Christoffers, *Eur. J. Org. Chem.* **1998**, *7*, 1259. (b) M. Sibi, S. Manyem, *Tetrahedron*, **2000**, *56*, 8033. (c) N. Krause, A. Hoffman-Röder, *Synthesis* **2001**, 171. (d) J. Christoffers, A. Baro, *Angew.Chem. Int. Ed.* **2003,** *42*, 1688; (e) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* **2005**, *105*, 933. (f) J. Christoffers, G. Koripelly, A. Rosiak, M. Rössle, *Synthesis* **2007**, 1279. (g) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701. (h) S. Sulzer-Mossé, A. Alexakis, *Chem. Commun.* **2007**, 3123. (i) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pamies and M. Diéguez, *Chem. Rev.* **2008**, *108*, 2796. (j) H. Pellissier, *Adv. Synth. Catal.* **2016**, *358*, 2194.

(3) Selected examples for Michael additions of 1,3-dicarbonyl compounds to enones, see: (a) R. Helder, H. Wynberg, *Tetrahedron Lett.* **1975**, *16*, 4057. (b) K. Hermann, H. Wynberg, *J. Org. Chem.* **1979**, *44*, 2238. (c) D. J. Carm, G. D. Y. Sogah, *J. Chem. Soc. Chem. Commun.* **1981**, 625. d) H. Brunner, B. Hammer, *Angew. Chem.* **1984**, *96*, 305; *Angew. Chem. Int. Ed.* **1984**, *23*, 312. (e) M. Yamaguchi, T. Shiraishi, M. Hirama, *Angew. Chem.* **1993**, *105*, 1243; *Angew. Chem. Int. Ed.* **1993**, *32*, 1176. (f) H. Sasai, T. Arai, M. Shibasaki, *J. Am. Chem. Soc.* **1994**, *116*, 1571. (g) H. Sasai, T. Arai, Y. Satow, K. N. Houk, M. Shibasaki, *J. Am. Chem. Soc.* **1995**, *117*, 6194. (h) M. Yamaguchi, T. Shiraishi, M. Hirama, *J. Org. Chem*. **1996**, *61*, 3520. (i) T. Arai, H. Sasai, K. Aoe, K. Okamura, T. Date, M. Shibasaki, *Angew. Chem.* **1996**, *108*, 103; *Angew. Chem. Int. Ed.* **1996**, *35*, 104. (j) Y. S. Kim, S. Matsunaga, J. Das, A. Sekine, T. Oshima, M. Shibasaki, *J. Am. Chem. Soc.* **2000**, *122*, 6506. (k) M. Nakajima, Y. Yamaguchi, S. Hashimoto, *Chem. Commun.* **2001**, 1596. (l) Y. Hamashima, D. Hotta, M. Sodeoka, *J. Am. Chem. Soc.* **2002**, *124*, 11240. (m) K. Majima, R. Takita, A. Okada, T. Oshima, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 15837. (n) N. Halland, P. S. Aburel, K. A. Jørgensen, *Angew. Chem.* **2003**, *115*, 685; *Angew. Chem. Int. Ed.* **2003**, *42*, 661. (o) N. Halland, T. Hansen, K. A. Jørgensen, *Angew. Chem.* **2003**, *115*, 5105; *Angew. Chem. Int. Ed.* **2003**, *42*, 4955. (p) K. R. Kundsen, C. E. T. Mitchell, S. V. Ley,

Chem. Commun. **2006**, 66.

(4) (a) Y. Hamashima, D. Hotta, M. Sodeoka, *J. Am. Chem. Soc.* **2002**, *124*, 11240. (b) Y. Hamashima, D. Hotta, N. Umebayashi, Y. Tsuchida, M. Sodeoka, *Adv. Synth. Catal.* **2005***, 347,* 1576. (c) J. Yang, W. Li, Z. Jin, X. Liang, J. Ye, *Org. Lett.* **2010**, *12*, 5218. (d) F. Wu, R. Hong, J. Khan, X. Liu, L. Deng, *Angew. Chem. Int. Ed.* **2006**, *45*, 4301. (e) N. R. Cichowicz, W. Kaplan, Y. Khomutnyk, B. Bhattarai, Z. Sun, P. Nagorny, *J. Am. Chem. Soc.* **2015**, *137*, 14341.

(5) (a) S. Bera, S. K. Das, T. Saha, G. Panda, *Tetrahedron Lett.* **2015**, *56*, 146. (b) H. Nemoto, N. Matsuhashi, M. Imaizumi, M. Nagai, K. Fukumoto, *J. Org. Chem.* **1990**, *55*, 5625. (c) D. Taub, R. D. Hoffsommer, H. L. Slates, N. L. Wendler, *J. Am. Chem. Soc.* **1958**, *80*, 4435. (d) G. V. Pillai, A. J. Smith, P. A. Hunt, P. B. Simpson, *Biochem. Pharmacol*. **2004**, *68*, 819.

(6) (a) N. Kumagai, S. Matsunaga, M. Shibasaki, *Org. Lett.* **2001**, *3*, 4251. (b) S. Harada, N. Kumagai, T. Kinoshita, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 2582. (c) Y.-Z. Hua, M.-M. Liu, P.-J. Huang, X. Song, M.-C. Wang, J.-B. Chang, *Chem. Eur. J.* **2015**, *21*, 11994.

(7) The stoichiometric amount of tin amide promoted *anti*-selective direct Michael addition of α-alkoxyketones to enone. (a) I. Shibata, K. Yasuda, Y. Tanaka, M. Yasuda, A. Baba, *J. Org. Chem.* **1998**, *63*, 1334. The stoichiometric amount of lithium diisopropylamide promoted *syn*-selective direct Michael addition of α-alkoxyacetate to enone. (b) S. Kanemasa, M. Nomura, E. Wada, *Chem. Lett.* **1991**, 1735.

(8) Enantioselective direct Michael addition of α-alkoxyketones to nitroalkenes was reported. (a) H. Huang, E. N. Jacobsen, *J. Am. Chem. Soc.* **2006**, *128*, 7170. catalytic cycloaddition of α-hydroxyketones with dicyanoalkenes including *anti*-selective Michael addition step of α-hydroxyketones to dicyanoalkenes was reported. (b) S. Tsunoi, Y. Seo, Y. Takano, I. Suzuki, I. Shibata *Org. Biomol. Chem.* **2016**, *14*, 1707.

(9) Intramolecular Direct catalytic Michael addition of α-oxyketone moiety to enone moiety (a) J. christensen, Ł. Albrecht, K. A. Jørgensen, *Chem. Asian. J.* **2013**, *8*, 648. (b) Y. Liu, A. Lu, K. Hu, Y. Wang, H. Song, Z. Zhou, C. Tang, *Eur. J. Org. Chem.* **2013**, 4836. (c) D. J. B. Antúnez, M. D. Greenhalgh, C. Fallan, A. M. Z. Slawin, A. D. Smith, *Org. Biomol. Chem*., **2016**, *14*, 7268.

(10)(a) A. Yanagisawa, S. Takeshita, Y. Izumi, K. Yoshida, *J. Am. Chem. Soc.* **2010**, *132*, 5328. (b) A. Yanagisawa, T. Satou, A. Izumiseki, Y. Tanaka, M. Miyagi, T. Arai, K. Yoshida, *Chem. Eur. J.* **2009**, *15*, 11450.

(11)The configuration of **3ea** was determined by X-ray structural analysis, see supporting information.

(12)The transmetalation between Bu_3SnOMe and $Sm(OTf)_3$ smoothly proceeded at ambient temperature and the process was observed by ^{13}C NMR.

(13)The coordination of alkoxyketone by samarium methoxide was observed by ^{13}C NMR.

(14)When Me_3SnOMe was used instead of Bu_3SnOMe, the *anti*-selectivity was quite changed (75% yield,

anti/syn = 77/23). This result suggested that the tin enolate generated in *situ* acted as a reactive species of Michael addition step.

(15)The reaction of tributyltin enolate derived from alkoxyketone with enone generates the *anti*-product. see. ref. 7a.

(16)D. A. Oare, C. H. Heathcock, *J. Org. Chem.* **1990**, *55*, 157.

(17)Selected example of Michael additions of tin enolates, see: a) I. Shibata, M. Nishio, A. Baba, H. Matsuda, *J. Chem. Soc. Chem. Commun.* **1983**, 1067. b) I Shibata, Y. Mori, H. Yamasaki, A. Baba, H. Matsuda, *Tetrahedron Lett.* **1993**, *34*, 6567. c) M. Yasuda, N. Ohigashi, I. Shibata, A. Baba, *J. Org. Chem.* **1999**, *64*, 2180. d) M. Yasuda, N. Ohigashi, A. Baba, *Chem. Lett.* **2000**, 1266. e) M. Yasuda, K. Chiba, N. Ohigashi, Y. Katoh, A. Baba, *J. Am. Chem. Soc.* **2003**, *125*, 7291.

(18)Y.-Q. Yang, Z. Chai, H.-F. Wang, X.-K. Chen, H.-F. Cui, C.-W. Zheng, H. Xiao, P. Li, G. Zhao, *Chem. Eur. J.* **2009**, *15*, 13295.

(19)The configuration of major isomer was determined by X-ray structural analysis of **9ba**.

(20)The reaction of **1b** with **2a** in EtCN at 60 °C for 24 h gave the corresponding product **3ab** (91% yield, *anti*/*syn* = 93/7).

(21)**Synthetic methods: 1d, 1f**; W. J. Kerr, R. J. Mudd, L. C. Paterson, J. A. Brown, *Chem. Eur. J.* **2014**, *20*, 14604. **1e**; Z. Wang, G. Yin, J. Qin, M. Gao, L. Cao, A. Wu, *Synthesis* **2008**, *22*, 3675. A. Ueda, T. Umeno, M. Doi, K. Akagawa, K. Kudo, M. Tanaka, *J. Org. Chem*. **2016**, *81*, 6343. **1g**; E. M. Phillips, M. Riedrich, K. A. Scheidt, *J. Am. Chem. Soc*. **2010**, *132*, 13179. **1h**; M. bandini, M. Fagioli, M. Garavelli, A. Melloni, V. Trigari, A. U.-Ronchi, *J. Org. Chem*. **2004**, *69*, 7511. N. Rodriguez, F. Manjolinho, M. F. Grünberg, L. J. Gooßen, *Chem. Eur. J*. **2011**, *17*, 13688. **1i**; J. Otera, Y. Fujita, S. Fukuzumi, *Tetrahedron* **1996**, *52*, 9409. **1n**; N. Molleti, N. K. Rana, V. K. Singh, *Org. Lett*. **2012**, *14*, 4322. **1o**; X-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P-H. Leung, *Organometallics* **2015**, *34*, 5196.

(22)**Synthetic methods: 2b, 2d**; N.Sakai, H. Hori, Y. Ogiwara, *Eur. J. Org. Chem*. **2015**, 1905. **2f, 2g**; R. M. Moriarty, O. Prakash, M. P. Duncan, R. K. Vaid, *J. Org. Chem.* **1987**, *52*, 1097. assignment: **2b**, **2d**; Y. Tamura, T. Yakura, Y. Shirouchi, J-I. Haruta, *Chem. Pharm. Bull.* **1985**, *33*, 1097. **2f**; P. Mizar, T. Wirth, *Angew. Chem. Int. Ed.* **2014**, *53*, 5993. **2g**; R. M. Moriarty, O. Prakash, M. P. Duncan, R. K. Vaid, *J. Org. Chem.* **1987**, *52*, 150.

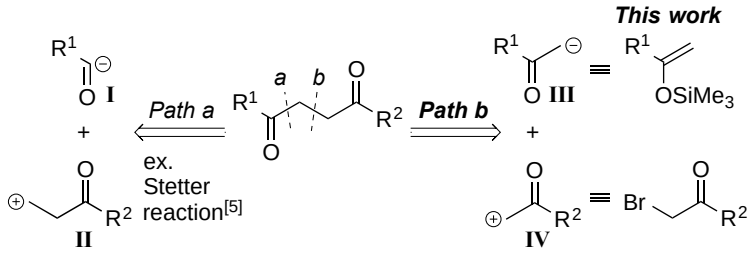
Chapter 2

Synthesis of 1,4-Dicarbonyl Compounds from Silyl Enol Ethers and Bromocarbonyls Catalyzed by an Organic Dye under Visible Light Irradiation

2-1. Introduction

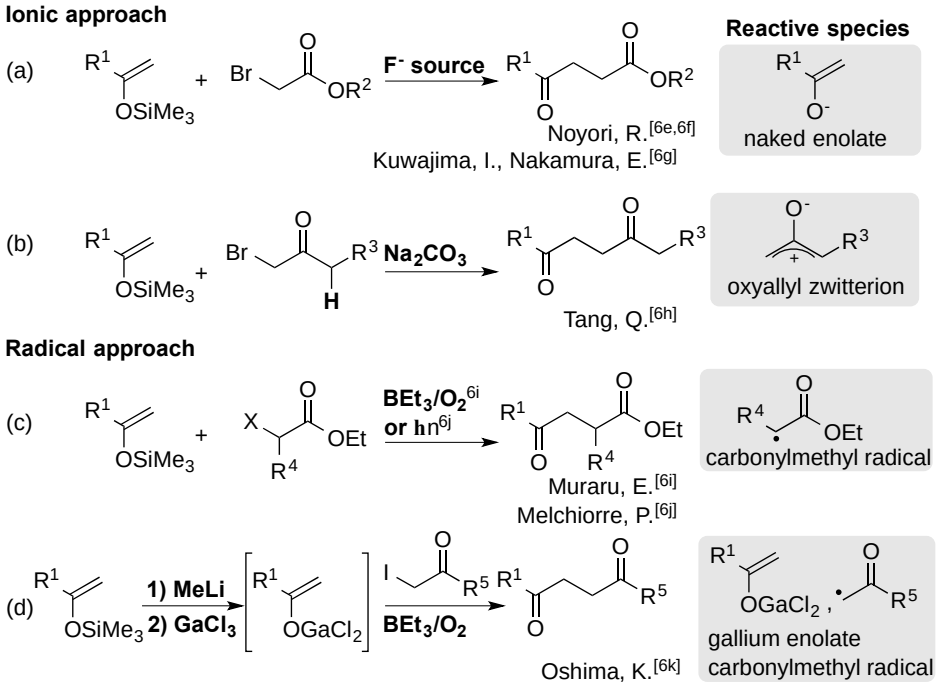
1,4-Dicarbonyl compounds are an important class of compounds as building blocks for biological molecules[1] and precursors for the Paal–Knorr synthesis, which gives five-membered heteroarenes.[2] Several synthetic methods have been developed to afford the broadly useful 1,4-dicarbonyl compounds.[3] Considering a retrosynthesis of the 1,4-dicarbonyl compounds, two strategies were designed as illustrated in Scheme 1: the reaction of an acyl anion equivalent **I** with a carbonylethyl cation **II** (path a) or the reaction of a carbonylmethyl anion **III** with a cation **IV** (path b). Methods based on path have been limited due to difficulties associated with controlling the reactivity at acyl anion **I**.[4] The only successful reaction is that involving the Breslow intermediates as acyl anion equivalents, which is generated by an *in situ* reaction between the aldehydes and carbenes, and unsaturated carbonyl compounds as equivalents for cation **II** (Stetter reaction).[5] Path b is exemplified by the reaction of enolates with α-halocarbonyls.[6] This reaction system intrinsically suffers from chemoselectivity problems because the α-halocarbonyls include two electrophilic moieties: carbonyl and halide groups. Previously, our group reported the synthesis of 1,4-dicarbonyls using highly coordinated tin enolates and α-halocarbonyls via a halo-substitution reaction.[6a] The carbonyl addition reaction of the tin enolates, which possess a high nucleophilicity, was avoided by controlling the reactivity of the tin enolates using ligands that formed higher-order tin enolates with a low reactivity toward carbonyl groups.[7] The selectivity was not perfect, however, and some amounts of carbonyl adducts accompanied the 1,4-dicarbonyls.[6a]

Scheme 1. Retrosynthesis of 1,4-dicarbonyl compounds.



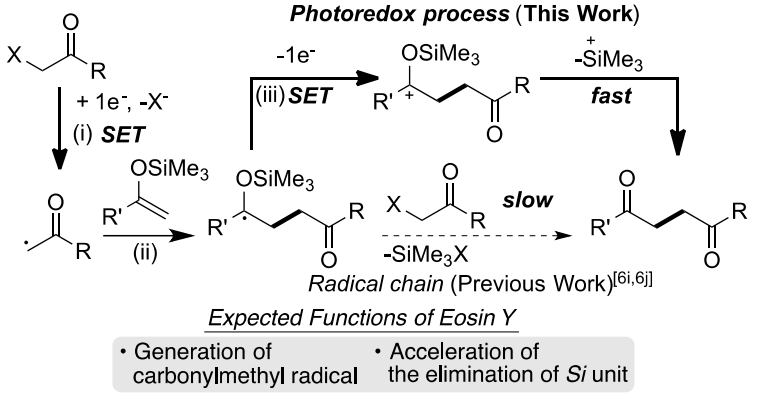
The use of moderately nucleophilic silyl enol ethers shows promise for providing a high chemoselectivity; however, these compounds are inert to halocarbonyls under thermal conditions in the absence of additives.[8] To the best of our knowledge, only four processes using silyl enol ethers and halocarbonyls have been identified for the synthesis of 1,4-dicarbonyls.[6e-6k] Fluoride anion–activated silyl enol ethers may be applied to the reaction with haloesters in ionic approaches (Scheme 2a)[6e-6g] The naked enolate species generated by fluoride anions *in situ* has a high nucleophilicity; therefore, the reaction of the haloester, with a carbonyl group that is less electrophilic than that of the haloketones, was established. Recently, Tang's group reported the reaction of silyl enol ethers with haloketones in the presence of weak bases to give 1,4-dicarbonyls (Scheme 2b).[6h] Although haloketones were applied to this system, the substrate scope was intrinsically limited to aliphatic substrates bearing an α'-hydrogen because the reaction requires the generation of a key oxyallyl zwitterion intermediate. In radical approaches, a radical initiator or photosensitizer promotes the coupling reaction to generate the reactive carbonylmethyl radical; however, only haloesters were used (Scheme 2c).[6i,6j] An alternative approach involves a reaction using gallium enolate generated by the treatment of silyl enol ethers and gallium chloride under basic conditions (Scheme 2d).[6k] This reaction was applied to haloketones, although the yield was low. As described above, the generality of the halocarbonyls has been quite limited.

Scheme 2. Reported syntheses of 1,4-dicarbonyls by reactions of silyl enol ethers with halocarbonyls.



Photoredox processes were recently developed using ruthenium or iridium complexes or organic dyes as photocatalysts.[9] Our group has reported the use of the eosin Y–catalyzed α-allylation of halocarbonyls using allyltrifluoroborate salts under visible light irradiation.[10] Eosin Y effectively generates carbonylmethyl radicals from halocarbonyls (E_{red}($BzCH_2Br/BzCH_2Br^{\bullet-}$) = –0.49 V vs. SCE) [11a] via single electron transfer (SET) from the photoexcited eosin Y (E^*_{ox}($eosinY^{\bullet+}$/eosinY*) = –1.11 V vs. SCE) [9g] and acceleration of the elimination of the borate moiety via single electron oxidation. The working hypothesis of the reaction between silyl enol ethers and halocarbonyls in the presence of eosin Y is shown in Scheme 3: i) the generation of a carbonylmethyl radical via single electron reduction of the halocarbonyls by eosin Y; ii) addition of the radical to silyl enol ethers; and iii) single electron oxidation to accelerate the elimination of the silyl moiety. Herein, we disclose a new strategy for synthesizing 1,4-dicarbonyl compounds from silyl enol ethers and halocarbonyls using eosin Y as a photoredox catalyst.

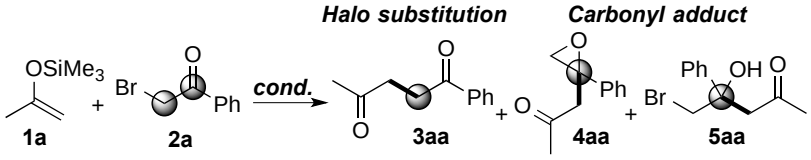
Scheme 3. Working hypothesis for the reaction of silyl enol ethers with halocarbonyls via a SET process.



2-2. Results and Discussion

First, we explored reported reaction systems for reactions of silyl enol ether **1a** with α-bromoketone **2a** (Table 1). In F^--accelerated reactions, the epoxide **4aa** was mainly produced via carbonyl addition of **1a** to **2a**, along with the targeted 1,4-dicarbonyl compound **3aa** (entry 1).[6g] In entry 2 involving Na_2CO_3,[6h] the reaction did not occur at all. Under radical conditions using Et_3B (entry 3),[6i] the selective formation of **3aa** was confirmed, but the yield was very low. The photochemical reaction catalyzed by *p*-anisaldehyde gave no coupling products (entry 4).[6j] A Mukaiyama-type reaction system catalyzed by $TiCl_4$[12] provided the halohydrin **5aa** via the addition of a carbonyl group (entry 5). In contrast with these reactions, eosin Y under visible light irradiation successfully produced **3aa** in a high yield and with perfect chemoselectivity (entry 6)

Table 1: Selectivity in the reactions of silyl enol ether **1a** with bromoketone **2a**.[a]

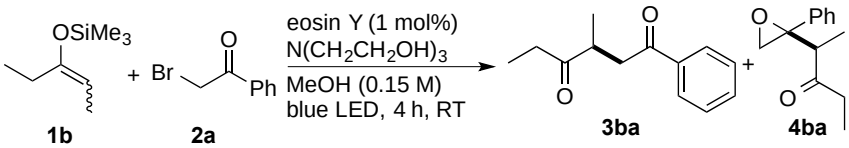


Entry	Conditions	Yield (%)		
		3aa	**4aa**	**5aa**
1	Bu_4NF, -78 °C to rt	6	32	0
2	Na_2CO_3, rt	0	0	0
3	Et_3B/O_2, rt	16	0	0
4	*p*-$MeOC_6H_4CHO$, CFL	0	0	0
5	$TiCl_4$, -78 °C to rt	0	0	30
6	**eosinY, $N(CH_2CH_2OH)_3$ blue LED (468 nm)**	**80**	**0**	**0**

[a] A detailed list of the reaction conditions is provided in the Experimental Section.

Investigations of the reaction conditions involving silyl enol ether **1b** and bromoketone **2a** are summarized in Table 2. Effective reaction conditions were identified employing 1 mol% eosin Y as a photocatalyst and 1 equiv triethanolamine as a reductive quencher under blue LED (468 nm) irradiation (entry 1). Although **3ba** was obtained using our reported allylation conditions,[10] the carbonyl adduct **4ba** was also obtained because the reactivity of the silyl enol ether activated by the fluoride anion was too high (entry 2). A low yield of **3ba** was observed in the presence of smaller amounts of triethanolamine (entries 3 and 4). Three equivalents of triethanolamine afforded **3ba** in

Table 2: Optimization of the reaction conditions.[a]



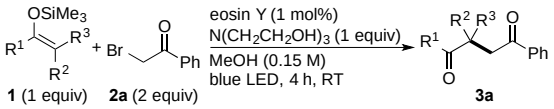
Entry	Modification of conditions	Yield (%)[b]	
		3ba	**4ba**
1	none	76(70)[c]	0
2[d]	CsF instead of $N(CH_2CH_2OH)_3$	27	18
3	without $N(CH_2CH_2OH)_3$	3	0
4	$N(CH_2CH_2OH)_3$ (0.5 equiv)	54	0
5	$N(CH_2CH_2OH)_3$ (3.0 equiv)	82	0
6	NEt_3 instead of $N(CH_2CH_2OH)_3$	45	0
7	$Ru(bpy)_3Cl_2$ instead of eosin Y	41	0
8	$Ir(ppy)_3$ instead of eosinY	76	0
9	erythrosine B instead of eosinY	75	0
10	eosin Y (0.5 mol%)	71	0
11	eosin Y (10 mol%)	81	0
12	**1b** (2 equiv), **2a** (1 equiv)	72	0
13	under air	0	0
14	without eosin Y or in the dark	0	0

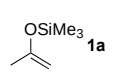
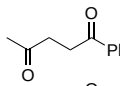
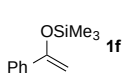
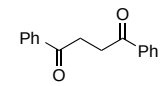
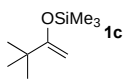
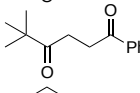
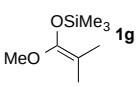
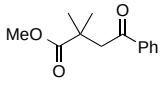
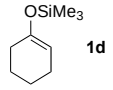
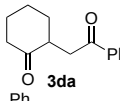
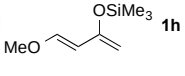
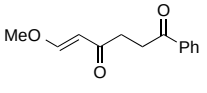
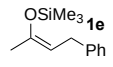
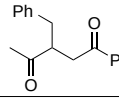
[a] Conditions: **1b** (0.3 mmol), **2a** (0.6 mmol), eosin Y (0.003 mmol), $N(CH_2CH_2OH)_3$ (0.3 mmol), MeOH (2 mL), room temperature, and 3 W blue LED (468 nm). [b] ^1H NMR yield with 1,1,1,2-tetrachloroethane as an internal standard. [c] Isolated yield. [d] DMF was used instead of MeOH as a solvent.

almost the same yield as was obtained using entry 1 (entry 5). Triethylamine was less effective as a reductive quencher than triethanolamine ($E_{ox}(TEOA^{\bullet+}/TEOA)$ = +0.82 V; $E_{ox}(NEt_3^{\bullet+}/NEt_3)$ = +0.99 V vs. SCE)[11b,11c] (entry 6). The transition metal photoredox catalyst $Ru(bpy)_3Cl_2$ gave **3ba** in a moderate yield (entry 7). In the case of $Ir(ppy)_3$, the coupling product **3ba** was obtained in a high yield comparable to that obtained using the eosin Y catalyst (entry 8). Erythrosine B also provided a catalytic activity comparable to that of eosin Y (entry 9). This coupling reaction was not very sensitive to the amount of eosin Y present (entries 10 and 11). Excess quantities of the silyl enol ether **1b** gave **3ba** in a 72% yield (entry 12). The reaction did not proceed under air, probably due to quenching of the excited triplet state of eosin Y by molecular oxygen (entry 13).[13] Control experiments revealed that both the organic dye and visible light irradiation were essential for the formation of **3ba** (entry 14).

With the optimized reaction conditions in hand, we investigated the scope of the silyl enol ethers **1** (Table 3). The silyl enol ethers **1a** and **1c** derived from acetone and *tert*-butyl methyl ketone gave the 1,4-dicarbonyl compounds **3aa** and **3ca**, respectively, without producing carbonyl adducts (entries 1 and 2). The cyclic silyl enol ether **1d** also produced the coupling product **3da** in a high yield (entry 3). The silyl enol ether bearing a phenyl group **1e** afforded the product **3ea** (entry 4). Although the yield of **3fa** was low, the reaction of **1f** derived from acetophenone proceeded (entry 5). The silyl ketene acetal **1g** yielded the coupling product **3ga** in a moderate yield (entry 6). The Danishefsky diene **1h** was applied to this coupling reaction system to give the dioxo-enol ether **3ha** (entry 7).

Table 3. Substrate scope of silyl enol ether **1**.[a]

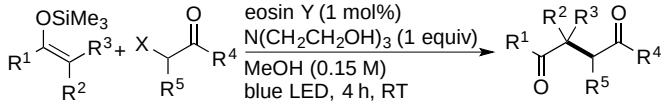


Entry	Silyl enolate **1**	Product **3**	Yield (%)[b]	Entry	Silyl enolate **1**	Product **3**	Yield (%)[b]
1	 **1a**	 **3aa**	80	5[e]	 **1f**	 **3fa**	12
2	 **1c**	 **3ca**	82	6	 **1g**	 **3ga**	26
3[c]	 **1d**	 **3da**	81	7[f]	 **1h**	 **3ha**	60
4[d]	 **1e**	 **3ea**	51				

[a] Conditions: silyl enol ether **1** (0.3 mmol), bromoacetophenone (0.6 mmol), eosin Y (0.003 mmol), $N(CH_2CH_2OH)_3$ (0.3 mmol), MeOH (2 mL), room temperature, and 3 W blue LED (468 nm). [b] Isolated yield. [c] **1d** (2 equiv), **2a** (1 equiv). [d] **1e** (1 equiv), **2a** (3 equiv). [e] **1f** (1 equiv), **2a** (2 equiv). [f] **1h** (3 equiv), **2a** (1 equiv).

We investigated the coupling reaction using various halocarbonyls **2** (Table 4). Reactions of phenacyl bromide possessing an alkoxy group **2b** or a chloro moiety **2c** with the silyl enol ether **1a** proceeded effectively to give the coupling products **3ab** or **3ac**, respectively (entries 1 and 2). The nitro-substituted haloketone **2d** gave a low yield (entry 3). A hydroxy group was compatible with these reaction conditions (entry 4). A bromoketone possessing a CF_3 group **2f** also gave the corresponding product **3af** (entry 5). The bromoester **2g** and the bromoamide **2h** were also used in this reaction to yield the coupling products **3ag** and **3ah**, respectively (entries 6 and 7). The secondary bromoketone **2i** afforded the desired product **3ai** in a moderate yield due to steric hindrance (entry 8). The bromomalonate **2j** gave the tricarbonyl compound **3dj** (entry 9). The addition of NaI accelerated the coupling reaction between **1b** and chloroketone **2k** (entries 10 and 11) via *in situ* halogen-exchange.

Table 4. Substrate scope of halocarbonyls **2**.[a]



1 **2** **3**

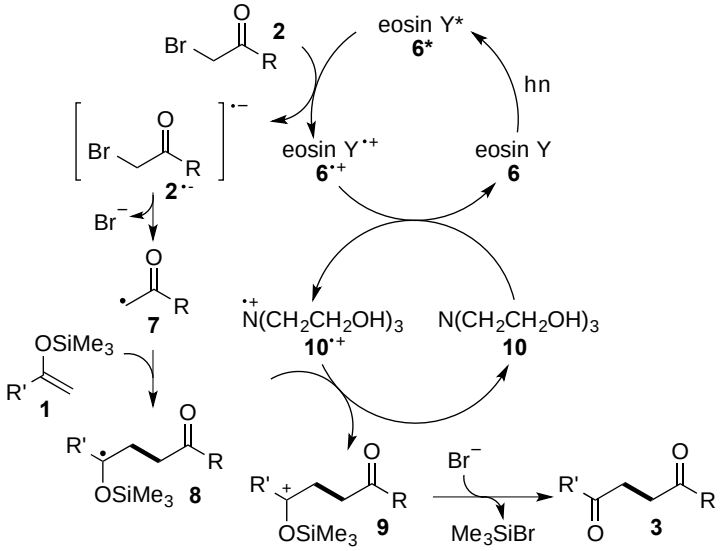
Entry	Enolate **1**	Halocarbonyls **2**	Product **3**	Yield (%)[b]
1	**1a**	X; *p*-OMe **2b**	**3ab**	93
2	**1a**	*p*-Cl **2c**	**3ac**	89
3	**1a**	*p*-NO_2 **2d**	**3ad**	15
4	**1a**	*p*-OH **2e**	**3ae**	88
5	**1a**	*m*-CF_3 **2f**	**3af**	38
6	**1a**	**2g**	**3ag**	63
7[c,d]	**1a**	**2h**	**3ah**	69
8[e]	**1a**	**2i**	**3ai**	48
9	**1d**	**2j**	**3dj**	53
10	**1b**	**2k**	**3bk**	11[f]
11[g]				64

[a] Conditions: silyl enol ether **1** (0.3 mmol), halocarbonyl **2** (0.6 mmol), eosin Y (0.003 mmol), $N(CH_2CH_2OH)_3$

(0.3 mmol), MeOH (2 mL), room temperature, and 3W blue LED (468 nm). [b] Isolated yield. [c] Solvent (MeOH:MeCN = 1:1). [d] **2h** (3 equiv). [e] **2i** (3 equiv). [f] ^{1}H NMR yield with 1,1,1,2-tetrachloroethane as an internal standard. [g] NaI (2 equiv) was added as an additive.

A plausible reaction mechanism is shown in Scheme 4. Blue LED irradiation generates the photoexcited eosin Y **6***. Then, **6*** reduces the bromocarbonyl **2** via SET to give $\mathbf{6}^{\bullet+}$ and the radical anion $\mathbf{2}^{\bullet-}$.[14] The reduction of $\mathbf{6}^{\bullet+}$ by triethanolamine **10** regenerates eosin Y **6** and produces a triethanolamine radical cation $\mathbf{10}^{\bullet+}$. The photocatalyst is effectively quenched using excess amounts of triethanolamine.[15] The elimination of Br^- from $\mathbf{2}^{\bullet-}$ affords the carbonylmethyl radical **7**. The radical **7** adds to the silyl enol ether **1** gives the siloxy-substituted carbon radical **8**. The radical **8** is oxidized by $\mathbf{10}^{\bullet+}$ to afford the cation **9** and triethanolamine **10**.[16] Finally, the elimination of the trimethylsilyl group from **9** produces the 1,4-dicarbonyl **3**.

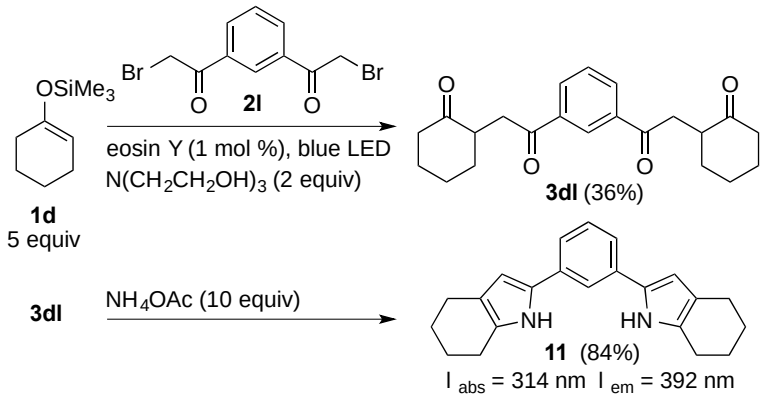
Scheme 4. Plausible reaction mechanism for eosin Y catalyzed radical coupling of silyl enol ethers **1** and bromocarbonyls **2**.



The utility of this protocol was demonstrated by synthesizing bis(pyrrolyl)arene, a useful fluorescence compound,[17a] through a combination of the present reaction system and the Paal–Knorr method (Scheme 5). The tetracarbonyl compound **3bl** was successfully synthesized by the reaction of **2l**, possessing two bromocarbonyl moieties, with the silyl enol ether **1b**. Treatment of **3bl** by the Paal–Knorr method afforded bis(pyrrolyl)arene **11**. Generally, the synthesis of these types of 1,3-bis(pyrrolyl)arenes requires a multi-step process involving expensive transition metal catalysts[17] or the use of highly toxic phosgene;[18] however, the sequential process developed here is safer and less

expensive. The molecular structures determined from X-ray diffraction analysis and UV-vis absorption and emission spectra of bispyrrole **11** are provided in the Experimental Section.

Scheme 5. Synthesis of Bis(pyrrol-2-yl)benzene Derivatives.



2-3. Conclusion

I developed a practical synthetic method for preparing 1,4-dicarbonyl compounds via a reaction between α-halocarbonyls and silyl enol ethers, accelerated by the inexpensive eosin Y as a photoredox catalyst under visible light irradiation. The halo-substitution reaction proceeded with perfect chemoselectivity without carbonyl adduct. Triethanolamine was found to function as an appropriate reductant to regenerate eosin Y. Various types of silyl enol ethers and α-bromocarbonyl compounds were applicable to this reaction. Finally, I demonstrated the utility of the present synthetic method for the preparation of dipyrrolarenes.

2-4. Experimental Section

General

New compounds were characterized by ^{1}H, ^{13}C, DEPT, COSY, HMQC, HMBC, IR, MS, HRMS, and MALDI-TOF MS. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were obtained using TMS as an internal standard. IR spectra were recorded as thin films. All reactions were carried out under nitrogen, and the reaction vessels were positioned at a distance of 3 cm from a 3 W blue LED (468 nm). Column chromatography was performed on silica gel. Bulb-to-bulb distillation (Kugelrohr) was accomplished at the oven temperatures and pressures indicated. Yields were determined by ^{1}H NMR using bromoform or 1,1,1,2-tetrachloroethane as an internal standard.

Materials

Dehydrated solvents, including *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), acetonitrile, hexane, diethyl ether (ether), tetrahydrofuran (THF), dichloromethane, 1,4-dioxane,

chloroform, toluene, acetone, ethyl acetate, methanol (MeOH), and ethanol (EtOH), were purchased and used as obtained. Bu_4NF, 2,2,2-trifluoroethanol, triethylborane, $TiCl_4$, *p*-anisaldehyde, and ammonium acetate were also purchased from commercial sources. The catalysts listed in Tables 1 and S2, and the silyl enol ethers **1a**, **1d**, **1f**, **1g**, and **1h** were purchased from commercial sources. The other silyl enol ethers **1b**, **1c**, and **1e** were synthesized according to a procedure established in a previous report. The α-halocarbonyls **2a**, **2b**, **2c**, **2d**, **2e**, **2f, 2g, 2i**, **2j**, and **2k** were purchased from commercial sources. The bromocarbonyls **2h** and **2l** were prepared by a known procedure. Tris(2-methoxyethyl)amine (Table S3, entry 7) and tris(2-mercaptoethyl)amine (Table S3, entry 8) were synthesized based on a previous report.[19,20] All other additives listed in Table S3 were purchased from commercial sources.

Selectivity in the Reactions of Silyl enol ether 1a with Bromoketone 2a (Table 1)

Entry 1[21]; To a solution of isopropenyloxytrimethylsilane (**1a**) (0.3 mmol) and 2-bromoacetophenone (**2a**) (0.36 mmol) in THF (1.6 mL) was dropwise added Bu_4NF (0.36 mmol, 0.36 mL, 1.0 M in THF) at -78 °C. The mixture was stirred while warming to RT for 12 h. The reaction mixture was diluted with Et_2O (20 mL) and washed with water (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure to obtain the crude products **3aa** (6% as NMR yield) and **4aa** (32% as NMR yield). These products were analyzed by ^1H NMR.[9]

Entry 2[22]; To a suspended solution of 2-bromoacetophenone (**2a**) (0.5 mmol) and Na_2CO_3 (0.6 mmol) in 2,2,2-trifluoroehanol (1 mL) was added isopropenyloxytrimethylsilane (**1a**) (1 mmol). The mixture was stirred at room temperature for 12 h. The reaction was quenched with water (5 mL), and the mixture was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure to obtain the crude product. The product was analyzed by ^1H NMR.

Entry 3[23]; To a solution of isopropenyloxytrimethylsilane (**1a**) (0.75 mmol) and 2-bromoacetophenone (**2a**) (0.3 mmol) in DMSO (1.5 mL) was added BEt_3 (0.3 mmol, 0.3 mL, 1.0 M in hexane) under air at RT. To this reaction mixture, BEt_3 (1.5 mmol, 1.5 mL, 1.0 M in hexane) divided into four aliquots was added every 30 min. After the addition of BEt_3, the mixture was stirred for 1 h, quenched with 1 N HCl aq. (5 mL), and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the volatiles were removed under reduced pressure to give the crude product **3aa** (in a 16% yield, as determined by NMR). The product was analyzed by ^1H NMR.[12]

Entry 4[24]; To a solution of isopropenyloxytrimethylsilane (**1a**) (0.6 mmol), 2-bromoacetophenone (**2a**) (0.3 mmol), 2,6-lutidine (0.3 mmol) in MeCN (0.6 mL) was added *p*-anisaldehyde (0.06 mmol) under nitrogen at RT. The reaction mixture was degassed via freeze pump thaw (x3 times), and the vessel was refilled with nitrogen. The vial was positioned approximately 10 cm away from the light source. A 26 W compact fluorescent light (CFL) was used. The mixture was irradiated at room temperature for 10 h. The reaction was quenched with water (5 mL), and the mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the volatiles were removed under reduced pressure to obtain the crude product. The product was analyzed by ^{1}H NMR.

Entry 5[25]; To a solution of $TiCl_4$ (0.36 mmol) and 2-bromoacetophenone (**2a**) (0.36 mmol) in CH_2Cl_2 (2 mL) was dropwise added isopropenyloxytrimethylsilane (**1a**) (0.3 mmol) at 0 °C, which was stirred for 1.5 h at the same temperature. The mixture was quenched with 1 N HCl aq. (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the volatiles were removed under reduced pressure to give the crude product **5aa** (in a 30% yield, as determined by NMR). The product was analyzed by ^{1}H NMR.[9]

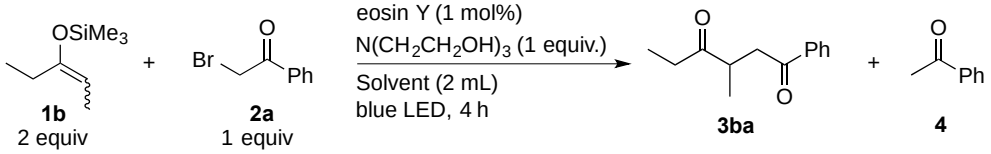
Entry 6; To a solution of eosin Y (0.0027 mmol, 0.0019 g) and 2-bromoacetophenone (0.60 mmol, 0.120 g) in MeOH (2 mL) was added triethanolamine (0.33 mmol, 0.0491 g) and isopropenyloxytrimethylsilane (0.372 mmol, 0.0484 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched with water (5 mL), extracted with Et_2O (3 x 20 mL), and washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 98:2) to give 1-phenylpentane-1,4-dione (0.30 mmol, 0.052 g, 80%). The analytical data agreed with previous reports.[26]

Experimental Procedure

To a suspended solution of eosin Y (0.003 mmol) and α-halocarbonyls **2** (0.6 mmol) in MeOH (2 mL) were added triethanolamine (0.3 mmol) and silyl enol ether **1** (0.3 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched with water (5 mL), extracted with Et_2O (3 x 20 mL), and washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the volatiles were removed under reduced pressure to give the crude product **3**. The product was analyzed by ^{1}H NMR. The purification steps are described in detail in the Product Data section.

Optimization Data

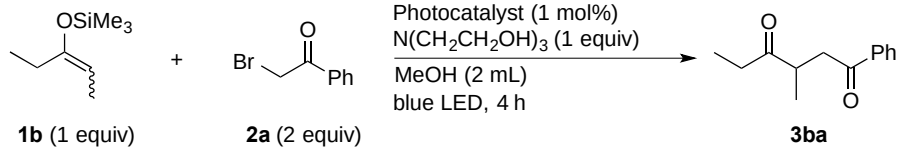
Table 5. Optimization of Solvents.



Entry	Solvent	Yield of **3ba**(%)[a]	Yield of **4**(%)[a]
1	DMF	20	4
2	DMSO	12	5
3	CH_3CN	44	2
4	Hexane	0	14
5	Ether	0	45
6	THF	0	33
7	CH_2Cl_2	54	22
8	1,4-dioxane	0	22
9	$CHCl_3$	11	8
10	Toluene	0	50
11	Acetone	28	18
12	CH_3CO_2Et	3	25
13	EtOH	55	3
14	**MeOH**	**72**	**0**
15[b]	**MeOH**	**76**	**0**

[a]Yields were determined by ^{1}H NMR. [b]**1b** (1 equiv), **2a** (2 equiv).

Table 6. Optimization of Photocatalyst.



Entry	Photocatalyst	Yield of **3ba**(%)[a]
1	**eosin Y**	**76**
2	erythrosine B	75
3	uranine	64
4	rose bengal	62
5	phloxine B	51
6	basic red 2	34
7[b]	bromopyrogall red	0
8[b]	rhodamine B	0
9[b]	resazurin	0
10	$Ir(ppy)_3$	76
11	$Ru(bpy)_3Cl_2$	41

[a]Yields were determined by ^{1}H NMR. [b]**1b** (2 equiv), **2a** (1 equiv)

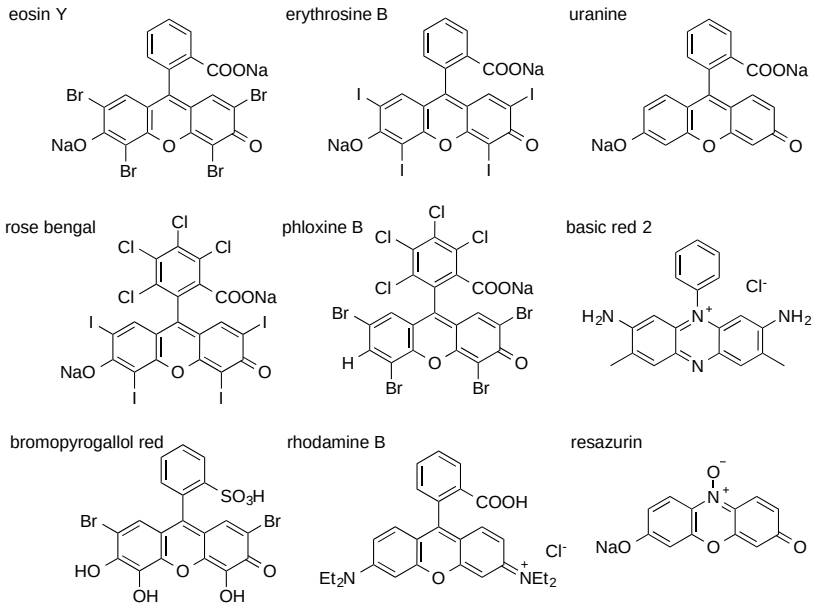
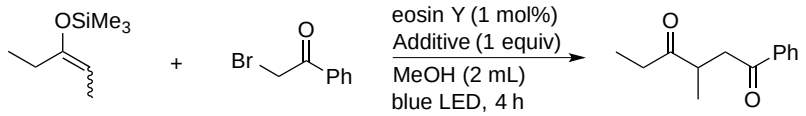
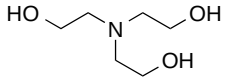
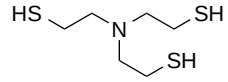
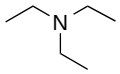
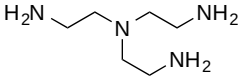
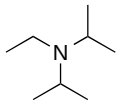
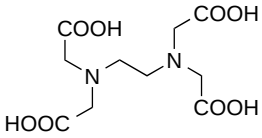
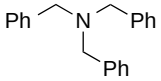
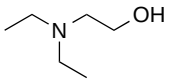
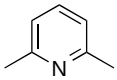
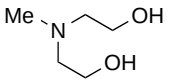
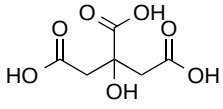
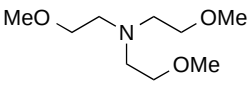
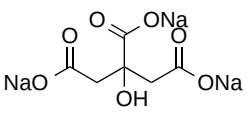


Table 7. Optimization of Reductive Quencher.



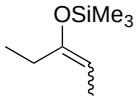
1b (1 equiv) **2a** (2 equiv) **3ba**

Entry	Additive	yield of **3ba**(%)[a]	Entry	Additive	yield of **3ba**(%)[a]
1		76	8		0
2		45	9		0
3		20	10		0
4		8			
5		46	11[b]		20
6		69	12[b]		0
7		59	13[b]		33

[a]Yield was determined by ^{1}H NMR. [b]**1b** (1 equiv), **2a** (2 equiv).

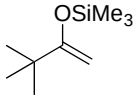
Synthesis of Substrates

Preparation of 3-trimetylsilyloxy-2-pentene (1b)[27]



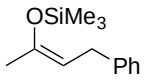
To a solution of $^{i}Pr_2NH$ (10.1 g, 100 mmol) in THF (100 mL) was added ^{n}BuLi (1.6 M in hexane, 63 mL, 100 mmol) at 0 °C. After stirring at 0 °C for 15 min, then to reaction mixture was added 3-pentanone (6.89 g, 80 mmol) dropwise at -78 °C. After stirred for 30 min at -78 °C, Me_3SiCl (10.9 g, 100 mmol) was added dropwise at -78 °C. The reaction mixture was allowed to reach room temperature and stirred for 30 min. Then, saturated $NaHCO_3$ aq (50 mL) was added and the solution was extracted with pentane (3 x 50 mL). The organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by distillation under reduced pressure to give the product as a colorless oil (12.0 g, 76% yield, *E*/*Z* = 5:1). The analytical data agreed with the previous report.

Preparation of 3,3-dimethyl-2-(trimethylsilyl)oxy-1-butene (1c)[28]



To a solution of $^{i}Pr_2NH$ (10.1 g, 100 mmol) in THF (100 mL) was added ^{n}BuLi (1.6 M in hexane, 63 mL, 100 mmol) at 0 °C. After stirring at 0 °C for 15 min, to the reaction mixture was added to 3,3-dimethyl-butan-2-one (8.0 g, 80 mmol) dropwise at -78 °C . The mixture was stirred at -78 °C for 1 h and then Me_3SiCl (10.9 g, 100 mmol) was dropwised to the mixture at -78 °C. The solution was stirred at -78 °C for 2 h and then warmed to rt for 1 h. Then, saturated $NaHCO_3$ aq (50 mL) was added and the solution was extracted with pentane (3 x 50 mL). The organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by distillation under reduced pressure to give the product as a colorless oil (10.3 g, 60% yield). The analytical data agreed with the previous report.

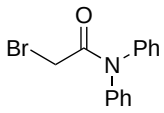
Preparation of 4-phenyl-2-(trimethylsilyl)oxy-2-butene (1e)[29]



To a suspended solution of $CuBr \cdot Me_2S$ (0.257 g, 1.25 mmol) in THF (30 mL) was added phenylmagnesium bromide (1.0 M in THF, 30 mL, 30 mmol) at -78 °C. Then, a solution of methyl vinyl ketone (1.66 g, 23.7 mmol), Me_3SiCl (5.4 g, 50mmol), and HMPA (10.7 g, 60 mmol) in THF (20 mL) was added dropwise. The solution was stirred at -78 °C for 2 h, then stirred at RT for 30 min. NEt_3 (7 mL) was added and diluted with hexane (100 mL). The mixture was washed with water, and the organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified

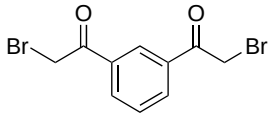
by distillation under reduced pressure to give the product as a colorless oil (2.5 g, 46% yield, *E*/*Z* = 3:2). The analytical data agreed with the previous report.

Preparation of 2-bromo-*N*,*N*-diphenylacetamide (2h)[30]



To a solution of *N,N*-diphenylamine (30 mmol, 5.1 g) and NEt_3 (30 mmol, 3.0 g) in CH_2Cl_2 (60 mL) at 0 °C was added bromoacetyl bromide (90 mmol, 18.2 g) in CH_2Cl_2 (10 mL), and the reaction was allowed to stir at room temperature for 16 h. The mixture was quenched by 1N HCl aq (20 mL), which was extracted with Et_2O (3 x 20 mL) and washed with brine (3 x 10 mL). The combined organic phases were dried over $MgSO_4$. The solvent was evaporated under reduced pressure to give a crude product. The crude product was purified by recrystallization from petroleum ether/methanol to give the product as a white solid (4.9 g, 56%). The analytical data agreed with the previous report.

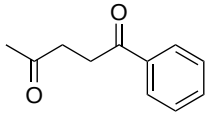
Preparation of 2-bromo-1-[3-(2-bromoacetyl)phenyl]ethanone (2l)[31]



To a suspended solution of 1,3-diacetylbenzene (10 mmol, 1.62 g)and *N*- bromosuccinimide (27 mmol, 4.75 g) in CCl_4 (10 mL) was added NH_4OAc (2 mmol, 0.159 g). The mixture was stirred under reflux for 12 h, then the mixture was filtered and the filtrate was washed with water and dried with $MgSO_4$. It was evaporated under reduced pressure to give a crude product (0.87 g, 27 %). It was purified by column chromatography (hexane/ethyl acetate = 70:30, column length 11 cm, diameter 21 mm silicagel) (0.37 g, 12%). The analytical data agreed with the previous report.

Product Date

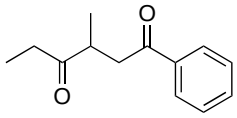
1-phenylpentane-1,4-dione (3aa)



To a solution of eosin Y (0.0027 mmol, 0.0019 g) and 2-bromoacetophenone (0.60 mmol, 0.120 g) in MeOH (2 mL) was added triethanolamine (0.33 mmol, 0.0491 g) and isopropenyloxytrimethylsilane (0.372 mmol, 0.0484 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm)

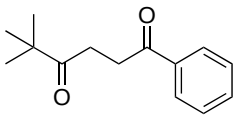
light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 98:2) to give 1-phenylpentane-1,4-dione (0.30 mmol, 0.052 g, 80%). The analytical data agreed with the previous report.[26]

3-methyl-1-phenylhexane-1,4-dione (3ba)



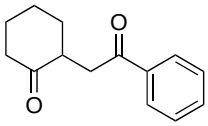
To a solution of eosin Y (0.0046 mmol, 0.0032 g) and 2-bromoacetophenone (0.60 mmol, 0.119 g) in MeOH (2 mL) was added triethanolamine (0.30 mmol, 0.0453 g) and 3-trimetylsilyloxy-2-pentene (0.31 mmol, 0.0484 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 3-methyl-1-phenylhexane-1,4-dione (0.21 mmol, 0.044 g, 70%). The analytical data agreed with the previous report.[32]

5,5-dimethyl-1-phenylhexane-1,4-dione (3ca)



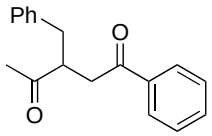
To a solution of eosin Y (0.003 mmol, 0.0021 g) and 2-bromoacetophenone (0.61 mmol, 0.121 g) in MeOH (2 mL) was added triethanolamine (0.32 mmol, 0.0477 g) and 3,3-dimethyl-2-(trimethylsilyl)oxy-1-butene (0.27 mmol, 0.0470 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 15,5-dimethyl-1-phenylhexane-1,4-dione (0.22 mmol, 0.055 g, 82%). The analytical data agreed with the previous report.[33]

2-phenacylcyclohexanone (3da)



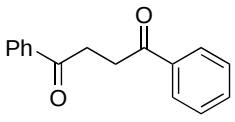
To a solution of eosin Y (0.0035 mmol, 0.0024 g) and 2-bromoacetophenone (0.30 mmol, 0.0605 g) in MeOH (2 mL) was added triethanolamine (0.30 mmol, 0.0448 g) and 1-(Trimethylsilyloxy)cyclohexene (0.61 mmol, 0.1029 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 2-phenacylcyclohexanone (0.25 mmol, 0.053 g, 81%). The analytical data agreed with the previous report.[34]

3-benzyl-1-phenylpentane-1,4-dione (3ea)



To a solution of eosin Y (0.0042 mmol, 0.0029 g) and 2-bromoacetophenone (0.91 mmol, 0.1804 g) in MeOH (2 mL) was added triethanolamine (0.32 mmol, 0.0486 g) and 4-phenyl-2-(trimethylsilyl)oxy-2-butene (0.28 mmol, 0.0613 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 3-benzyl-1-phenylpentane-1,4-dione (0.14 mmol, 0.038 g, 51%). The analytical data agreed with the previous report.[35]

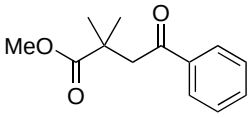
1,4-diphenylbutane-1,4-dione (3fa)



To a solution of eosin Y (0.0026 mmol, 0.0018 g) and 2-bromoacetophenone (0.30 mmol, 0.0605 g) in MeOH (2 mL) was added triethanolamine (0.34 mmol, 0.0510 g) and

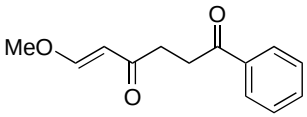
1-Phenyl-1-trimethylsilyloxyethylene (0.93 mmol, 0.1792 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 1,4-diphenylbutane-1,4-dione (0.036 mmol, 0.0086 g, 12%). The analytical data agreed with the previous report.[26]

methyl 2,2-dimethyl-4-oxo-4-phenylbutyrate (3ga)



To a solution of eosin Y (0.003 mmol, 0.0021 g) and 2-bromoacetophenone (0.6 mmol, 0.1194 g) in MeOH (2 mL) was added triethanolamine (0.30 mmol, 0.0451 g) and 1-methoxy-2-methyl-1-trimethylsiloxy-1-propene (0.29 mmol, 0.0508 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give methyl 2,2-dimethyl-4-oxo-4-phenylbutyrate (0.076 mmol, 0.0167 g, 26%). The analytical data agreed with the previous report.[36]

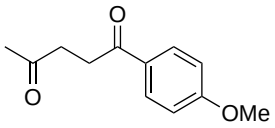
(*E*)-6-methoxy-1-phenylhex-5-ene-1,4-dione (3ha)



To a solution of eosin Y (0.0038 mmol, 0.0026 g) and 2-bromoacetophenone (0.31 mmol, 0.0618 g) in MeOH (2 mL) was added triethanolamine (0.33 mmol, 0.0488 g) and 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene (0.88 mmol, 0.1515 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 7:3) to give (*E*)-6-methoxy-1-phenylhex-5-ene-1,4-dione (0.19 mmol, 0.041 g,

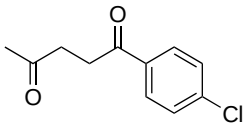
60%). mp: 57 °C-59 °C. IR: (KBr) 1678 (CO), 1662 (CO) cm^{-1}, ^1H NMR: (400 MHz, $CDCl_3$) 8.05 (d, *J* = 7.4 Hz, 2H, *o*), 7.70 (d, *J* = 12.8 Hz, 1H, 1-H), 7.57 (t, *J* = 7.4 Hz, 1H, *p*), 7.46 (t, *J* = 7.4 Hz, 2H, *m*), 5.69 (d, *J* = 12.8 Hz, 1H, 2-H), 3.73 (s, 3H, 1-OCH_3), 3.35 (t, *J* = 6.5 Hz, 2H, 5-H_2), 2.95 (t, *J* = 6.5 Hz, 2H, 4-H_2); ^{13}C NMR: (100 MHz, $CDCl_3$); 198.8 (s, C-6), 197.7 (s, C-3), 162.7 (d, C-1), 136.7 (s, *i*), 133.1 (d, *p*), 128.5 (d, *m*), 128.0 (d, *o*), 105.4 (d, C-2), 57.4 (q, 1-OCH_3), 34.5 (t, C-4), 32.5 (t, C-5); MS: (CI, 70 eV) m/z 219 (M + 1, 100), 161 (19); HRMS: (CI, 70 eV) Calculated ($C_{13}H_{15}O_3$) 219.1016 (M^+) Found: 219.1024.

1-(4-methoxyphenyl)pentane-1,4-dione (3ab)



To a solution of eosin Y (0.0039 mmol, 0.0027 g) and 2-bromo-4'-methoxyacetophenone (0.61 mmol, 0.1397 g) in MeOH (2 mL) was added triethanolamine (0.32 mmol, 0.0481 g) and isopropenyloxytrimethylsilane (0.30 mmol, 0.0396 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 1-(4-methoxyphenyl)pentane-1,4-dione (0.28 mmol, 0.059 g, 93%). The analytical data agreed with the previous report.[37]

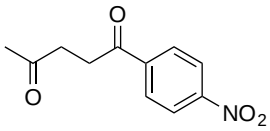
1-(4-chlorophenyl)pentane-1,4-dione (3ac)



To a solution of eosin Y (0.0030 mmol, 0.0021 g) and 2-bromo-4'-chloroacetophenone (0.61 mmol, 0.1433 g) in MeOH (2 mL) was added triethanolamine (0.31 mmol, 0.0472 g) and isopropenyloxytrimethylsilane (0.28 mmol, 0.0369 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give 1-(4-chlorophenyl)pentane-1,4-dione (0.25 mmol, 0.053 g, 89%). The

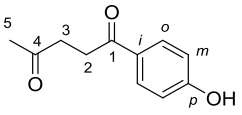
analytical data agreed with the previous report.[38]

1-(4-nitrophenyl)pentane-1,4-dione (3ad)



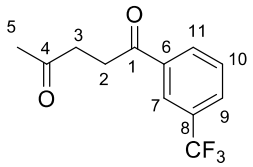
To a solution of eosin Y (0.0039 mmol, 0.0027 g) and 2-bromo-4'-nitroacetophenone (0.30 mmol, 0.0738 g) in MeOH (2 mL) was added triethanolamine (0.30 mmol, 0.0453 g) and isopropenyloxytrimethylsilane (0.61 mmol, 0.0797 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give the product (0.045 mmol, 0.010 g, 15%). The analytical data agreed with the previous report.[39]

1-(4-hydroxyphenyl)pentane-1,4-dione (3ae)



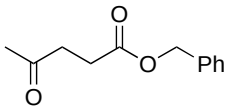
To a solution of eosin Y (0.0030 mmol, 0.0021 g) and 2-bromo-4'-hydroxyacetophenone (0.62 mmol, 0.1325 g) in MeOH (2 mL) was added triethanolamine (0.32 mmol, 0.0477 g) and isopropenyloxytrimethylsilane (0.31 mmol, 0.0409 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with AcOEt (3 x 20 mL) and washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product (0.28 mmol, 0.0537 g, 88%). mp: 92-95 °C IR: (KBr) 3211 (OH) 1692 (CO), 1662 (CO) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.81 (d, J = 8.8 Hz, 2H, *o*), 6.83 (d, J = 8.8 Hz, 2H, *m*), 3.21 (t, J = 6.1 Hz, 2H, 2-H_2), 2.90 (t, J = 6.1 Hz, 2H, 3-H_2), 2.28 (s, 3H, 5-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 209.5 (s, C-1), 197.5 (s, C-4), 161.1 (s, C-*p*), 130.6 (d, C-*o*), 129.0 (s, C-*i*), 115.4 (d, C-*m*), 37.2 (t, C-3), 32.0 (t, C-2), 30.2 (q, C-5) MS: (EI, 70 eV) m/z 192 (M^+, 9), 121 (COC_6H_4OH, 100), 93 (C_6H_4OH, 13) HRMS: (EI, 70 eV) Calculated ($C_{11}H_{12}O_3$) 192.0786 (M^+) Found: 192.0784.

1-(3-trifluorophenyl)pentane-1,4-dione (3af)



To a solution of eosin Y (0.0036 mmol, 0.0025 g) and 2-bromo-1-[3-(trifluoromethyl)phenyl]ethanone (0.30 mmol, 0.0801 g) in MeOH (2 mL) was added triethanolamine (0.30 mmol, 0.0448 g) and isopropenyloxytrimethylsilane (0.60 mmol, 0.0782 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with AcOEt (3 x 20 mL) and washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product (0.11 mmol, 0.027 g, 37%). bp: 145 °C (6 Torr) IR: (neat) 1720 (CO), 1693 (CO) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.22 (s, 1H, 7-H), 8.15 (d, J = 7.7 Hz, 1H, 11-H), 7.81 (d, J = 7.7 Hz, 1H, 9-H), 7.60 (t, J = 7.7 Hz, 1H, 10-H), 3.27 (t, J = 6.5 Hz, 2H, 2-H), 2.91 (t, J = 6.5 Hz, 2H, 3-H), 2.25 (s, 3H, 5-H) ^{13}C NMR: (100 MHz, $CDCl_3$) 206.9 (C-4), 197.2 (C-1), 137.2 (C-6), 131.23 (quartet coupling with F was observed; $^2J_{CF}$ = 31.1 Hz, C-8), 131.17 (C-11), 129.5 (quartet coupling with F was observed; $^3J_{CF}$ = 3.7 Hz, C-9), 129.3 (C-10), 125.0 (quartet coupling with F was observed; $^3J_{CF}$ = 3.7 Hz, C-7), 123.7 (quartet coupling with F was observed; $^1J_{CF}$ = 266 Hz, CF_3), 36.9 (C-3), 32.4 (C-2), 30.0 (C-5) MS: (EI, 70 eV) m/z 244 (M^+, 14), 229 ($CF_3C_6H_4COCH_2CH_2CO$, 57), 173 ($CF_3C_6H_4CO$, 100), 145 ($CF_3C_6H_4$,62) HRMS: (CI, 70 eV) Calculated ($C_{12}H_{12}F_3O_2$) 245.0789 ($M+H^+$) Found: 245.0787.

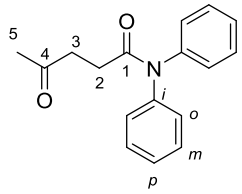
benzyl levulinate (3ag)



To a solution of eosin Y (0.0030 mmol, 0.0021 g) and benzyl 2-bromoacetate (0.63 mmol, 0.1434 g) in MeOH (2 mL) was added triethanolamine (0.33 mmol, 0.0494 g) and isopropenyloxytrimethylsilane (0.35 mmol, 0.0452 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 8:2) to give the product

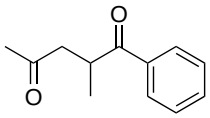
(0.22 mmol, 0.045 g, 63%). The analytical data agreed with the previous report.[40]

4-oxo-*N*,*N*-diphenylpentanamide (3ah)



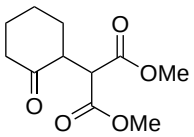
To a solution of eosin Y (0.0036 mmol, 0.0025 g) and 2-bromo-*N*,*N*-diphenylacetamide (0.30 mmol, 0.0878 g) in MeOH (1 mL) and MeCN (1 mL) were added triethanolamine (0.35 mmol, 0.0522 g) and isopropenyloxytrimethylsilane (0.89 mmol, 0.116 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with AcOEt (3 x 20 mL) and the solvent was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the product (0.21 mmol, 0.056 g, 69%). mp: 93-95 °C IR: (KBr) 1714 (CO), 1663 (CO) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.32 (br, 10H, Ph x 2), 2.78 (t, J = 5.8 Hz, 2H, 3-H_2), 2.49 (t, J = 5.8 Hz, 2H, 2-H_2), 2.19 (s, 3H, 5-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 207.5 (C-4), 171.9 (C-1), 142.6 (C-*i*), 128.9-126.4 (br, C-*o*, C-*m*, and C-*p*), 38.3 (C-3), 29.9 (C-5), 29.4 (C-2) MS: (EI, 70 eV) m/z 267 (M^+, 6.8), 169 (100), 99 (M^+-NPh_2, 34) HRMS: (EI, 70 eV) Calculated ($C_{17}H_{17}NO_2$) 267.1259 (M^+) Found: 267.1257.

1-phenyl-2-methyl-1,4-pentanedione (3ai)



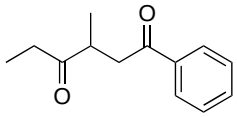
To a solution of eosin Y (0.0039 mmol, 0.0027 g) and 2-bromopropiophenone (0.91 mmol, 0.1932 g) in MeOH (2 mL) were added triethanolamine (0.30 mmol, 0.0451 g) and isopropenyloxytrimethylsilane (0.29 mmol, 0.0381 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give the product (0.14 mmol, 0.027 g, 48%). The analytical data agreed with the previous report.[41]

dimethyl 2-(2-oxocyclohexyl)malonate (3dj)



To a solution of eosin Y (0.0030 mmol, 0.0021 g) and dimethyl bromomalonate (0.91 mmol, 0.1923 g) in MeOH (2 mL) were added triethanolamine (0.33 mmol, 0.0495 g) and 1-(trimethylsilyloxy)cyclohexene (0.32 mmol, 0.0538g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the product (0.17 mmol, 0.0384 g, 53%). The analytical data agreed with the previous report.[42]

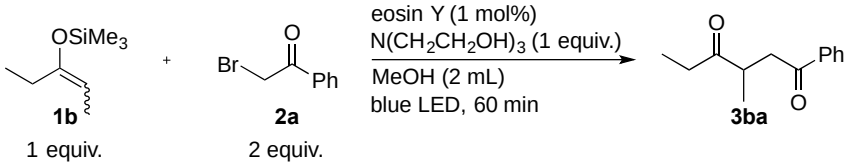
3-methyl-1-phenylhexane-1,4-dione (3bk)



To a solution of eosin Y (0.0035 mmol, 0.0024 g) and 2-chloroacetophenone (0.60 mmol, 0.0921 g) and sodium iodide (0.62 mmol, 0.0926 g) in MeOH (2 mL) were added triethanolamine (0.50 mmol, 0.0740 g) and isopropenyloxytrimethylsilane (0.31 mmol, 0.0488 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with Et_2O (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 95:5) to give the product (0.20 mmol, 0.0407 g, 64%). The analytical data agreed with the previous report.[26]

Effect of Photoirradiation on the Reaction

The reaction of **1b** with **2a** was performed with or without visible light irradiation. The time profile of the reaction is shown in Figure S1. These results indicated that continuous irradiation with blue LED was essential for promoting the reaction, and the contribution of the radical chain mechanism to this reaction was small.



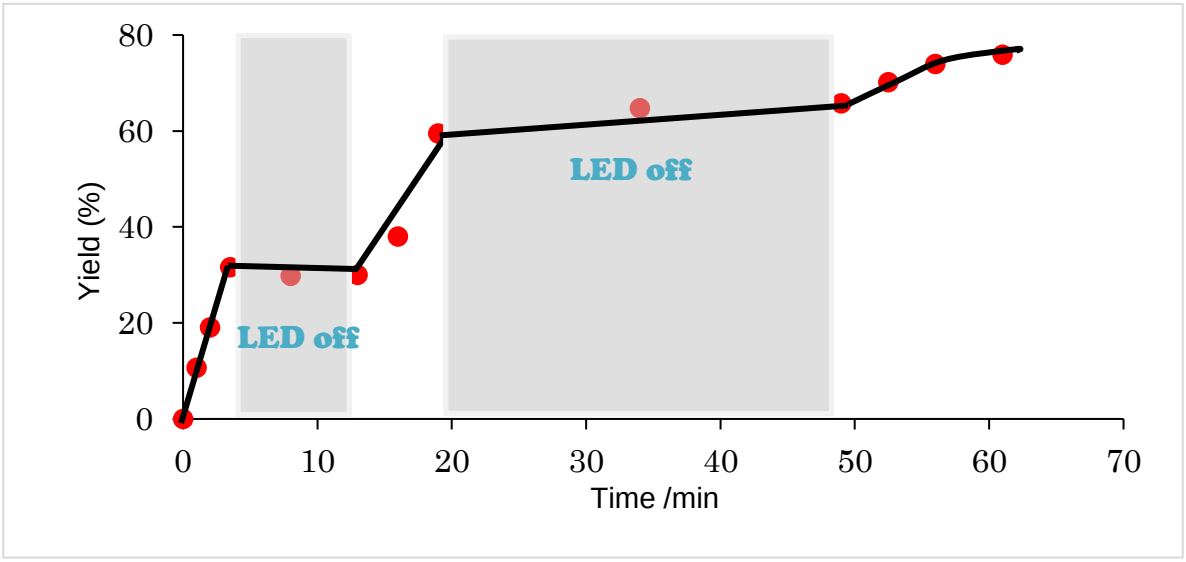


Figure 1. Time profile of the reaction of **1b** with **2a**.[a]

[a]The yield of **3ba** was determined by GC with dodecane as an internal standard.

Stern-Vormer Fluorescence Quenching Studies[43]

Fluorescence quenching studies were performed using a JACSO FP-6600 spectrofluorometer. In each experiment, the photocatalyst and various concentrations of the quencher were combined in MeOH in screw-top 1.0 cm quartz cuvettes. The emission quenching of the eosin Y monosodium salt was achieved using a photocatalyst concentration of 5.0 x 10^{-7} M under excitation at 536 nm. (The eosin Y monosodium salt showed a stronger linear correlation compared to the eosin Y disodium salt.) The emission intensity was observed at 550 nm. Plots were constructed according to the Stern–Volmer equation $I_0/I = 1 + k_q\tau_0[Q]$.[43,44]

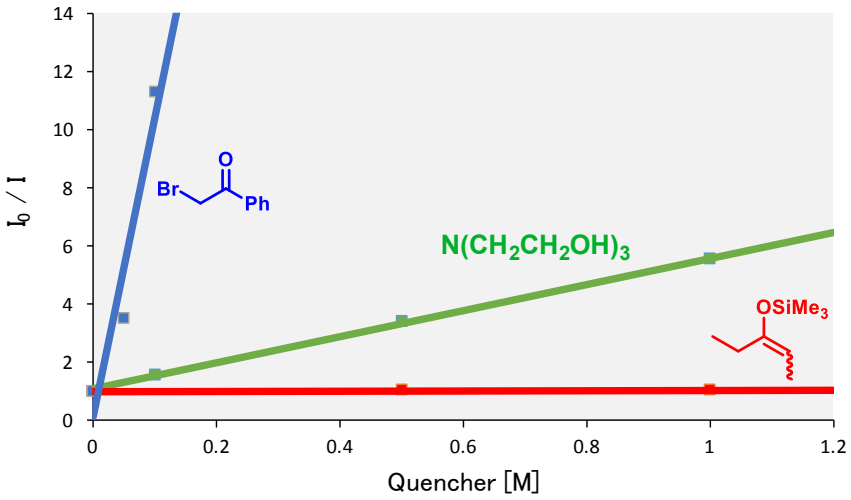
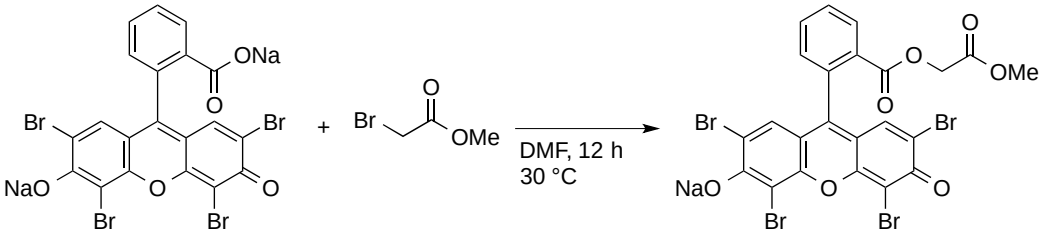


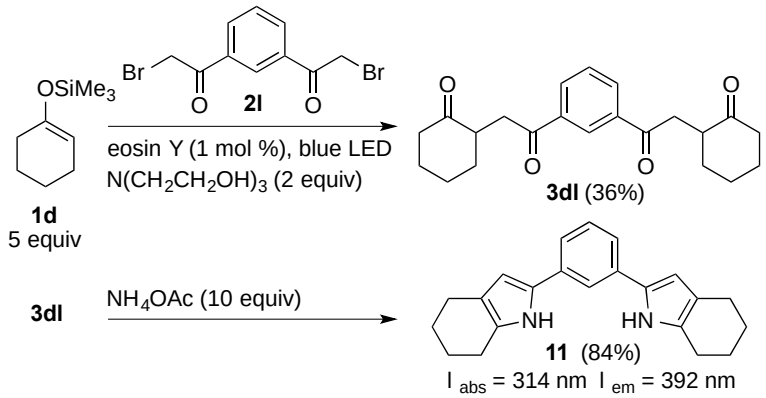
Figure 2. Stern–Volmer plots for the quenching of the eosin Y monosodium salt emission at RT.

Synthesis of Eosin Y Monosodium Salt from Eosin Y Disodium Salt

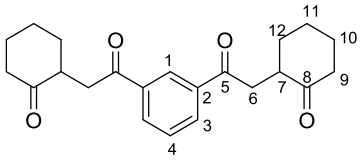


To a suspended solution of eosin Y (0.10 mmol, 0.061 g) in DMF (2 mL) was added bromo methylacetate (0.30 mmol, 0.043 g) at RT. The mixture was stirred for 12 h at 30 °C and then was concentrated under reduced pressure. The residue was diluted with acetone (20 mL) and filtered off. The volatiles were removed under reduced pressure to give eosin Y monosodium salts as a red solid (0.059 g, 80%). IR: (KBr) 1727 (CO) cm^{-1} ^1H NMR: (400 MHz, d_6-DMSO) 8.24 (d, J = 8.0 Hz, 1H, 3-H), 7.90 (t, J = 7.5, 6.6 Hz, 1H, 5-H), 7.81 (t, J = 8.0, 6.6, 1H, 4-H), 7.52 (d, J = 7.5, 1H, 6-H), 6.89 (s, 2H, 7-H x 2), 4.71 (s, 2H, 2-H_2), 3.51 (s, 3H, 1-H_3) ^{13}C NMR: (100 MHz, d_6-DMSO) 168.3 (s), 167.6 (s), 164.2 (s), 152.9 (s), 150.3 (s), 134.0 (4), 133.5 (d, C-5), 130.8 (d, C-3 and C-6), 130.2 (d, C-4), 129.0 (d, C-7), 128.6 (s), 118.5 (s), 109.3 (s), 99.4 (s), 61.5 (t, C-3), 51.8 (q, C-1) MALDI-TOF MS: Calculated ($C_{23}H_{11}Br_4O_7$) 714.7238 Found: 714.7233 (M^+-Na) ^1H and ^{13}C NMR charts are listed below.

Synthesis of Bis(pyrrol-2-yl)benzene Derivatives (Scheme 5)

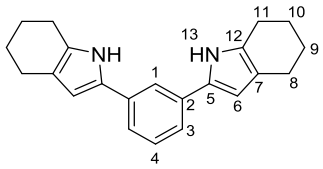


2,2'-(1,3-phenylenebis(2-oxoethane-2,1-diyl))bis(cyclohexan-1-one) (3dl)



To a solution of eosin Y (0.0036 mmol, 0.0025 g) and 2-bromo-1-[3-(2-bromoacetyl)phenyl]ethanone (0.30 mmol, 0.0963 g) in MeOH (1 mL) and MeCN (1 mL) were added triethanolamine (0.68 mmol, 0.1026 g) and 1-(trimethylsilyloxy)cyclohexene (1.8 mmol, 0.3126 g). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched by water (5 mL), which was extracted with AcOEt (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the product (0.11 mmol, 0.038 g, 36%) as the mixture of diastereomers (d.r. = 50:50). mp: 95-100 °C IR: (KBr) 1708 (CO), 1685 (CO) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) one diastereomer: 8.57 (s, 1H, 1-H), 8.18 (d, *J* = 7.7 Hz, 2H, 3-H x 2), 7.57 (t, *J* = 7.7 Hz, 1H, 4-H), 3.63 (dd, *J* = 17.6, 7.0 Hz, 2H, 1-H^A x 2) 3.23-3.16 (m, 2H, 7-H x 2), 2.72 (dd, *J* = 17.6, 5.3 Hz, 2H, 6-H^B x 2), 2.50-2.39 (m, 4H, 9-H_2 x 2), 2.23-2.14 (m, 4H, 12-H^A x 2 and 10-H^A x 2), 1.94-1.55 (m, 6H, 11-H_2 x 2 and 10-H^A x 2), 1.55-1.44 (m, 2H, 12-H^A x 2) another diastereomer: 8.57 (s, 1H, 1-H), 8.18 (d, *J* = 7.7 Hz, 2H, 3-H x 2), 7.57 (t, *J* = 7.7 Hz, 1H, 4-H), 3.63 (dd, *J* = 17.6, 7.0 Hz, 2H, 1-H^A x 2) 3.23-3.16 (m, 2H, 7-H x 2), 2.70 (dd, *J* = 17.6, 5.3 Hz, 2H, 6-H^B x 2), 2.50-2.39 (m, 4H, 9-H_2 x 2), 2.23-2.14 (m, 4H, 12-H^A x 2 and 10-H^A x 2), 1.94-1.55 (m, 6H, 11-H_2 x 2 and 10-H^A x 2), 1.55-1.44 (m, 2H, 12-H^A x 2) ^{13}C NMR: (100 MHz, $CDCl_3$) 211.4 (s, C-8), 198.0 (s, C-5), 137.4 (s, C-2), 132.3 (d, C-3), 129.0 (d, C-4), 127.7 (d, C-1), 46.6 (d, C-7), 41.9 (t, C-9), 38.6 (t, C-6), 34.3 (t, C-12), 28.0 (t, C-10), 25.4(t, C-11) HRMS: (EI, 70 eV) Calculated ($C_{22}H_{26}O_4$) 354.1831 (M^+) Found: 354.1828.

2-[3-(4,5,6,7-tetrahydro-1H-indole-2-yl)phenyl]-4,5,6,7-tetrahydro-1H-indole (11)[45]



To a solution of 2,2'-[(1,3-phenylenebis(2-oxoethane-2,1-diyl))bis(cyclohexan-1-one) (0.30 mmol, 0.107 g) in EtOH (1.5 mL) was added NH_4OAc (3.0 mmol, 0.232 g). The mixture was stirred at 80 °C for 1 h. The mixture was quenched by sat. $NaHCO_3$ (5 mL), which was extracted with AcOEt (3 x 20 mL) and was washed with brine (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give a crude product. The residual oil was purified by silica gel column chromatography (CH_2Cl_2) to give the product (0.25 mmol, 0.080 g, 84%) IR: (KBr) 3367 (N-H) cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.00 (br, 2H, NH x 2), 7.48 (s, 1H, 1-H), 7.30 (t, J = 6.8 Hz, 1H, 4-H), 7.22 (d, J = 6.8 Hz, 2H, 3-H x 2) 6.32 (d, J = 2.4, 2H, 6-H x 2) 2.66 (t, 4H, 11-H_2 x 2), 2.57 (t, 4H, 8-H_2 x 2), 1.90-1.77 (m, 8H, 10-H_2 x 2 and 9-H_2 x 2) ^{13}C NMR: (100 MHz, $CDCl_3$) 133.6 (s, C-2), 130.2 (s, C-5), 129.2 (d, C-4), 128.5 (s, C-12), 120.7 (d, C-3), 119.0 (s, C-7), 118.5 (d, C-1), 105.3 (d, C-6), 23.7, 23.4, 22.9 HRMS: (EI, 70 eV) Calculated ($C_{22}H_{24}N_2$) 316.1939 (M^+) Found: 316.1938.

Photophysical Properties of 11

Measurements of the photophysical data: UV-visible absorption spectra were recorded on a *JASCO* V-650 spectrometer with a resolution of 0.2 nm. A *JASCO* FP-8500 spectrometer was used to measure the emission spectra of solution samples with a resolution of 0.2 nm.

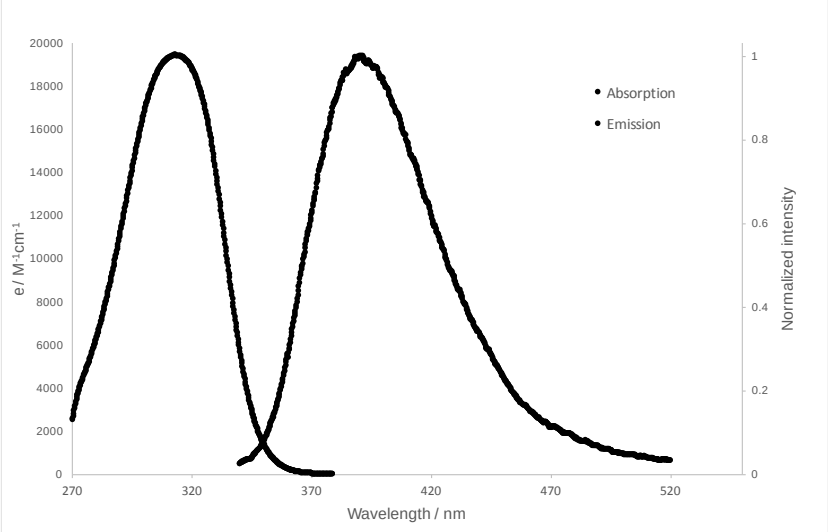


Figure 3. Absorption and emission spectra of **11**.

Table 8. Photophysical date of bispyrrolebenzene **11**.

Absorption		Fluorescence
λ_{max} / nm	ε / $M^{-1}cm^{-1}$	λ_{em} / nm
314	19400	392

2-5. References

(1) (a) S.-H. Li, J. Wang, X.-M. Niu, Y.-H. Shen, H.-J. Zhang, H.- D. Sun, M.-L. Li, Q.-E. Tian, Y. Lu, P. Cao, Q.-T. Zheng, *Org. Lett.* **2004**, *6*, 4327. (b) P. Lu, A. Mailyan, Z. Gu, D. M. Guptill, H. Wang, H. M. L. Davies, *J. Am. Chem. Soc.* **2014**, *136*, 17738. (c) C. Z. I. Dubovyk, K. E. Lazarski, R. J. Thomson, *J. Am. Chem. Soc.* **2014**, *136*, 17750. (d) P. Lu, Z. Gu, A. Zakarian, *J. Am. Chem. Soc.* **2013**, *135*, 14552. (e) F. Peng, S. J. Danishefsky, *J. Am. Chem. Soc.* **2012**, *134*, 18860. (f) A. Furusaki, T. Matsumoto, H. Ogura, H. Takayanagi, A. Hirano, S. Omura, *J. Chem. Soc., Chem. Commun*. **1980**, 698. (g) Y. Enomoto, K. Shiomi, M. Hayashi, R. Masuma, T. Kawakubo, K. Tomosawa, Y. Iwai, S. Omura *J. Antibiot*. **1996**, *49*, 50. (h) T. Kosuge, K. Tsuji, K. Hirai, K. Yamaguchi, T. Okamoto, Y. Iitaka, *Tetrahedron Lett.* **1981**, *22*, 3417.

(2) (a) C. Paal, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2756. (b) L. Knorr, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2863. (c) B. M. Trost, G. A. Doherty, *J. Am. Chem. Soc.* **2000**, *122*, 3801. (d) V. Amarnath, D. C. Anthony, K. Amarnath, W. M. Valentine, L. A. Wetterau, D. G. Graham, *J. Org. Chem.* **1991**, *56*, 6924. (e) V. Amarnath, K. Amarnath, *J. Org. Chem.* **1995**, *60*, 301. (f) Z. Kaleta, B. T. Makowski, T. Soos, R. Dembinski, *Org. Lett.* **2006**, *8*, 1625.

(3) See. ref. 5, 6.

(4) (a) Y. Obora, Y. Ogawa, Y. Imai, T. Kawamura, Y. Tsuji, *J. Am. Chem. Soc.* **2001**, *123*, 10489. (b) Y. Obora, M. Nakanishi, M. Tokunaga, J. Tsuji, *J. Org. Chem.* **2002**, *67*, 5835. (c) Y. Hanzawa, N. Tabuchi, T. Taguchi, *Tetrahedron Lett.* **1998**, *39*, 6249. (d) H. Sakurai, K. Tanabe, K. Narasaka, *Chem. Lett.* **1999**, *28*, 309; (e) B. Adrian G, *Acc. Chem. Res.* **1974**, *7*, 77. (f) O. W., Jr. Lever, *Tetrahedron* **1976**, *32*, 1943. (g) D. Seyferth, R. C. Hui, W.-L. Wang, C. Archer, *J. Org. Chem.* **1993**, *58*, 5843. (h) T. Hiiro, Y. Morita, T. Inoue, N. Kambe, A. Ogawa, I. Ryu, N. Sonoda, *J. Am. Chem. Soc.* **1990**, *112*, 455. (i) D. Seyferth, R. M. Weinstein, *J. Am. Chem. Soc.* **1982**, *104*, 5534.

(5) (a) H. Stetter, *Angew. Chem. Int. Ed.* **1976**, *15*, 639. (b) S. R. Yetra, A. Patra, A. T. Biju, *Synthesis* **2015**, *47*, 1357. (c) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511. (d) A. T. Biju, N. Kuhl, F. Glorius, *ACC. Chem. Res.* **2011**, *44*, 1182. (e) S. Esposti, D. Dondi, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2007**, *46*, 2531.

(6) (a) M. Yasuda, T. Oh-hata, I. Shibata, A. Baba, H. Matsuda, *J. Chem. Soc., Perkin Trans. 1* **1993**, 859. (b) M. Yasuda, Y. Katoh, I. Shibata, A. Baba, H. Matsuda, N. Sonoda, *J. Org. Chem.* **1994**, *59*, 4386.

(c) M. Yasuda, S. Tsuji, Y. Shigeyoshi, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 7440. (d) C. Liu, Y. Deng, J. Wang, Y. Yang, S. Tang, A. Lei, *Angew. Chem. Int. Ed.* **2011**, *50,* 7337. (e) R. Noyori, I. Nishida, J. Sakata, *Tetrahedron Lett.* **1980**, 21, 2085. (f) R. Noyori, I. Nishida, J. Sakata, *J. Am. Chem. Soc.* **1983**, *105*, 1598. (g) I. Kuwajima, E. Nakamura, M. Shimizu, *J. Am. Chem. Soc.* **1982**, *104*, 1025. (h) J. Luo, Q. Jiang, H. Chen, Q. Tang, *RSC Adv.*, **2015**, *5*, 67901. (i) E. Baciocchi, E. Muraglia, *Tetrahedron Lett.* **1994**, 35, 2763. (j) E. Arceo, E. Montroni, P. Melchiorre, *Angew. Chem. Int. Ed.* **2014**, *53*, 12064. (k) S. Usugi, H. Yorimitsu, H. Shinokubo, K. Oshima, *Bull. Chem. Soc. Jpn.* **2002**, 75, 2049.

(7) M. Yasuda, K. Chiba, A. Baba, *J. Am. Chem. Soc.* **2000**, *122*, 7549.

(8) The reaction of the silyl enolate **1b** with the bromoketone **2a** in MeOH or MeCN solutions did not proceed at all under reflux conditions, although the reaction of tin enolate with bromoketone gave the carbonyl adduct. See ref. 6a.

(9) For recent reviews on photoredox catalyst, see: (a) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322. (b) M. Reckenthäler, A. G. Griesbeck, *Adv. Synth. Catal*. **2013**, *355*, 2727. c) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102. (d) M. Teplý, *Collect. Czech. Chem. Commun.* **2011**, *76*, 859. (e) M. N. Hopkinson, B. Sahoo, J-L. Li, F. Glorius *Chem. Eur. J.* **2014**, *20*, 3874. (f) T. Koike, M. Akita, *Inorg. Chem. Front.*, **2014**, *1*, 562. (g) D. P. Hari, B. König, *Chem. Commun.* **2014**, *50*, 6688. (h) D. Ravelli, S. Protti, M. Fagnoni, *Chem. Rev.* **2016**, *116*, 9850. (i) K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev.* **2016**, *116*, 10035. (j) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075. (k) D.kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566. (l) Zoller, D. C. J.; Fabry, D. C.; Ronge, M. A.; Rueping, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 13264. (m) S. Choi, T. Chatterjee, W. J. Choi, Y. You, E. J. Cho, *ACS Catal.* **2015**, *5*, 4796. (n) J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff, D. W. C. MacMillan, *Nature,* **2015**, *524*, 330.

(10) I. Suzuki, N. Esumi, M. Yasuda. *Asian J. Org. Chem.* **2016**, *5*, 179.

(11) (a) D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77. (b) R. J. Crutchley, A. B. P. Lever, *J. Am. Chem. Soc.* **1980**, *102*, 7129. (c) D. D. M. Wayner, J. J. Dannenberg, D. Griller, *Chem. Phys. Lett.* **1986**, *131*, 189.

(12) (a) T. Mukaiyama, K. Narasaka, K. Banno, *Chem. Lett.* **1973**, *2*, 1011. (b) T. Mukaiyama, K. Banno, K. Narasaka, *J. Am. Chem. Soc.* **1974**, *96*, 7503.

(13) (a) F. Stracke, M. Heupel, E. Thiel, *J. Photochem. Photobiol., A* **1999**, *126*, 51. (b) J. Zhang, L. Wang, Q. Liu, Z. Yang, Y. Huang, *Chem. Commun.* **2013**, *49*, 11662. (c) D. P. Hari, B. König, *Org. Lett.* **2011**, *13*, 3852.

(14) The luminescence quenching studies of eosin Y are presented in Experimental Section.

(15) Excess amount of a tertiary amine were used to effectively quench the photocatalyst. a) M. A.

Cismesia, T. P. Yoon, *Chem. Sci*. **2015**, *6*, 5426. b) A. G. Amador, E. M. Sherbrook, T. P. Yoon, *J. Am. Chem. Soc.* **2016**, *138*, 4722.

(16) A mechanism was proposed in which the tertiary amine radical cation works as a oxidant of the alkyl radical species. See ref. 15.

(17) (a) M. S. M. Saroukou, T. Skalski, W. G. Skene, W. D. Lubell, Tetrahedron, **2014**, *70*, 450. (b) J-I. Setsune, M. Toda, K. Watanabe, P. K. Panda, T. Yoshida, *Tetrahedron. Lett.* **2006**, *47*, 7541. (c) C. Eerdun, S. Hisanaga, J-I. Setsune, *Chem. Eur. J.* **2015**, *21*, 239.

(18) (a) J. L. Sessler, D. An, W-S. Cho, V. Lynch, M. Marquez, *Chem. Eur. J.* **2005**, *11*, 2001. (b) E. Turac, M. Ak, E. Sahmetlioglu, M. K. Sener, M. A. Kaya, *Russ. J. Gen. Chem.* **2011**, *81*, 2510.

(19) L. Corda, G. Delogu, E. Maccioni, G. Podda, J. M. B. Fernandez, *J. Heterocyclic. Chem.* **1994**, *31*, 1337.

(20) L. Sun, C-Y. Hong, C-Y. Pan, *J. Am. Chem. Soc*. **2012**, *134*, 20581.

(21) I. Kuwajima, E. Nakamura, M. Shimizu, *J. Am. Chem. Soc.* **1982**, *104*, 1025.

(22) J. Luo, Q. Jiang, H. Chen, Q. Tang, *RSC Adv.*, **2015**, *5*, 67901.

(23) E. Baciocchi, E. Muraglia, *Tetrahedron Lett.* **1994**, 35, 2763.

(24) E. Arceo, E. Montroni, P. Melchiorre, *Angew. Chem. Int. Ed.* **2014**, *53*, 12064.

(25) T. Mukaiyama, K. Narasaka, K. Banno, *Chem. Lett.* **1973**, *2*, 1011.

(26) X-W. Lan, N-X. Wang, W. Zhang, J-L. Wen, C-B. Bai, Y. Xing, Y-H. Li, *Org. Lett*. **2015**, *17*, 4460.

(27) R. E.Tirpak, M. W. Rathke, *J. Org. Chem*. **1982**, *47*, 5099.

(28) L. Huang, X. Zhang, Y. Zhang, *Org. Lett*. **2009**, *11*, 3730.

(29) S. Matsuzawa, Y. Horiguchi, E. Nakamura, I. Kuwajima, *Tetrahedron* **1989**, *45*, 349.

(30) L. A. McAllister, K. L. Truner, S. Brand, M. Stefaniak, D. J. Procter, *J. Org. Chem*. **2006**, *71*, 6497.

(31) (a) K. Tanemura, T. Suzuki, Y. Nishida, K. Satsumabayashi, T. Horaguchi, *Chem. Commun.* **2004**, 470. (b) N. Tada, K. Ban, S. Hirashima, T. Miura, A. Itoh, *Org. Biomol. Chem.* **2010**, *8*, 4701.

(32) O. Borto, G. Fantin, M. Fogagnolo, P. P. Giovannini, A. Massi, S. Pacifico, *Org. Biomol. Chem.* **2011**, *9*, 8437.

(33) M. Yasuda, S. Tsuji, Y. Shigeyoshi, A. Baba, *J. Am. Chem. Soc*. **2002**, *124*, 7440.

(34) Y. Yasu, T. Koike, M. Akita, *Chem. Commun*. **2012**, *48*, 5355.

(35) B. B. Parida, P. P. Das, M. Niocel, J. K. Cha, *Org. Lett*. **2013**, *15*, 1780.

(36) Y. Kohno, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1995,** *68*, 322.

(37) E. O. Reilly, C. Iglesias, D. Ghislieri, J. Hopwood, J. L. Galman, R. C. Lloyd, N. J. Turner, *Angew. Chem. Int. Ed*. **2014**, *53*, 2447.

(38) S. Xue, L-Z. Li, Y-K. Liu, Q-X. Guo, *J. Org. Chem*. **2006**, *71*, 215–218.

(39) Q. Zhang, Y-F. Qiao, M. Huang, H-D. Liang, R-J. Zhou, *Heteroatom Chem*. **2009**, *20*, 425.

(40) A. J. Wills, Y. Krishnan-Ghosh, S. Balasubramanian, *J. Org. Chem*. **2002**, *67*, 6646.

(41) G-Z. Wang, R. Shang, W-M. Cheng, Y. Fu, *Org. Lett*. **2015**, *17*, 4830.

(42) K. Miura, N. Fujisawa, H. Saito, D. Wang, A. Hosomi, *Org. Lett*. **2001**, *3*, 2591.

(43) C. K. Prier, D. W. C. MacMillan, *Chem*. *Sci*. **2014**, *5*, 4173.

(44) N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings: Menlo Park, CA, 1978.

(45) M. Naik, S. Ghorpade, L. K. Jena, G. Gorai, A. Narayan, S. Guptha, S. Sharma, N. Dinesh, P. Kaur, R. Nandishaiah, J. Bhat, G. Balakrishnan, V. Humnabadkar, V. Ramachandran, L. K. Naviri, P. Khadtare, M. Panda, P. S. Iyer, M. Chatterji, *ACS Med. Chem. Lett.* **2014**, *5*, 1005.

Chapter 3

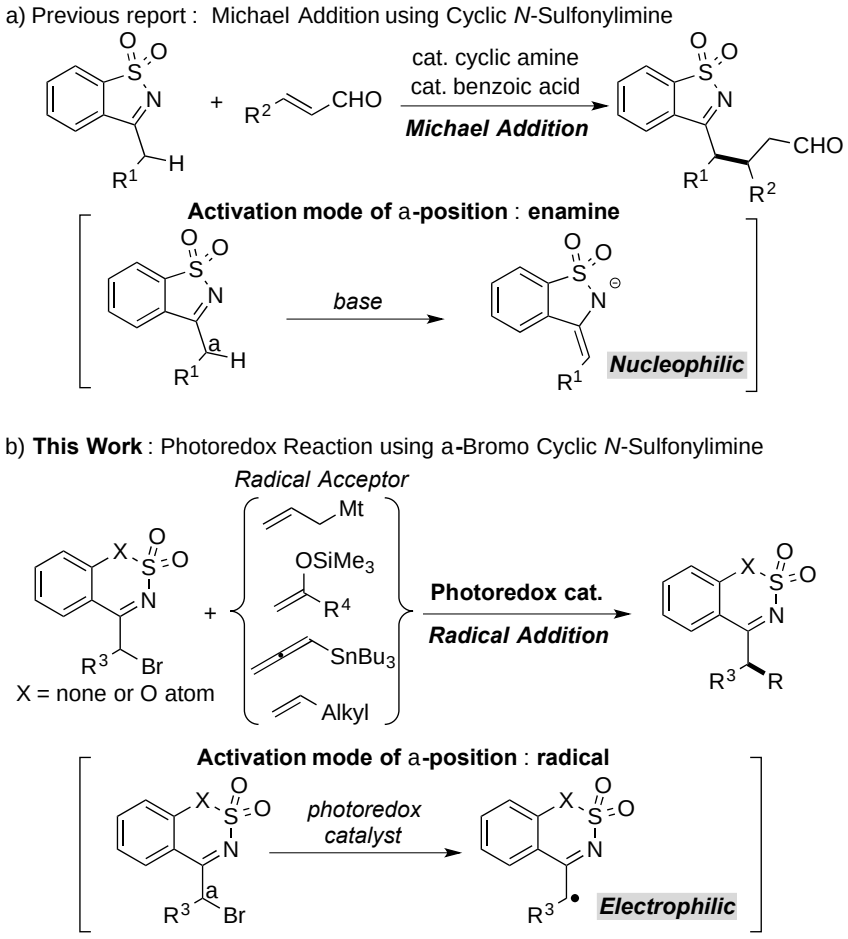
Generation of α-Iminyl Radicals from α-Bromo Cyclic *N*-Sulfonylimines and Application to Coupling with Various Radical Acceptors Using a Photoredox Catalyst

3-1. Introduction

Cyclic *N*-sulfonylimines are useful and valuable substrates for the synthesis of chiral α-tertiary amines, annulation reactions and Michael additions in organic synthesis.[1] Furthermore, a cyclic *N*-sulfonylimine moiety can serve as an effective functional group to improve biological activity.[2] Therefore, the development of a novel method for the synthesis of cyclic *N*-sulfonylimines has attracted considerable attention. In general, two approaches are utilized for the synthesis of cyclic *N*-sulfonylimines: i) the reaction of organomagnesium or lithium nucleophiles with saccharin; [3] and, ii) the reaction of sulfamoyl chloride, NH_2SO_2Cl, with ketones.[1a,1g] However, their compatibility with functional groups is extremely poor due to both the high nucleophilicity of employed organometallic nucleophiles and to the high reactivity of sulfamoyl chloride, which often leads to undesired side reactions. As an improved approach, the Michael addition of cyclic *N*-sulfonylimines to electron-deficient olefins catalyzed by proline derivatives has been developed (Scheme 1a).[1d] Due to the high acidity of α-proton of *N*-sulfonylimines, the generation of enamines smoothly proceeded to afford the Michael adduct under mild reaction conditions.[1d,1e,1f,1i] However, these reactions only proceeded with electrophiles such as unsaturated aldehydes or simple aldehydes because generated enamines behave as nucleophiles. Recently, radical reactions catalyzed by a photoredox catalyst have gained much attention in organic chemistry because this method allows the selective generation of radicals under mild conditions.[4] An α-halocarbonyl compound is one of the most useful precursors that is used to generate radicals at the α-positon of carbonyl groups, and it reacts with various radical acceptors.[5] Our group has reported the organic dye-catalyzed radical coupling of α-bromocarbonyls with allyl trifluoroborate salts or silyl enol ethers.[6] Therefore, I envisaged that α-bromo cyclic *N*-sulfonylimine would be a suitable precursor for an α-iminyl radical to synthesize cyclic *N*-sulfonylimine-containing molecules because the electron-withdrawing ability of the sulfonyl group facilitates single-electron reduction by a photoredox catalyst and increases the electrophilicity of α-iminyl radicals to behave as an electrophilic radical species. Herein, I report the visible-light-promoted radical coupling reaction of α-bromo *N*-sulfonylimines[7] with various nucleophilic radical acceptors in the presence of a photoredox catalyst (Scheme 1b). To the best of our knowledge, this is the first example of the generation of an α-iminyl radical from α-halo imine and its

utilization in organic synthesis.[8,9]

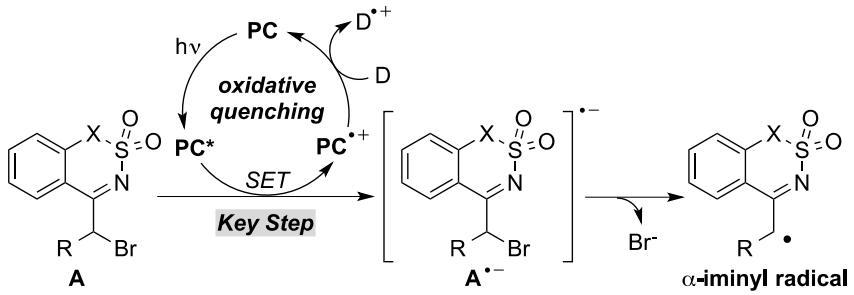
Scheme 1. Introduction of a cyclic *N*-sulfonylimine unit via the activation of the α-position of an imine.



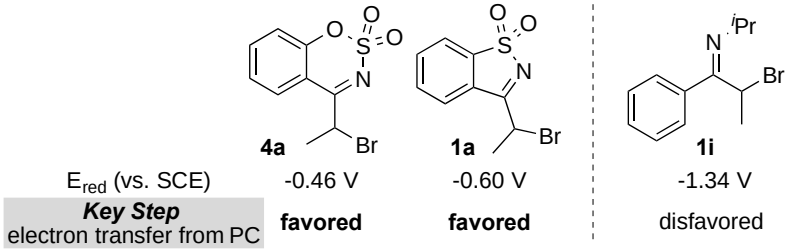
3-2. Results and Discussion

Based on previous reports,[5,6] the important step in the generation of an α-iminyl radical would include a single electron transfer from an excited photocatalyst (**PC***) to α-bromo *N*-sulfonylimine **A** under visible light irradiation (Scheme 2). Therefore, I measured the reduction potential of α-bromo ketimines by cyclic voltammetry to evaluate the feasibility of the reduction process.[10] The reduction potentials of **1a**, **4a**, and **1i** were determined as –0.60, –0.46, and –1.34 V vs. SCE, respectively (Scheme 3). According to these values, α-bromo *N*-sulfonylimines **1a** and **4a** are more easily reduced than the simple *N*-alkyl-substituted α-bromo imine **1i**, which suggests that commercially available photoredox catalysts such as eosin Y, erythrosine B, and $Ru(bpy)_3^{2+}$ could reduce α-bromo *N*-sulfonylimines **1a** and **4a** to give the α-iminyl radical (The oxidation potential of photoexcited photoredox catalyst; $E^*_{ox}(eosinY^{\bullet+}/eosinY^*) = -1.11$ V vs. SCE[4d]; E^*_{ox}(erythrosine $B^{\bullet+}$/ erythrosine B *) = –1.17 V vs. SCE[11]; $E^*_{ox}([Ru(bpy)_3]^{3+}/ [Ru(bpy)_3]^{2+*}) = -0.81$ V vs. SCE[4c]).

Scheme 2. Generation of an α-iminyl radical via a photoredox reaction.



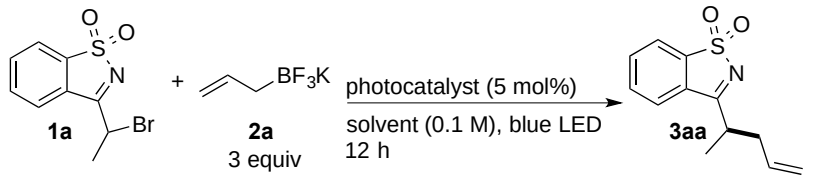
Scheme 3. The reduction potential of α-bromoketimines.



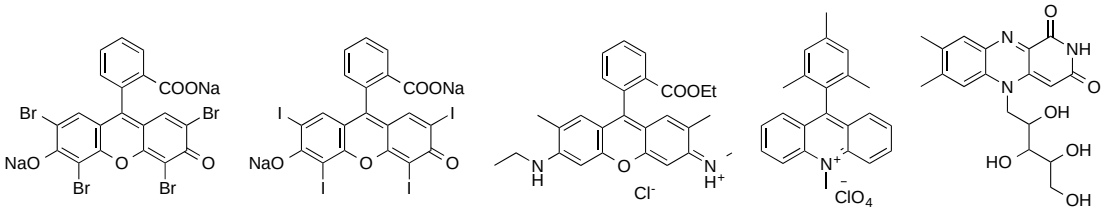
First, I chose the allylation of α-bromo *N*-sulfonylimines **1a** with allyl trifluoroborates **2a** in the presence of photoredox catalysts as a model radical reaction to optimize the reaction conditions. When the reaction using eosin Y (5 mol%) and CsF (3 equiv) was carried out in DMF under visible-light irradiation by blue LED (468 nm), the allylation product **3aa** was not observed (Table 1, entry 1). This was the condition for our previously reported system of α-allylation for α-bromoketones via allylboron compounds.[6a] However, the conditions in the absence of CsF gave **3aa** with in a moderate yield of 54% (entry 2). After the screening of organic dyes and transition metal photoredox catalysts under irradiation by blue LED (468 nm) or green LED (525 nm) (entries 3-8), the combination of erythrosine B with blue LED was found to be the most effective (entry 3). Interestingly, in eosin Y-, erythrosine B-, and rhodamine 6G-catalyzed reactions, irradiation by blue LED rather than green LED gave high yields in spite of their maximum absorption wavelength (λ_{max}) close to an emission wavelength of green LED. Perhaps, the use of a visible light of a slightly different wave length from a λ_{max} of photocatalysts could keep a low concentraton of a generated iminyl radical species to avoid undesired side reactions such as homocoupling of iminyl radicals. Several polar solvents were investigated by using erythrosine B and blue LED (entries 9-12), in particular, the reaction carried out in MeCN afforded **3aa** in a satisfying 86% yield (entry 10). Control experiments in entries 13 and 14 revealed that both the organic dye and visible light irradiation were essential in the formation of **3aa**. Furthermore, the addition of TEMPO (2 equiv) inhibited the reaction (entry 15), which suggests that the generation of a radical species was involved in the reaction. When the emission intensity was

decreased, the yield became slightly lower (entry 16). A larger scale experiment also gave a reasonable yield (entry 17).

Table 1. Optimization of reaction conditions of α-bromo *N*-sulfonylimine **1a** with allyl trifluoroborate **2a**.[a]



entry	photocatalyst	solvent	yield (%)[b]	
			blue LED	Green LED
1[c]	eosinY	DMF	0	
2	eosinY	DMF	54	39
3	erythrosine B	DMF	74	46
4	rhodamine 6G	DMF	65	49
5	Mes-Acr$^+$ClO$_4^-$	DMF	74	18
6	riboflavine	DMF	72	25
7	Ir(ppy)$_3$	DMF	68	70
8	Ru(bpy)$_3$PF$_6$	DMF	62	65
9	erythrosine B	DMF/MeCN	78	
10	erythrosine B	MeCN	86(85)[d]	75
11	erythrosine B	MeOH	58	
12	erythrosine B	EtOAc	32	
13	none	MeCN	0	
14[f]	erythrosine B	MeCN	0	
15[g]	erythrosine B	MeCN	0	
16[h]	erythrosine B	MeCN	61	
17[i]	erythrosine B	MeCN	77	

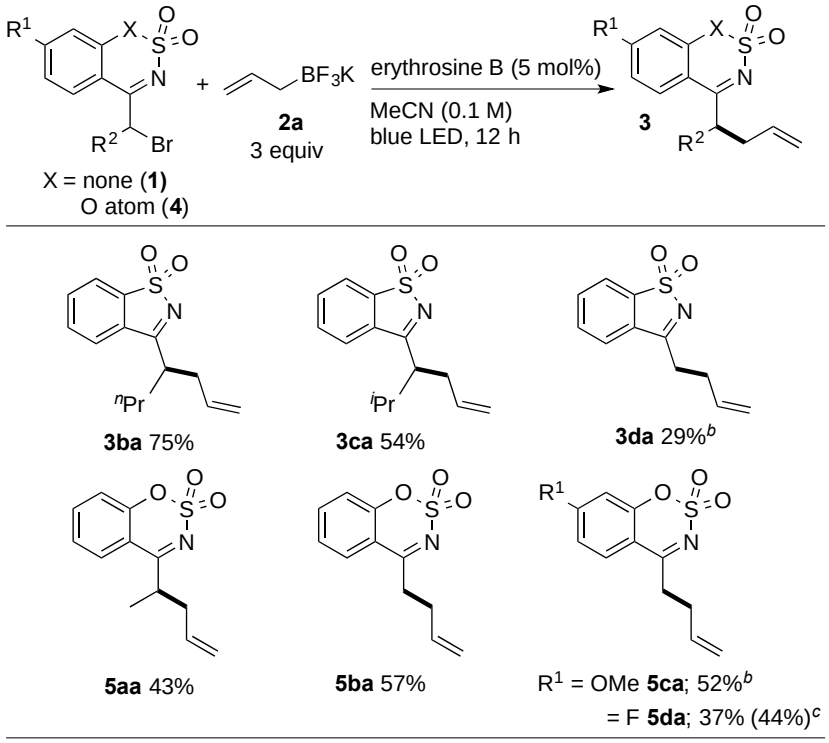


[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), photocatalyst (5 mol%), solvent (1 mL), 12 h under irradiation of 3 W blue LED (468 nm) or 3 W green LED (525 nm). [b] Yields were determined by ^{1}H NMR with 1,1,1,2-tetrachloroethane as an internal standard. [c] CsF (3 equiv) was used as an additive. [d] Isolated Yield. [f] no irradiation. [g] TEMPO (2 equiv) was added. [h] The half-shielded blue LED was used. [i] Reaction conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), photocatalyst (1 mol%), solvent (1 mL), blue LED (468 nm), 12 h.

With the optimized conditions in hand (Table 1, entry 10), the scope of the allylation of α-bromo *N*-sulfonylimines was explored (Scheme 4). More sterically hindered ketimine bearing ^{n}Pr and ^{i}Pr groups (**1b** and **1c**) than Me group (**1a**) furnished the corresponding products **3ba** and **3ca** in 75% and

54% yields, respectively. The primary bromoimine **1d** reacted to provide the allylated product **3da**, albeit in a low yield. The reaction of a six-membered cyclic *N*-sulfonylketimine **4** was also investigated. Ketimines **4a** and **4b** underwent the allylation reaction to give the products **5aa** and **5ba** in moderate yields, respectively. Although a decreased yield was observed in the reaction using electron-deficient ketimine **4d**, electron-rich ketimine **4c** gave the product **5ca** in 52% yield.

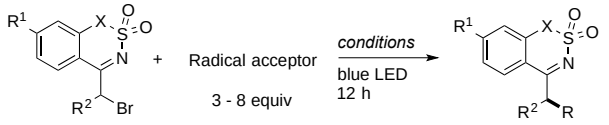
Scheme 4. Allylation of α-bromo *N*-sulfonylimines **1** by allyl trifluoroborate **2a**.[a]



[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), erythrosine B (5 mol%), solvent (1 mL), blue LED (468 nm), 12 h. [b] MeOH was used instead of MeCN. [c] $Ru(bpy)_3PF_6$ (5 mol%) was used as a photocatalyst.

Next, I evaluated the scope of a visible-light-induced reaction of α-bromo *N*-sulfonylimines with various radical acceptors in the presence of a photoredox catalyst (Table 2). The allylation of five-membered bromoimine **1a** and six-membered one **4a** by allylstannane **2b** proceeded to afford **3aa** and **5aa** in high yields, respectively (entries 1 and 2). Although allylated products were not obtained in the reaction of allylsilane **2c** catalyzed by erythrosine B, the use of $Ru(bpy)_3(PF_6)_2$ gave coupling products **3da** and **5ba**, respectively (entries 3 and 4). Bromoimines reacted with silyl enol ethers **2d** and **2e** to yield 1,4-imino ketones (entries 5-8). Methallylstannane **2f** and allenylstannane **2g** also worked as radical acceptors to give the coupling products **3af** and **3dg** in 71 and 39% yields, respectively (entries 9 and 10). The radical coupling reaction using bromoimime **1i**, which has higher reduction potential than α-bromo *N*-sulfonylimines, did not proceed (entry 11).

Table 2. Reaction of α-bromo *N*-sulfonylimines **1** and **4** with various radical acceptors[a,b]

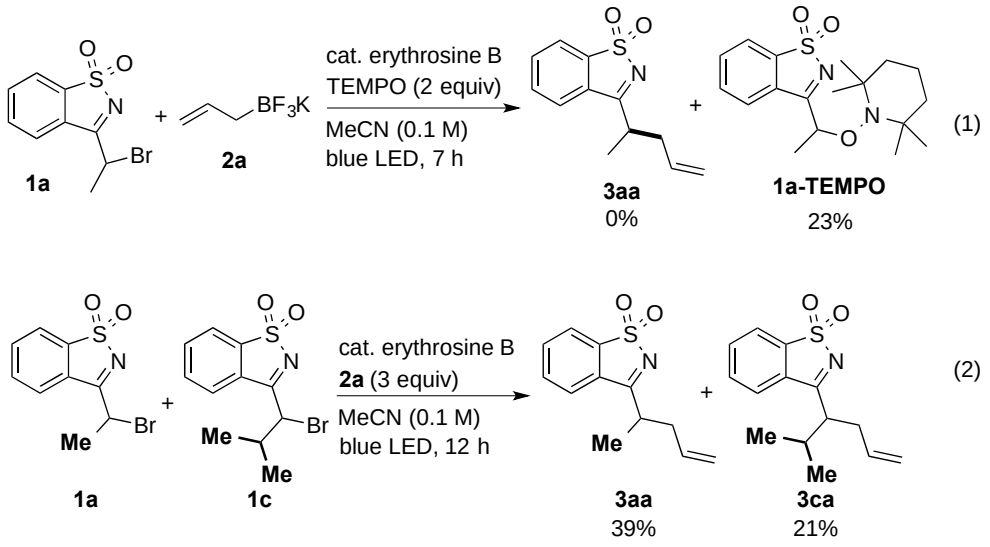


Entry	Bromoimine	Radical acceptor	Product	Yield (%)[c]
1	**1a**	**2b**	**3aa**	87[a]
2	**4a**	**2b**	**5aa**	81[a]
3	**1d**	**2c**	**3da**	0[a] 48[b]
4	**4b**	**2c**	**5ba**	0[a] 40[b]
5	**1d**	**2d**	**3dd**	(28)[a,d] 65[b]
6	**4b**	**2d**	**5bd**	65[a] (60)[b,d]
7	**1d**	**2e**	**5de**	51[b]
8	**4b**	**2e**	**5be**	30[b]
9	**1a**	**2f**	**3af**	71[b]
10	**1d**	**2g**	**3dg**	39[b]
11	**1i**	**2a**	**3ia**	0[b]

[a] Reaction conditions A: **1** (0.1 mmol), **2** (3-8 equiv), erythrosine B (5 mol%), blue LED (468 nm), 12 h. [b] conditions B: **1** (0.1 mmol), **2** (3-8 equiv), $Ru(bpy)_3(PF_6)_2$ (5 mol%), blue LED (468 nm), 12 h. [c] Isolated Yield. [d] Yields were determined by ^1H NMR with 1,1,1,2-tetrachloroethane as an internal standard.

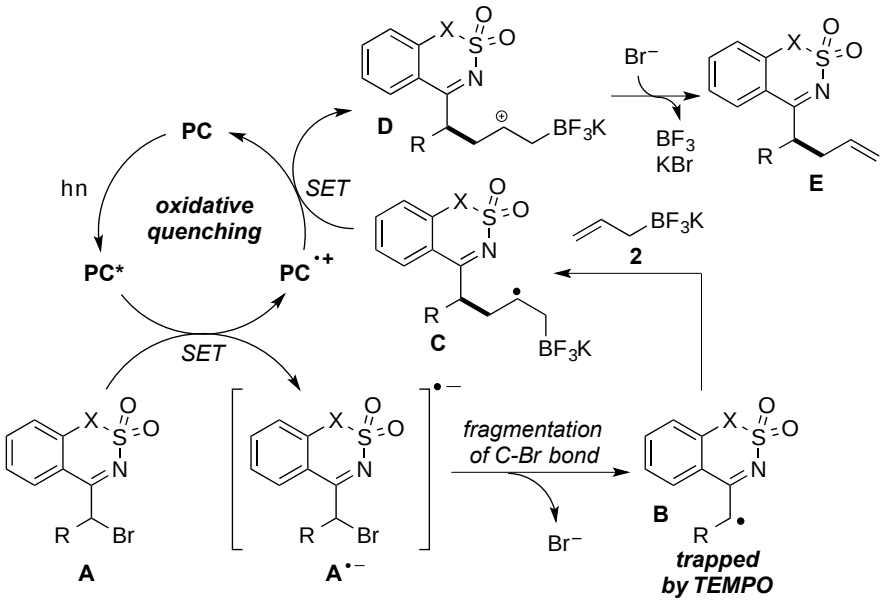
The generation of an α-iminyl radical from α-bromo *N*-sulfonylimines **1a** was investigated. The loading of TEMPO (2,2,6,6-tetramethylpiperidine-N-oxyl radical) to the reaction system, as shown in Eq. (1), produced the compound **1a-TEMPO**, and coupling product **3aa** was not obtained at all. This result clearly shows that the present coupling reaction involves the generation of an α-iminyl radical. Next, the luminescence quenching studies of erythrosine B with α-bromo ketimine **1a** and allyl trifluoroborates **2a** were investigated to reveal the reaction mechanism.[12] The results supported an

oxidative quenching mechanism with an effective electron transfer from the photoexcited erythrosine B to α-bromo ketimine **1a**. To evaluate the steric effect on this photoredox reaction, a mixture of α-bromo *N*-sulfonylimines **1a** and **1c** were treated with allyl trifluoroborane **2a** in the presence of erythrosine B (Eq. [2]). Methyl substituted substrate **1a** was quickly reacted with **2a** prior to *iso*-propyl substituted substrate **1c** in spite of almost the same reduction potential (E_{red}(**1a**/ **1a**$^{\bullet-}$) = -0.60 V vs. SCE; E_{red}(**1c**/ **1c**$^{\bullet-}$) = -0.64 V vs. SCE).

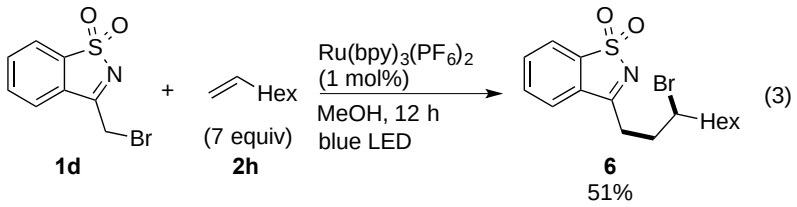


The dependence of the present radical reaction on light was further studied by employing a periodic "on/off" light conditions.[13] Turning off the light resulted in a dramatically low rate, which excludes a radical chain mechanism. A plausible reaction mechanism is shown in Scheme 5. The irradiation of visible light to photoredox catalyst (**PC**; erythrosine B or $Ru(bpy)_3(PF_6)_2$) generates the excited catalyst **PC***. Then, single-electron transfer (SET) from **PC*** to α-bromo *N*-sulfonylimines **A** occurs to form PC radical cation (**PC**$^{\bullet+}$) and radical anion **A**$^{\bullet-}$. Then, the fragmentation of C-Br bond affords α-iminyl radical **B**. The radical **B** adds to the acceptor such as allyl trifluoroborate **2a** to afford radical intermediates **C**, and the intermediates **C** is oxidized by **PC**$^{\bullet+}$ to generate the cation **D** and **PC** is regenerated. Finally, the fragmentation of **D** leads to the product **E**. The preference of **1a** over **1c** in the competitive reaction (Eq. [2]) is explained by less steric hindrance in the addition of radical **B** to radical acceptor **2a**. When allylsilane **2c** was used as a radical acceptor, it was nessesary to use $Ru(bpy)_3(PF_6)_2$ instead of erythrosine B. This is probably because $Ru(bpy)_3^{3+}$ has greater potential for oxidation compared with that of the erythrosine B radical cation, and promotes oxidation from radical **C** to **D** (E_{ox}(erythrosine B$^{\bullet+}$/erythrosine B) = 0.71 V vs. SCE[11]; E_{ox}($Ru(bpy)_3^{3+}$/ $Ru(bpy)_3^{2+}$) = 1.29 V vs. SCE[4c]).

Scheme 5. Proposed reaction mechanism.



In order to demonstrate the additional utility of α-iminyl radicals derived from α-bromo *N*-sulfonylimines, intermolecular atom transfer radical addition (ATRA) was performed using a photoredox catalyst.[5e] The reaction of bromoketimine **1d** with 1-octene **2h** in the presence of $Ru(bpy)_3(PF_6)_2$ under visible light irradiation proceeded to afford the ATRA product **6** [Eq. (3)].[14] This method is an efficient route to obtain cyclic *N*-sulfonylimine-containing molecules by using simple alkenes other than organometallic nucleophiles such as organoborates, silanes, and stannanes.



3-3. Conclusion

I have developed a practical protocol under mild conditions for the synthesis of *N*-sulfonylimine derivatives by using photoredox catalysts, α-bromo *N*-sulfonylimines, and radical acceptors. This is the first report on the generation of an α-iminyl radical from haloimines via the single-electron reduction of a photoredox catalyst. The key for this radical generation was the incorporation of a sulfonyl group into an imine moiety, which facilitated a single-electron reduction by the photoredox catalyst and stabilized the α-iminyl radical. The methodology reported here displays a broad substrate scope of radical acceptors to give the coupling products and ATRA product effectively.

3-4. Experimental Section

General

New compounds were characterized by ^{1}H, ^{13}C, COSY, HMQC, HMBC, IR, MS, HRMS. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL AL-400 spectrometer (JEOL, Tokyo, Japan) in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data are reported as follows: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in hertz, and integration. IR spectra were recorded as thin films. Mass spectrometry (MS) and High resolution mass spectrometry (HRMS) was performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University. Medium-pressure column chromatography was carried out on a YAMAZEN Flash Purification System, which is equipped with a 254 nm UV detector. The absorption wave of photocatalyst was measured by JASCO V-630. All reactions were carried out in dry solvents under nitrogen atmosphere, and the reaction vessels were positioned at a distance of 5 cm from a 3 W blue LED (468 nm) or a 3W green LED (525 nm). NMR Yields were determined by ^{1}H NMR using 1,1,1,2-tetrachloroethane as an internal standard.

Materials

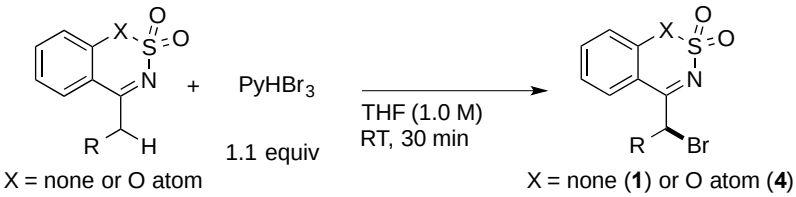
Dehydrated solvents, including acetonitrile, *N,N*-dimethylformamide (DMF), ethyl acetate, methanol (MeOH), and ethanol (EtOH), were purchased (Wako Pure Chemical Industries) and used as obtained. Cyclic *N*-sulfonylimines were synthesized based on the literature procedure.[15] The synthesis of α-bromo cyclic imines were shown in the section of Preparation of Bromoimines. Bromoimine **1i** was synthesized based on the reported method.[16] Radical acceptors **2a**, **2b**, **2c**, **2e**, **2h** were purchased from commercial sources (Tokyo Chemical Industry). The other radical acceptor **2d**, **2f, 2g** were synthesized based on the literature procedure.[17] The catalysts in Table 1 and Table S1 were purchased from commercial sources (Sigma-Aldrich).

Experimental Procedure

To a solution of photoredox catalyst (1-5 mol%) and α-bromo *N*-sulfonylimines 1(0.100 mmol) in MeCN (1.0 mL) were added radical acceptors (3-8 equiv). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was obtained. The product was analyzed by ^{1}H NMR. The purification steps are described in detail in the Product Data section.

Preparation of Bromoimines

General Procedure

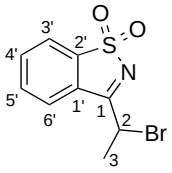


X = none or O atom

X = none (**1**) or O atom (**4**)

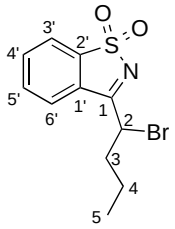
To a solution of the corresponding imine (6.0 mmol) in THF (6 mL) at 25 °C was added pyridinium bromide perbromide (6.6 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was finally purified by recrystallization from EtOAc and hexane to afford the bromoimine **1** or **4**.

3-(1-bromoethyl)benzo[*d*]isothiazole 1,1-dioxide (1a)



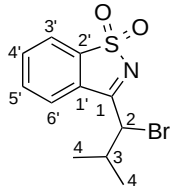
To a solution of the corresponding imine (1.51 g, 7.73 mmol) in THF (7 mL) at 25 °C was added pyridinium bromide perbromide (2.72 g, 8.50 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq. (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a white solid (1.96 g, 93 % yield). mp: 109-110 °C IR: (KBr) 1558, 1336, 1174 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.95-7.91 (m, 1H), 7.91-7.86 (m, 1H), 7.79-7.74 (m, 2H), 5.23 (q, J = 6.8 Hz, 1H, 2-H), 2.15 (d, 3H, J = 6.8 Hz, 3-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 172.2 (s, C-1), 140.2 (s, C-2'), 133.9 (d), 133.8 (d), 129.2 (s, C-1'), 124.9 (d), 122.7 (d), 37.7 (d, C-2), 21.1 (q, C-3) MS: (EI, 70 eV) *m*/*z* 275 (M^+ + 2, 2), 273 (M^+, 2), 195 (49), 194 (100), 130 (36), 103 (47), 76 (28) HRMS: (EI, 70 eV) calcd for ($C_9H_8BrNO_2S$) 272.9459 (M^+) found *m*/*z* 272.9462

3-(1-bromobutyl)benzo[*d*]isothiazole 1,1-dioxide (1b)



To a solution of the corresponding imine (3.35 g, 15.0 mmol) in THF (15 mL) at 25 °C was added pyridinium bromide perbromide (5.28 g, 16.5 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq (20 mL). The aqueous layer was extracted with EtOAc (30 mL x 2), then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a white solid (4.22 g, 93 % yield). mp: 88-90 °C IR: (KBr) 1556, 1331, 1178 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.92-7.88 (m, 2H), 7.85-7.74 (m, 2H), 5.09 (t, J = 7.2 Hz, 1H, 2-H), 2.32 (q, J = 7.2 Hz, 2H, 3-H_2), 1.76-1.64 (m, 1H, 4-H^A), 1.61-1.48 (m, 1H, 4-H^B), 1.01 (t, J = 7.6 Hz, 3H, 5-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 171.8 (s, C-1), 139.9 (s, C-2'), 133.9 (d), 133.7 (d), 129.1 (s, C-1'), 125.0 (d), 122.5 (d), 43.6 (d, C-2), 35.9 (t, C-3), 20.6 (t, C-4), 13.2 (q, C-5) MS: (EI, 70 eV) *m*/*z* 303 (M^+ + 2, 0.1), 301 (M^+, 0.1), 261 (74), 259 (68), 222 (20), 194 (86), 181 (100), 103 (35), 76 (30) HRMS: (EI, 70 eV) calcd for ($C_{11}H_{12}BrNO_2S$) 300.9772 (M^+) found *m*/*z* 300.9773

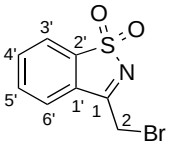
3-(1-bromo-2-methylpropyl)benzo[*d*]isothiazole 1,1-dioxide (1c)



To a solution of the corresponding imine (1.00 g, 4.48 mmol) in THF (5 mL) at 25 °C was added pyridinium bromide perbromide (1.60 g, 5.00 mmol) in portions. After stirred for 30 min at 45 °C, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq (10 mL). The aqueous layer was extracted with EtOAc (20 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a white solid (0.353 g, 24 % yield). mp: 108-110 °C IR: (KBr) 1554, 1333, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.96-7.89 (m, 2H), 7.79-7.73 (m, 2H), 4.80 (d, J = 9.2 Hz, 1H, 2-H), 2.66-2.57 (m, 1H, 3-H), 1.33 (d, J = 7.2 Hz, 4-H_3), 1.11 (d, J = 7.2 Hz, 4-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 171.4 (s, C-1), 140.1 (s, C-2'),

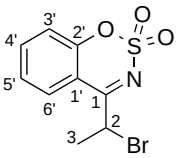
133.8 (d), 133.7 (d), 129.3 (s, C-6'), 125.1 (d), 122.7 (d), 52.2 (d, C-2), 32.2 (t, C-3), 21.1 (q, C-4), 20.4 (q, C-4) MS: (EI, 70 eV) *m*/*z* 303 (M^+ + 2, 0.2), 301 (M^+, 0.2), 261 (100), 259 (94), 222 (29), 208 (42), 181 (86), 143 (20), 116 (22), 115 (25), 76 (23)HRMS: (CI, 70 eV) calcd for ($C_{11}H_{13}BrNO_2S$) 301.9850 (M^+ + 1) found *m*/*z* 301.9854

3-(bromomethyl)benzo[*d*]isothiazole 1,1-dioxide (1d)



To a solution of the corresponding imine (3.00 g, 16.6 mmol) in THF (20 mL) at 25 °C was added pyridinium bromide perbromide (5.84 g, 18.3 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq. (20 mL). The aqueous layer was extracted with EtOAc (40 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a white solid (2.10 g, 49 % yield). mp: 146-148 °C IR: (KBr) 1552, 1333, 1174 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.97-7.91 (m, 1H), 7.90-7.84 (m, 1H), 7.82-7.76 (m, 2H), 4.55 (s, 1H, 2-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 169.3 (s, C-1), 140.0 (s, C-2'), 134.1 (d), 134.0 (d), 129.0 (s, C-1'), 124.9 (d), 122.8 (d), 23.1(t, C-2) MS: (EI, 70 eV) *m*/*z* 261 (M^+ + 2, 44), 259 (M^+, 44), 181 (69), 152 (100), 133 (37), 117 (32), 90 (31), 89 (61), 77 (42), 76 (93), 50 (66) HRMS: (EI, 70 eV) calcd for ($C_8H_6BrNO_2S$) 258.9303 (M^+) found *m*/*z* 258.9303

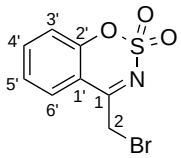
4-(1-bromoethyl)benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (4a)



To a solution of the corresponding imine (0.400 g, 1.89 mmol) in THF (2 mL) at 25 °C was added pyridinium bromide perbromide (0.640 g, 2.00 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq. (5 mL). The aqueous layer was extracted with EtOAc (10 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a brown solid (0.287 g, 52 % yield). mp: 68-71 °C IR: (neat) 1597, 1554, 1386, 1182 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.96 (d, J = 8.0 Hz, 1H, 6'-H), 7.74 (t, J = 8.0 Hz, 1H, 4'-H), 7.44 (t, J = 8.0 Hz, 1H, 5'-H), 7.32 (d, J =

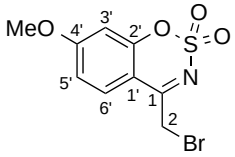
8.0 Hz, 1H, 3'-H), 5.40 (q, *J* = 6.8 Hz, 1H, 2-H), 2.05 (d, *J* = 6.8 Hz, 3H, 3-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 175.4 (s, C-1), 154.1 (s, C-2'), 137.4 (d, C-4'), 127.9 (d, C-6'), 126.0 (d, C-5'), 119.3 (d, C-3'), 114.3 (s, C-1'), 40.4 (d, C-2), 20.6 (q, C-3) MS: (EI, 70 eV) *m*/*z* 291 (M^+ + 2, 17), 289 (M^+, 16), 211 (42), 210 (100), 147 (35), 146 (71), 132 (34), 119 (37), 118 (23), 91 (51), 65 (22), 64 (27), 63 (30) HRMS: (EI, 70 eV) calcd for ($C_9H_8BrNO_3S$) 288.9408 (M^+) found *m*/*z* 288.9405

4-(bromomethyl)benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (4b)



To a solution of the corresponding imine (1.25 g, 6.34 mmol) in THF (7 mL) at 25 °C was added pyridinium bromide perbromide (2.24 g, 7.00 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq. (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a brown solid (1.12 g, 64 % yield). mp: 98-100 °C IR: (KBr) 1597, 1554, 1387, 1182 cm^{-1} ^{1}H NMR: (400 MHz, $CDCl_3$) 7.92 (d, *J* = 8.0 Hz, 1H, 6'-H), 7.77 (t, *J* = 8.0 Hz, 1H, 4'-H), 7.45 (t, *J* = 8.0 Hz, 1H, 5'-H), 7.33 (d, *J* = 8.0 Hz, 1H, 3'-H), 4.53 (s,2H, 2-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 173.1 (s, C-1), 154.1 (s, C-2'), 137.8 (d, C-4'), 128.4 (d, C-6'), 126.1 (d, C-5'), 119.4 (d, C-3'), 114.1 (s, C-1'), 27.9 (t, C-2) MS: (EI, 70 eV) *m*/*z* 277 (M^+ + 2, 31), 275 (M^+, 31), 197(78), 196 (100), 133 (32), 132 (97), 105 (34), 104 (47), 102 (26), 78 (21), 77 (40), 64 (35), 63 (42), 51 (22) HRMS: (EI, 70 eV) calcd for ($C_8H_6BrNO_3S$) 274.9252 (M^+) found *m*/*z* 274.9256

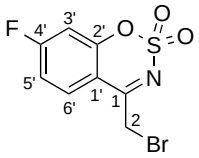
4-(bromomethyl)-7-methoxybenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (4c)



To a solution of the corresponding imine (0.30 g, 1.3 mmol) in THF (3.0 mL) at 25 °C was added pyridinium bromide perbromide (0.46 g, 1.4 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a brown solid (0.237

g, 60 % yield). mp: 144-145 °C IR: (KBr) 1621, 1579, 1379, 1188, 1120 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.80 (d, *J* = 9.2 Hz, 1H, 6'-H), 6.92 (dd, *J* = 9.2, 2.4 Hz, 1H, 5'-H), 6.77 (d, *J* = 2.4 Hz, 1H, 3'-H), 4.45 (s, 2H, 2-H_2), 3.95 (s, 3H, OMe) ^{13}C NMR: (100 MHz, $CDCl_3$) 172.3 (s, C-1), 167.0 (s, C-4'), 156.9 (s, C-2'), 130.1 (d), 113.7 (d), 107.6 (s, C-1'), 103.4 (d), 56.6 (q, OMe), 28.2 (t, C-2) MS: (EI, 70 eV) *m*/*z* 307 (M^+ + 2, 32), 305 (M^+, 31), 227 (100), 226 (34), 163 (26), 162 (63), 148 (38), 134 (21), 120 (25), 79 (23), 51 (25) HRMS: (EI, 70 eV) calcd for ($C_9H_8BrNO_4S$) 304.9357 (M^+) found *m*/*z* 304.9359

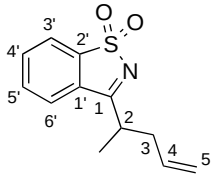
4-(bromomethyl)-7-fluorobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (4d)



To a solution of the corresponding imine (0.800 g, 3.72 mmol) in THF (5 mL) at 25 °C was added pyridinium bromide perbromide (2.24 g, 7.00 mmol) in portions. After stirred for 30 min, the generated white precipitate was filtered off, and the filtrate was poured into saturated NH_4Cl aq (10 mL). The aqueous layer was extracted with EtOAc (15 mL x 2), and then the combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in *vacuo*, the crude product was purified by recrystallization from EtOAc and hexane to afford the bromoimine as a brown solid (1.12 g, 64 % yield). mp: 80-81 °C IR: (KBr) 1614, 1554, 1382, 1201, 1115 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.96 (dd, *J* = 8.8 Hz, $^4J_{HF}$ = 6.0 Hz, 1H, 6'-H), 7.19-7.14 (m, 1H, 5'-H), 7.07 (dd, $^3J_{HF}$ = 8.8 Hz, *J* = 2.4 Hz, 1H, 3'-H), 4.50 (s, 2H, 2-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 172.1 (s, C-1), 167.3 (s, d, $^1J_{CF}$ = 266 Hz, C-4'), 156.2 (s, $^3J_{CF}$ = 14.0 Hz, C-2'), 131.0 (d, d, $^3J_{CF}$ = 11.6 Hz, C-6'), 114.3 (d, d, $^2J_{CF}$ = 22.3 Hz, C-5'), 111.0 (s, d, $^4J_{CF}$ = 3.3 Hz, C-1'), 107.5 (d, d, $^2J_{CF}$ = 25.6 Hz, C-3'), 27.9 (t, C-2) MS: (EI, 70 eV) *m*/*z* 295 (M^+ + 2, 19), 293 (M^+, 20), 215 (100), 214 (82), 151 (28), 150 (63), 123 (38), 122 (49), 96 (30), 95 (25), 82 (35), 81 (24) HRMS: (EI, 70 eV) calcd for ($C_8H_5BrFNO_3S$) 292.9158 (M^+) found *m*/*z* 292.9158

Product Date

3-(pent-4-en-2-yl)benzo[*d*]isothiazole 1,1-dioxide (3aa)



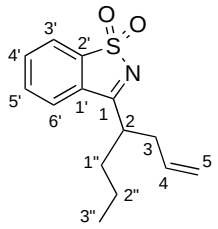
To a solution of erythrosin B (0.0047 g, 0.0053 mmol) and bromoimine **3aa** (0.0253 g, 0.0923 mmol)

in MeCN (1.0 mL) were added potassium allyltrifluoroborate **2** (0.0444 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL x 3) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3aa** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3aa** as a colorless oil (0.0184 g, 0.0782 mmol, 85%).

To a solution of erythrosin B (0.0044 g, 0.0050 mmol) and bromoimine **3aa** (0.0259 g, 0.0945 mmol) in MeCN (1.0 mL) were added allyltributylstannane (**2)** (0.0993 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was diluted with Et_2O (15 mL) and washed by NH_4F aq (10%, 20 mL). The obtained white precipitate was filtered off, and the filtrate was extracted with EtOAc (3 x 10 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3aa** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3aa** as a colorless oil (0.0194 g, 0.0824 mmol, 87%)

IR: (neat) 1554, 1454, 1336, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.95-7.91 (m, 1H), 7.77-7.71 (m, 3H), 5.83 (ddt, *J* = 17.6, 10.4, 7.2 Hz, 1H, 4-H), 5.15-5.09 (m, 2H, 5-H_2), 3.30 (sext, *J* = 7.2 Hz, 1H, 2-H), 2.69 (ddd, *J* = 17.6, 7.2, 6.4 Hz, 1H, 3-H^A), 2.42 (ddd, *J* = 17.6, 7.2, 6.4 Hz, 1H, 3-H^B), 1.42 (d, *J* = 7.2 Hz, 3H, 2-Me) ^{13}C NMR: (100 MHz, $CDCl_3$) 179.5 (s, C-1), 140.1 (s, C-2'), 134.4 (d), 133.8 (d), 133.5 (d), 130.7 (s, C-1'), 123.9 (d, C-4), 122.6 (d), 118.1 (t, C-5), 38.2 (t, C-3), 35.4 (d, C-2), 17.5 (q, 2-Me) MS: (EI, 70 eV) *m*/*z* 235 (M^+, 6), 220 (M^+ - Me, 20), 170 (61), 156 (100), 143 (32), 130 (43), 129 (45), 128 (26), 104 (26), 103 (40), 77 (23), 76 (26), 68 (23) HRMS: (CI, 70 eV) calcd for ($C_{12}H_{14}NO_2S$) 236.0745 (M^+ + 1) found *m*/*z* 236.0742

3-(hept-1-en-4-yl)benzo[*d*]isothiazole 1,1-dioxide (3ba)

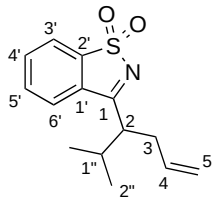


To a solution of erythrosin B (0.0046 g, 0.0052 mmol) and bromoimine **1b** (0.0312 g, 0.103 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0444 g, 0.300 mmol). The mixture

was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3ba** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3ba** as a yellow oil (0.0204 g, 0.0775 mmol, 75%).

IR: (neat) 1556, 1454, 1340, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.95-7.91 (m, 1H), 7.76-7.69 (m, 3H), 5.77 (ddt, J = 17.2, 10.0, 7.2 Hz, 1H, 4-H), 5.12-5.02 (m, 2H, 5-H_2), 3.23 (quint, J = 6.4 Hz, 1H, 2-H), 2.64 (ddd, J = 12.8, 6.4, 6.4 Hz, 1H, 3-H^A), 2.51 (ddd, J = 12.8, 6.4, 6.4 Hz, 1H, 3-H^B), 1.96-1.86 (m, 1H, 1"-H^A), 1.79-1.70 (m, 1H, 1"-H^B), 1.43-1.33 (m, 2"-H_2), 0.92 (t, J = 7.6 Hz, 3H, 3"-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 179.3 (s, C-1), 140.1 (s, C-2'), 134.5 (d), 133.8 (d), 133.5 (d, C-4), 131.3 (s, C-1'), 124.0 (d), 122.7 (d), 118.0 (t, C-5), 40.6 (d, C-2), 37.0 (t, C-3), 34.8 (t, C-1"), 20.4 (t, C-2"), 14.1 (q, C-3") MS: (EI, 70 eV) *m*/*z* 263 (M^+, 0.2), 234 (31), 222 (22), 221 (100), 220 (39), 156 (75), 129 (27), 103 (20) HRMS: (CI, 70 eV) calcd for ($C_{14}H_{18}NO_2S$) 264.1058 (M^+ + 1) found *m*/*z* 264.1055

3-(2-methylhex-5-en-3-yl)benzo[*d*]isothiazole 1,1-dioxide (3ca)

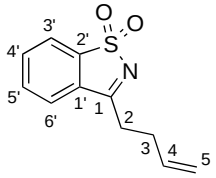


To a solution of erythrosin B (0.0050 g, 0.0057 mmol) and bromoimine **1c** (0.0306 g, 0.101 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0456 g, 0.308 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3ca** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3ca** as a colorless liquid (0.0144 g, 0.0547 mmol, 54%).

IR: (neat) 1552, 1338, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.93-7.91 (m, 1H), 7.77-7.68 (m, 3H), 5.72 (ddt, J = 16.8, 10.0, 7.6 Hz, 1H, 4-H), 5.06 (d, J = 16.8 Hz, 1H, 5-H^A), 4.96 (d, J = 10.0 Hz, 1H,

5-H^B), 3.07-3.02 (m, 1H, 2-H), 2.68 (ddd, *J* = 14.0, 7.6, 7.2 Hz, 1H, 3-H^A), 2.56 (ddd, *J* = 14.0, 7.6, 7.2 Hz, 1H, 3-H^B), 2.25-2.17 (m, 1H, 1"-H), 1.05 (d, J = 7.2 Hz, 2"-H_3), 1.03 (d, *J* = 7.2 Hz, 2"-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 179.1 (s, C-1), 139.9 (s, C-2'), 134.7 (d), 133.7 (d), 133.4 (d), 132.0 (s, C-1'), 124.1 (d, C-4), 122.6 (d), 117.7 (t, C-5), 47.1 (d, C-2), 34.2 (t, C-3), 31.6 (t, C-1"), 20.9 (q, C-2"), 19.8 (q, C-2") MS: (EI, 70 eV) *m*/*z* 263 (M^+, 0.3), 248 (36), 222 (24), 221 (100), 220 (63), 157 (21), 156 (80), 129 (26) HRMS: (CI, 70 eV) calcd for ($C_{14}H_{18}NO_2S$) 264.1058 (M^+ + 1) found *m*/*z* 264.1060

3-(but-3-en-1-yl)benzo[*d*]isothiazole 1,1-dioxide (3da)



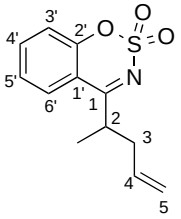
To a solution of erythrosin B (0.0040 g, 0.0045 mmol) and bromoimine **1d** (0.0260 g, 0.100 mmol) in MeOH (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0473 g, 0.320 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3da** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3da** as a white solid (0.0064 g, 0.029 mmol, 29%).

To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0054 g, 0.0063 mmol) and bromoimine **1d** (0.0280 g, 0.108 mmol) in MeOH (1.0 mL) were added Allyltrimethylsilane (**2c**) (0.0708 g, 0.620 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3da** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3da** as a white solid (0.0114 g, 0.0515 mmol, 48%).

^{1}H NMR: (400 MHz, $CDCl_3$)7.93-7.91 (m, 1H), 7.78-7.68 (m, 3H), 5.94 (ddt, *J* = 17.4, 10.0, 6.8 Hz, 1H, 4-H), 5.18-5.08 (m, 2H, 5-H_2), 3.08 (t, *J* = 7.2 Hz, 2H, 2-H_2), 2.69-2.65 (m, 2H, 3-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 175.5, 139.8, 135.8, 133.9, 133.6, 131.2, 123.8, 122.5, 116.6, 30.5, 29.1 The

analytical data agreed with the previous report.[4]

4-(pent-4-en-2-yl)benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (5aa)

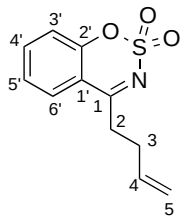


To a solution of erythrosin B (0.0039 g, 0.0044 mmol) and bromoimine **4a** (0.0277 g, 0.0955 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0444 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5aa** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5aa** as a colorless oil (0.0104 g, 0.0413 mmol, 43%).

To a solution of erythrosin B (0.0059 g, 0.0067 mmol) and bromoimine **4a** (0.0272 g, 0.0938 mmol) in MeCN (1.0 mL) were added allyl tributylstannane (**2b**) (0.0993 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was diluted with Et_2O (15 mL) and washed by NH_4F aq (10%, 20 mL). The obtained white precipitate was filtered off, and the filtrate was extracted with EtOAc (3 x 10 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5aa** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5aa** as a colorless oil (0.0190 g, 0.0756 mmol, 81%).

IR: (neat) 1597, 1552, 1390, 1190 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.84 (d, J = 8.0 Hz, 1H, 6'-H), 7.72 (t, J = 8.0 Hz, 1H, 4'-H), 7.40 (t, J = 8.0 Hz, 1H, 5'-H), 7.32 (d, J = 8.0 Hz, 1H, 3'-H), 5.79 (ddt, J = 16.8, 9.6, 7.6 Hz, 1H, 4-H), 5.13-5.06 (m, 2H, 5-H_2), 3.50 (sext, J = 7.2 Hz, 1H, 2-H), 2.68-2.61 (m, 1H, 3-H^A), 2.39-2.32 (m, 1H, 3-H^B), 1.36 (d, J = 7.2 Hz, 3H, 2-Me) ^{13}C NMR: (100 MHz, $CDCl_3$) 183.7 (s, C-1), 153.9 (s, C-2'), 136.8 (d, C-4'), 134.5 (d, C-4), 127.7 (d, C-6'), 125.8 (d, C-5'), 119.5 (d, C-3'), 118.0 (t, C-5), 115.8 (s, C-1'), 38.7 (t, C-3), 38.3 (d, C-2), 18.3 (q, 2-Me) MS: (EI, 70 eV) *m*/*z* 251 (M^+, 57), 236 (M^+ - Me, 100), 186 (61), 172 (54), 91 (26) HRMS: (EI, 70 eV) calcd for ($C_{12}H_{13}NO_3S$) 251.0616 (M^+) found *m*/*z* 251.0619

4-(but-3-en-1-yl)benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (5ba)

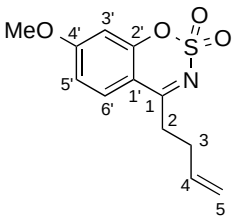


To a solution of erythrosin B (0.0039 g, 0.0044 mmol) and bromoimine **4b** (0.0251 g, 0.0909 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0458 g, 0.310 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5ba** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5ba** as a yellow oil (0.0124 g, 0.0523 mmol, 57%).

To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0043 g, 0.0050 mmol) and bromoimine **4b** (0.0247 g, 0.0895 mmol) in MeOH (1.0 mL) were added allyltrimethylsilane (**2c**) (0.0571 g, 0.500 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5ba** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5ba** as a yellow oil (0.0084 g, 0.0354 mmol, 40%).

IR: (neat) 1599, 1554, 1389, 1188 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.83 (d, J = 8.0 Hz, 1H, 6'-H), 7.72 (t, J = 8.0 Hz, 1H, 4'-H), 7.40 (t, J = 8.0 Hz, 1H, 5'-H), 7.30 (d, J = 8.0 Hz, 1H, 3'-H), 5.91 (ddt, J = 17.6, 10.4, 6.4 Hz, 4-H, 1H), 5.16-5.07 (m, 2H, 5-H_2), 3.15 (t, J = 8.0 Hz, 2H, 2-H_2), 2.59 (q, J = 6.4 Hz, 2H, 3-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 179.3 (s, C-1), 153.5 (s, C-2'), 136.9 (d, C-4'), 135.7 (d, C-4), 127.8 (d, C-6'), 125.9 (d, C-5'), 119.3 (d, C-3'), 116.6 (t, C-5), 116.1 (s, C-1'), 35.0 (t, C-2), 29.4 (t, C-3) MS: (EI, 70 eV) *m*/*z* 237 (M^+, 35), 222 (49), 173 (40), 172 (100), 91 (26) HRMS: (EI, 70 eV) calcd for ($C_{11}H_{11}NO_3S$) 237.0460 (M^+) found *m*/*z* 237.0461

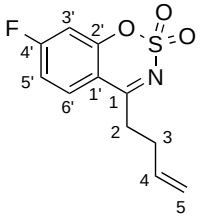
4-(but-3-en-1-yl)-7-methoxybenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (5ca)



To a solution of erythrosin B (0.0042 g, 0.0048 mmol) and bromoimine **4c** (0.0250 g, 0.0817 mmol) in MeOH (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0444 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5ca** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5ca** as a yellow oil (0.0114 g, 0.0426 mmol, 52%)

IR: (neat) 1622, 1589, 1540, 1379, 1192 cm^{-1} H NMR: (400 MHz, $CDCl_3$) 7.72 (d, J = 8.8 Hz, 1H, 6'-H), 6.88 (dd, J = 8.8, 2.0 Hz, 1H, 5'-H), 6.74 (d, J = 2.0 Hz, 1H, 3'-H), 5.89 (ddt, J = 17.2, 10.4, 7.6 Hz, 1H), 5.12 (d, J = 17.2 Hz, 1H, 5-H^A), 5.07 (d, J = 10.4 Hz, 1H, 5-H^B), 3.06 (t, J = 7.6 Hz, 2H, 2-H_2), 2.56 (q, J = 7.6 Hz, 2H, 3-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 178.6 (s, C-1), 166.4 (s, C-4'), 156.0 (s, C-2'), 135.9 (d, C-4), 129.5 (d, C-6'), 116.4 (t, C-5'), 113.4 (d, C-5'), 109.6 (s, C-1'), 103.0 (d, C-3'), 56.3 (q, O*Me*), 34.9 (t, C-2), 29.7 (t, C-3) MS: (EI, 70 eV) *m*/*z* 267 (M^+, 100), 266 (36), 252 (52), 203 (33), 202 (98), 188 (63) HRMS: (EI, 70 eV) calcd for ($C_{12}H_{13}NO_4S$) 267.0565 (M^+) found *m*/*z* 267.0561.

4-(but-3-en-1-yl)-7-fluorobenzo[*e*][1,2,3]oxathiazine 2,2-dioxide (5da)



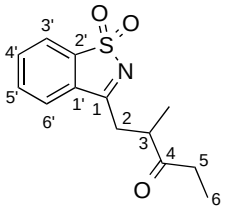
To a solution of erythrosin B (0.0044 g, 0.0050 mmol) and bromoimine **4d** (0.0246 g, 0.0836 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0444 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then

the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5da** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5da** as a yellow oil (0.0080 g, 0.0313 mmol, 37%)

To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0043 g, 0.0050 mmol) and bromoimine **4d** (0.0262 g, 0.0891 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate (**2a**) (0.0481 g, 0.325 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5da** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5da** as a yellow viscous oil (0.0100 g, 0.0391 mmol, 44%).

IR: (neat) 1610, 1560, 1390, 1198, 1117 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.86 (dd, J = 8.4 Hz, $^4J_{HF}$ = 6.0 Hz, 1H, 6'-H), 7.14-7.09 (m, 5'-H), 7.03 (dd, $^3J_{HF}$ = 8.0 Hz, J = 2.4 Hz, 1H, 3'-H), 5.89 (ddt, J = 17.2, 10.8, 6.4 Hz, 1H, 4-H), 5.16-5.07 (m, 2H, 5-H_2), 3.11 (t, J = 7.6 Hz, 2H, 2-H_2), 2.59 (q, J = 7.6 Hz, 2H, 3-H_2) ^{13}C NMR: (100 MHz, $CDCl_3$) 178.4 (s, C-1), 166.9 (s, d, $^1J_{CF}$ = 264 Hz, C-4'), 155.4 (s, d, $^3J_{CF}$ = 13.0 Hz, C-2'), 135.5 (d, C-4), 130.3 (d, d, $^3J_{CF}$ = 11.6 Hz, C-6'), 116.7 (t, C-5), 114.0 (d, d, $^2J_{CF}$ = 22.2 Hz, C-5'), 113.0 (s, C-1'), 107.2 (d, d, $^2J_{CF}$ = 25.5 Hz, C-3'), 35.2 (t, C-2), 29.4 (d, C-3) MS: (EI, 70 eV) *m*/*z* 255 (M^+, 35), 240 (47), 191 (36), 190 (100) HRMS: (EI, 70 eV) calcd for ($C_{11}H_{10}FNO_3S$) 255.0365 (M^+) found *m*/*z* 255.0364

1-(1,1-dioxidobenzo[*d*]isothiazol-3-yl)-2-methylpentan-3-one (3dd)

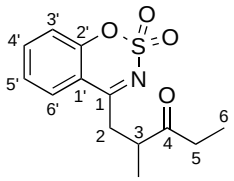


To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0019 g, 0.0022 mmol) and bromoimine **1d** (0.0227 g, 0.0873 mmol) in MeCN (1.0 mL) were added 3-trimetylsilyloxy-2-pentene (**2d**) (0.0886 g, 0.560 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After

concentration in *vacuo*, the crude product **3dd** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3dd** as a yellow viscous oil (0.0150 g, 0.0565 mmol, 65%).

IR: (neat) 1712, 1558, 1456, 1336, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.91-7.88 (m, 1H), 7.77-7.73 (m, 3H), 3.54-3.40 (m, 2H, 2-H^A and 3-H), 2.84 (dd, J = 17.6, 4.4 Hz, 1H, 2-H^B), 2.74-2.56 (m, 2H, 5-H_2), 1.30 (d, J = 6.8 Hz, 3H, 3-Me), 1.08 (t, J = 6.8 Hz, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 213.2 (s, C-4), 175.2 (s, C-1), 139.5 (s, C-2'), 133.9 (d), 133.6 (d), 131.1 (s, C-1'), 124.0 (d), 122.4 (d), 42.1 (d, C-3), 34.5 (t, C-5), 33.4 (t, C-2), 17.4 (q, 3-Me), 7.74 (q, C-6) MS: (EI, 70 eV) *m*/*z* 265 (M^+, 46), 156 (45), 155 (29), 142 (27), 141 (100), 129 (24), 128 (39), 115 (55) HRMS: (EI, 70 eV) calcd for ($C_{13}H_{15}NO_3S$) 265.0773 (M^+) found *m*/*z* 265.0773

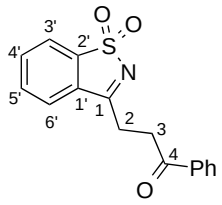
1-(2,2-dioxidobenzo[*e*][1,2,3]oxathiazin-4-yl)-2-methylpentan-3-one (5bd)



To a solution of erythrosin B (0.0049 g, 0.0056 mmol) and bromoimine **4b** (0.0262 g, 0.0949 mmol) in MeCN (1.0 mL) were added 3-trimetylsilyloxy-2-pentene (**2d**) (0.0900 g, 0.568 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5bd** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5bd** as a colorless viscous liquid (0.0174 g, 0.0618 mmol, 65%)

IR: (neat) 1712, 1608, 1556, 1392, 1190 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.88 (d, J = 7.6 Hz, 1H, 6'-H), 7.71 (t, J = 8.0 Hz, 1H, 4'-H), 7.39 (t, J = 8.0 Hz, 1H, 5'-H), 7.28 (d, J = 8.0 Hz, 1H, 3'-H), 3.64 (dd, J = 18.0, 9.2 Hz, 1H, 2-H^A), 3.46-3.37 (m, 1H, 3-H), 2.94 (dd, J = 18.0, 4.4 Hz, 1H, 2-H^B), 2.65 (m, 2H, 5-H_2), 1.26 (d, J = 7.2 Hz, 3H, 3-Me), 1.10 (t, J = 7.2 Hz, 3H, 6-H_3) ^{13}C NMR: (100 MHz, $CDCl_3$) 213.4 (s, C-4), 178.5 (s, C-1), 153.6 (s, C-2'), 137.0 (d, C-4'), 127.9 (d, C-6'), 125.9 (d, C-5'), 119.1 (d, C-3'), 116.2 (s, C-1'), 41.4 (d, C-3), 37.9 (d, C-2), 34.7 (t, C-5), 17.2 (q, 3-Me), 7.79 (q, C-6) MS: (EI, 70 eV) *m*/*z* 281 (M^+, 0.2), 252 (62), 161 (28), 57 (100) HRMS: (EI, 70 eV) calcd for ($C_{13}H_{15}NO_4S$) 281.0722 (M^+) found *m*/*z* 281.0718

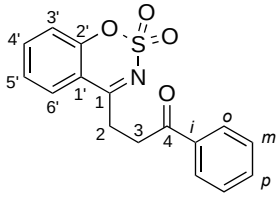
3-(1,1-dioxidobenzo[*d*]isothiazol-3-yl)-1-phenylpropan-1-one (3de)



To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0026 g, 0.0030 mmol) and bromoimine **1d** (0.0280 g, 0.108 mmol) in MeCN (1.0 mL) were added 1-phenyl-1-trimethylsilyloxyethylene (**2e**) (0.1230 g, 0.324 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3de** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3de** as a yellow solid (0.0164 g, 0.0548 mmol, 51%).

mp: 168-170 °C IR: (KBr) 1689, 1558, 1389, 1325, 1238, 1171 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.03 (d, J = 7.6 Hz, 2H), 7.93-7.91 (m, 1H), 7.85-7.82 (m, 1H), 7.79-7.75 (m, 2H), 7.61 (t, J = 7.6 Hz, 2H), 7.50 (t, J = 7.6 Hz, 2H), 3.69 (t, J = 6.4 Hz, 2H), 3.45 (t, J = 6.4 Hz, 2H) ^{13}C NMR: (100 MHz, $CDCl_3$) 197.3 (s, C-4), 175.7 (s, C-1), 139.7 (s), 136.1 (s), 134.0 (d), 133.7 (d), 133.6 (d), 131.2 (s), 128.7 (d), 128.1 (d), 124.0 (d), 122.4 (d), 33.8 (t), 25.1 (t) MS: (EI, 70 eV) *m*/*z* 299 (M^+, 0.04), 105 (100), 77 (39) HRMS: (CI, 70 eV) calcd for ($C_{16}H_{13}NO_3S$) 300.0694 (M^+ + 1) found *m*/*z* 300.0694

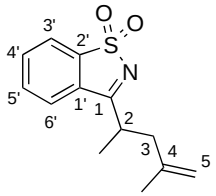
3-(2,2-dioxidobenzo[*e*][1,2,3]oxathiazin-4-yl)-1-phenylpropan-1-one (5be)



To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0150 g, 0.0174 mmol) and bromoimine **4b** (0.0298 g, 0.108 mmol) in MeCN (5.0 mL) were added 1-phenyl-1-trimethylsilyloxyethylene (**2e**) (0.1230 g, 0.324 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (20 mL) and the aqueous layer was extracted with EtOAc (30 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **5be** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **5be** as as a colorless viscous liquid (0.0398 g, 0.126 mmol, 30%).

mp: 119-120 °C IR: (KBr) 1681, 1599, 1552, 1404, 1205, 1163 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 8.01 (d, *J* = 8.0 Hz, 2H, *o*), 7.97 (dd, *J* = 8.0, 1.6 Hz, 1H, 6'-H), 7.71 (td, *J* = 8.0, 1.6 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 8.4 Hz, 2H), 7.41 (t, *J* = 8.4 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 3.61-3.58 (m, 2H), 3.55-3.51 (m, 2H) ^{13}C NMR: (100 MHz, $CDCl_3$) 197.4 (s, C-4), 179.0 (s, C-1), 153.3 (s, C-2'), 137.0 (s), 136.2 (s), 133.5 (d), 128.7 (d), 128.1 (d), 127.9 (d), 125.9 (d), 119.0 (d), 116.2 (s, C-1'), 33.3 (t), 29.4 (t) MS: (EI, 70 eV) *m*/*z* 315 (M^+, 4), 105 (100), 77 (26) HRMS: (EI, 70 eV) calcd for ($C_{16}H_{13}NO_4S$) 315.0565 (M^+) found *m*/*z* 315.0564

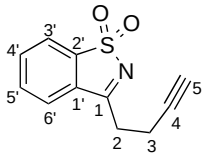
3-(4-methylpent-4-en-2-yl)benzo[*d*]isothiazole 1,1-dioxide (3af)



To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0014 g, 0.0016 mmol) and bromoimine **1a** (0.0333 g, 0.121 mmol) in MeCN (1.0 mL) were added tributyl(2-methylallyl)stannane (**2f)** (0.1035 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was diluted with Et_2O (30 mL) and washed by NH_4F (aq) (10%, 20 mL). The obtained white precipitate was filtered off, and the filtrate was extracted with Et_2O (3 x 10 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3af** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3af** as a colorless oil (0.0214 g, 0.0858 mmol, 71%).

IR: (neat) 1554, 1452, 1338, 1174 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.95-7.91 (m, 1H), 7.77-7.70 (m, 3H), 4.85 (s, 1H, 5-H^A), 4.78 (s, 1H, 5-H^B), 3.41 (sext, *J* = 7.0 Hz, 1H, 2-H), 2.66 (dd, *J* = 14.0, 7.0 Hz, 1H, 3-H^A), 2.35 (dd, *J* = 14.0, 7.0 Hz, 1H, 3-H^B), 1.79 (s, 3H, 4-Me), 1.39 (d, *J* = 7.0 Hz, 3H, 2-Me) ^{13}C NMR: (100 MHz, $CDCl_3$) 179.8 (s, C-1), 141.6 (s), 140.2 (s), 133.8 (d), 133.5 (d), 130.7 (s), 123.8 (d), 122.7 (d), 113.6 (t, C-5), 42.2 (t, C-3), 33.7 (d, C-2), 22.4 (q, 4-Me), 17.6 (q, 2-Me) MS: (EI, 70 eV) *m*/*z* 249 (M^+, 0.05), 149 (35), 144 (21), 126 (27), 92 (100), 83 (36), 55 (63) HRMS: (EI, 70 eV) calcd for ($C_{13}H_{15}NO_2S$) 249.0823 (M^+) found *m*/*z* 249.0822

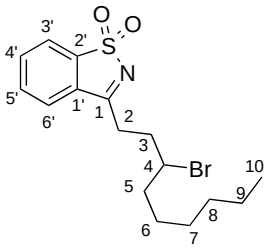
3-(but-3-yn-1-yl)benzo[*d*]isothiazole 1,1-dioxide (3dg)



To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0015 g, 0.0017 mmol) and bromoimine **1d** (0.0270 g, 0.104 mmol) in MeCN (1.0 mL) were added allenyltributylstannane (**2g**) (0.1067 g, 0.324 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was diluted with Et_2O (15 mL) and washed by NH_4F aq (10%, 20 mL). The obtained white precipitate was filtered off, and the filtrate was extracted with EtOAc (3 x 10 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **3dg** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **3dg** as a white solid (0.0088 g, 0.0401 mmol, 39%).

mp: 139-140 °C IR: (neat) 3292, 1562, 1330, 1167 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.95-7.91 (m, 1H), 7.80-7.77 (m, 3H), 3.24 (t, J = 7.2 Hz, 2H, 2-H_2), 2.82 (td, J = 7.2, 2.8 Hz, 2H, 3-H_2), 2.05 (t, J = 2.8 Hz, 1H, 5-H) ^{13}C NMR: (100 MHz, $CDCl_3$) 174.1 (s, C-1), 139.7 (s, C-2'), 134.0 (d), 133.8 (d), 130.9 (s, C-1'), 123.8 (d), 122.6 (d), 81.7 (s, C-4), 70.0 (d, C-4), 30.3 (d, C-2), 14.5 (d, C-3) MS: (EI, 70 eV) *m*/*z* 219 (M^+, 2), 155 (100), 154 (64), 128 (94), 127 (33), 103 (27), 76 (29), 50 (23) HRMS: (CI, 70 eV) calcd for ($C_{11}H_{10}NO_2S$) 220.0432 (M^+ + 1) found *m*/*z* 220.0431

3-(3-bromononyl)benzo[*d*]isothiazole 1,1-dioxide (6)



To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0017 g, 0.0019 mmol) and bromoimine **1d** (0.0496 g, 0.191 mmol) in MeCN (2.0 mL) were added 1-octene (**2h**) (0.160 g, 1.43 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **6** was obtained. The residual oil was purified by silica gel column chromatography (hexane/ethyl acetate = 75:25) to give **6** as a colorless oil (0.0374 g, 0.0968 mmol, 51%).

IR: (neat) 2929, 2858, 1608, 1560, 1454, 1338, 1176 cm^{-1} ^1H NMR: (400 MHz, $CDCl_3$) 7.93-7.91 (m, 1H), 7.77-7.76 (m, 3H), 4.24-4.18 (m, 1H, 4-H), 3.32 (ddd, J = 18.0, 8.8, 4.8 Hz, 1H, 2-H^A), 3.20 (ddd, J = 18.0, 8.8, 6.8 Hz, 1H, 2-H^B), 2.55-2.46 (m, 1H, 3-H^A), 2.34-2.24 (m, 1H, 3-H^B), 2.00-1.84 (m, 2H, 5-H_2), 1.62-1.24 (m, 8H, 6-H_2, 7-H_2, 8-H_2 and 9-H_2) 0.90 (t, J = 7.2 Hz, 3H, 10-H_3) ^{13}C NMR: (100

MHz, $CDCl_3$) 175.5 (s, C-1), 139.5 (s, C-2'), 134.0 (d), 133.7 (d), 131.1 (s, C-1'), 123.9 (d), 122.4 (d), 57.2 (d, C-4), 39.4 (t, C-5), 33.9 (t, C-3), 31.6 (t), 29.4 (t), 28.6 (t), 27.5 (t), 22.5 (t), 14.0 (q, C-10) MS: (EI, 70 eV) *m*/*z* 371 (M^+, 0.02), 226 (65), 222 (22), 206 (67), 198 (95), 194 (100), 181 (42), 156 (73), 143 (59), 115 (45), 103 (34) HRMS: (CI, 70 eV) calcd for ($C_{16}H_{23}BrNO_2S$) 372.0633 (M^+ + 1) found *m*/*z* 372.0634

The Redox Potential of photoexcited state of Erythrosine B

The redox potentials of triplet state erythrosine B* ($E^*_{ox}(EB^{\bullet+}/EB^*)$ and $E^*_{red}(EB^*/EB^{\bullet-})$) were estimated based on triplet energy($\mathbf{T_1}$)[18] and the redox potential of the ground state of erythrosine B ($E_{ox}(EB^{\bullet+}/EB)$ and $E_{red}(EB/EB^{\bullet-})$)[19] by the following equation.[20]

$E^*_{red}(EB^*/EB^{\bullet-}) = E_{red}(EB/EB^{\bullet-}) + \mathbf{T_1}$

= -1.18+1.88 = 0.70 V

$E^*_{ox}(EB^{\bullet+}/EB^*) = E_{ox}(EB^{\bullet+}/EB) - \mathbf{T_1}$

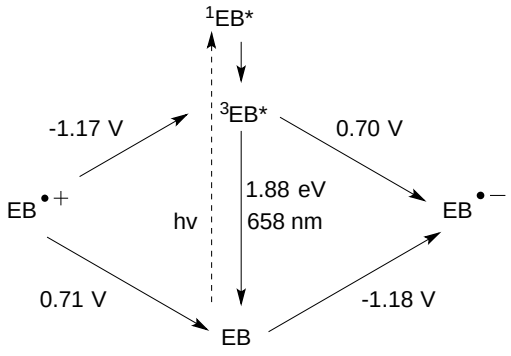
= 0.71-1.88 = -1.17 V

$\mathbf{T_1}$, $E_{red}(EB/EB^{\bullet-})$ and $E_{ox}(EB^{\bullet+}/EB)$ shown in below were applied to this equation.

$\mathbf{T_1}$: 1.88 eV[18] (658 nm)

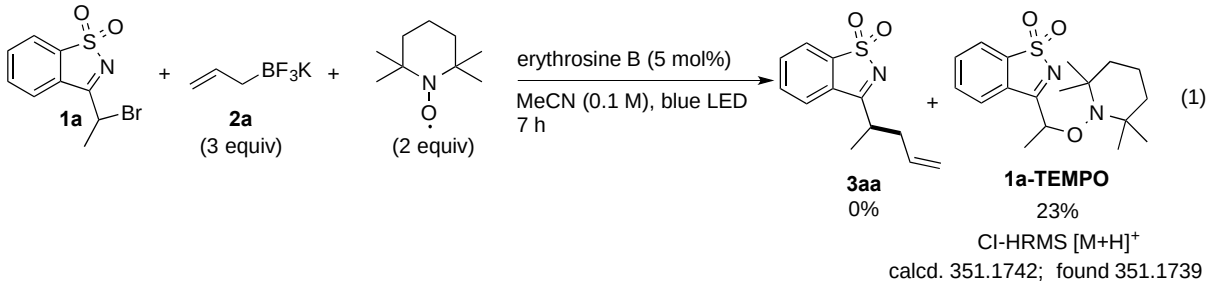
$E_{red}(EB/EB^{\bullet-})$ = -1.14 V vs Ag/AgCl[19] (-1.18 V vs SCE)[20]

$E_{ox}(EB^{\bullet+}/EB)$ = 0.75 V vs Ag/AgCl[19] (0.71 V vs SCE)[20]



Scheme 6. Redox potetial of erythrosine B.

Radical Trapping Experiments with TEMPO (Eq. [1])



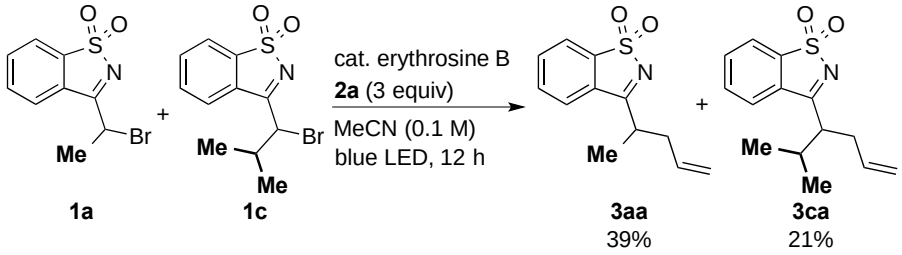
To a solution of erythrosin B (0.0044 g, 0.0050 mmol) and bromoimine **1a** (0.0274 g, 0.100 mmol) and TEMPO (0.0313 g, 0.200 mmol) in MeCN (1.0 mL) were added potassium allyltrifluoroborate **2a** (0.0444 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 7 h. After concentration in *vacuo*, the crude mixture was purified directly by silica gel column chromatography (hexane/ethyl acetate = 65:35) to give **1a-TEMPO** as brown solid (0.0081 g, 0.0231 mmol, 23%). **1a-TEMPO** was characterized by ^{1}H NMR and HRMS.

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

8.09-8.07 (m, 1H), 7.94-7.91 (m, 1H), 7.76-7.71 (m, 2H), 5.13 (q, J = 7.2 Hz, 1H, 2-H), 1.68 (d, J = 7.2 Hz, 3H, 3-H_3), 1.51-1.15 (m, 12H), 0.96 (br, 3H), 0.82 (br, 3H)

HRMS: (CI, 70 eV) calcd for ($C_{18}H_{27}N_2O_3S$) 351.1742 (M^+ + 1) found *m*/*z* 351.1739

The reaction of the mixture of α-bromo *N*-sulfonylimines 1a and 1c with allyl trifluoroborates 2a (Eq. [2])



To a solution of erythrosin B (0.0044 g, 0.0050 mmol) and bromoimine **1a** (0.0274 g, 1.00 mmol) and **1c** (0.0308 g, 0.100 mmol) in MeCN (1.0 mL) were added allyl trifluoroborates **2a** (0.0447 g, 0.300 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 4 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After concentration in *vacuo*, Yields and recoveries were determined by ^{1}H NMR with bromoform as an internal standard.

Stern-Volmer Fluorescence Quenching Studies[21]

Fluorescence quenching studies were performed using a JACSO FP-6600 spectrofluorometer. In each experiment, the photocatalyst and various concentrations of the quencher were combined in MeCN in screw-top 1.0 cm quartz cuvettes. The emission quenching of the erythrosine B monosodium salt was achieved using a photocatalyst concentration of 5.0 x 10^{-5} M under excitation at 548 nm. (The erythrosine B monosodium salt showed a stronger linear correlation compared to the erythrosine B disodium salt.) The emission intensity was observed at 566 nm. Plots were constructed according to the Stern–Volmer equation $I_0/I = 1 + k_q\tau_0[Q]$.[21,22]

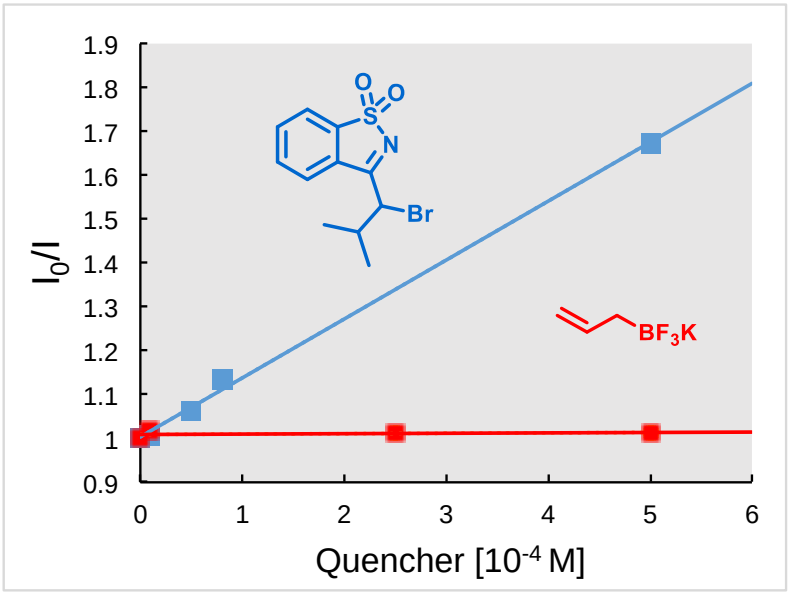
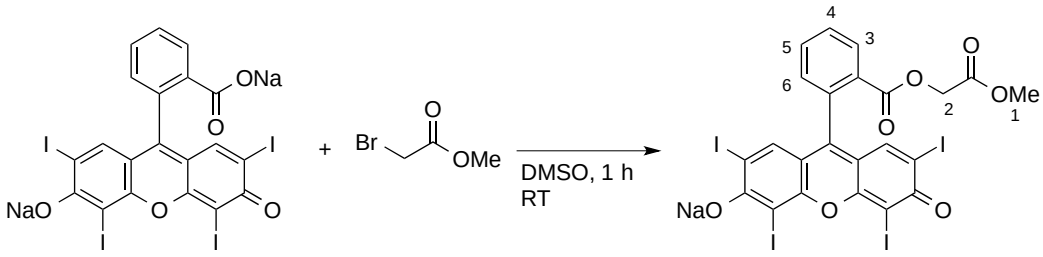


Figure 1. Stern–Volmer plots for the quenching of the erythrosine B monosodium salt emission at RT.

Synthesis of Erythrosine B Monosodium Salt from Erythrosine B Disodium Salt



To a solution of erythrosine B (0.079 mmol, 0.069 g) in DMSO (1 mL) was added bromo methylacetate (0.16 mmol, 0.024 g) at room temperature. The mixture was stirred for 1 h at room temperature, and then was concentrated under reduced pressure. The residue was diluted with acetone (5 mL) and the generated solid was filtered off. The filtrate are concentrated under reduced pressure to give erythrosine B monosodium salts as a red solid (0.049 g, 67%). IR: (KBr) 1731 (CO) cm^{-1} ^1H NMR: (400 MHz, DMSO-d_6) 8.23 (d, J = 7.5 Hz, 1H, 3-H), 7.89 (t, J = 7.5 Hz, 1H), 7.80 (t, J = 7.5,

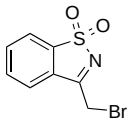
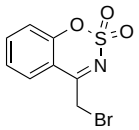
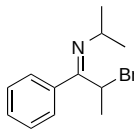
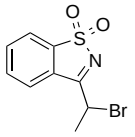
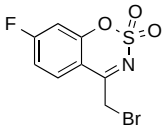
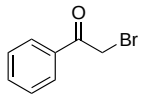
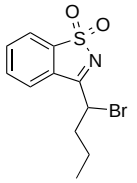
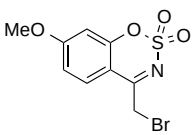
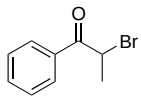
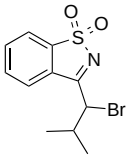
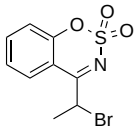
1H), 7.50 (d, J = 7.5, 1H, 6-H), 7.14 (s, 2H, 7-H x 2), 4.71 (s, 2H, 2-H_2), 3.51 (s, 3H, 1-H_3) ^{13}C NMR: (100 MHz, DMSO-d_6) 171.3 (s), 167.6 (s), 164.2 (s), 157.1 (s), 148.2 (s), 136.4 (d), 134.1 (s), 133.5 (d), 130.8 (d), 130.9 (d), 130.1 (d), 128.6 (s), 111.5 (s), 96.1 (s), 75.8 (s), 61.5 (t, 2-C), 52.0 (q, 1-C) FAB MS: Calculated ($C_{23}H_{11}I_4O_7$) 906.6683 Found: 906.6697 (M^+) ^{1}H and ^{13}C NMR charts are listed below.

Cyclic Voltammetry Measurements[23]

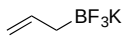
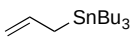
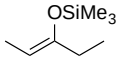
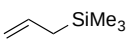
Cyclic voltammetry was performed using a ALS-600 (BAS Inc.) system, a glassy carbon working electrode, a platinum wire counter electrode, and a Ag/$AgNO_3$ reference electrode. Cyclic voltammograms in a MeCN solution of bromoimine or bromoketone (1 mM) containing 0.1M of Bu_4NClO_4 as an electrolyte were measured starting from 0 V towards negative potential at scan rate of 100 mV/s, and Cyclic voltammograms in a MeCN solution of radical acceptor (1 mM) containing 0.1M of Bu_4NClO_4 as an electrolyte were measured starting from 0 V towards positive potential at scan rate of 100 mV/s. All the potentials were corrected against SCE ($E_{SCE} = E_{Ag/AgNO3} + 0.33$ V).
The reduction potentials (E_{red}) of haloimines and haloketones, and the oxidation potentials (E_{ox}) of radical acceptors were shown below.

Scheme 7. The reduction potentials (E_{red}) of haloimines and haloketones.

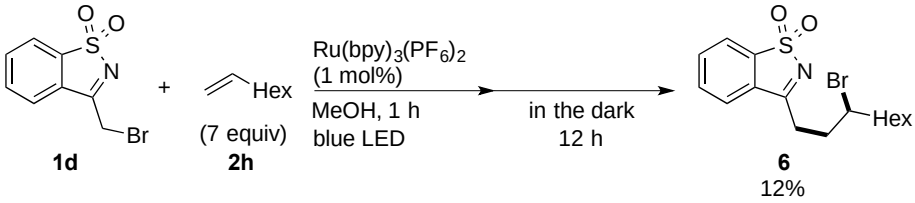
$E_{SCE} = E_{Ag} + 0.33$ V

substrate	*Ered*	substrate	*Ered*	substrate	*Ered*
	–0.58 V		–0.46 V		–1.34 V
	–0.60 V		–0.48 V		–1.15 V
	–0.61 V		–0.56 V		–1.20 V
	–0.64 V		–0.46 V		

Scheme 8. The oxidation potentials (E_{ox}) of radical acceptors.

substrate	*Eox*	substrate	*Eox*
	1.22 V		1.60 V
	1.08 V		1.34 V
	1.73 V		2.26 V

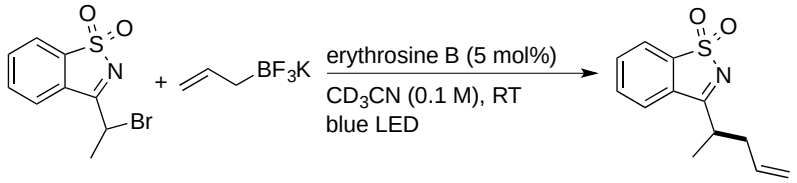
Mechanistic Study for ATRA Reaction



1d **2h** **6** 12%

To a solution of $Ru(bpy)_3(PF_6)_2$ (0.0008 g, 0.001 mmol) and bromoimine (0.0262 g, 0.101 mmol) in MeOH (1.0 mL) were added 1-octane (0.0770 g, 0.700 mmol). The mixture was stirred at room temperature under 3 W blue LED (468 nm) light irradiation for 1 h. Then, the reaction mixture was further stirred in the dark for 12 h. The mixture was quenched with water (5 mL) and the aqueous layer was extracted with EtOAc (10 mL x 3), then the combined organic layer was washed with brine (5 mL x 3) and dried over $MgSO_4$. After concentration in *vacuo*, the crude product **6** was obtained, and the yield was determined by ^{1}H NMR (1,1,1,2-tetrachloroethane was used as an internal standard).

Effect of Photo irradiation on the Reaction



To a solution of erythrosin B (0.0052 g, 0.0075 mmol), bromoimine **1a** (0.0439 g, 0.150 mmol), and 1,3,5-trimethylbenzene as an internal standard (0.0149 g, 0.1 mmol) in CD_3CN (1.5 mL) were added potassium allyltrifluoroborate **2a** (0.0666 g, 0.450 mmol). The yield of product **3aa** was determined by ^{1}H NMR. This reaction was performed with or without visible light irradiation. The time profile of the reaction is shown below. These results indicated that continuous irradiation with blue LED was essential for promoting the reaction, and the contribution of the radical chain mechanism to this

reaction was small.

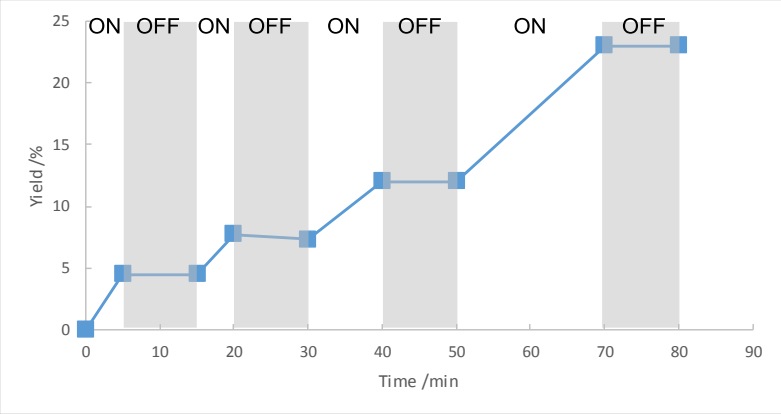
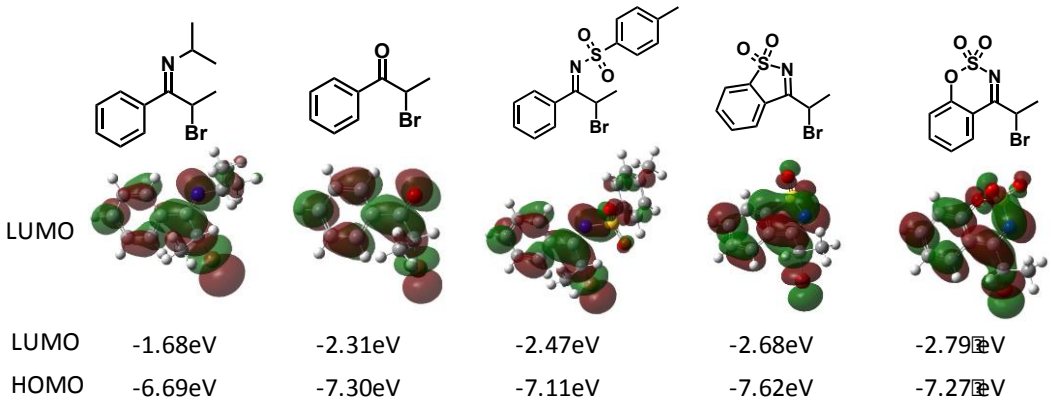


Figure 2. Time profile of the reaction of **1a** with **2a**.

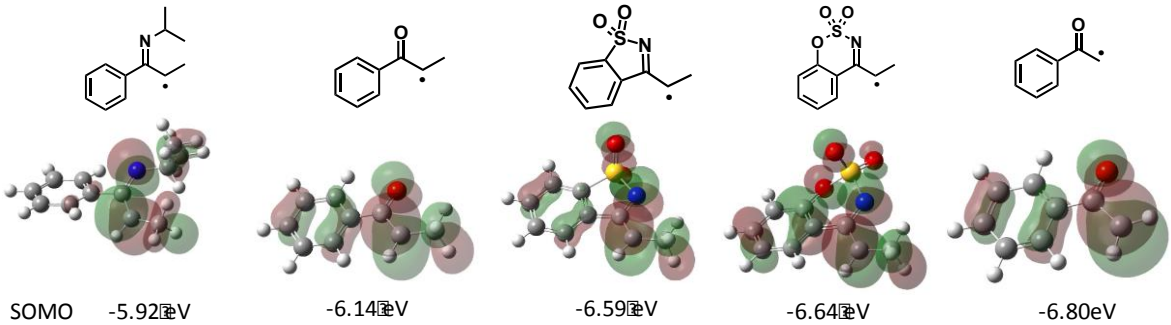
HOMO and LUMO energy of bromoimines and bromoketones.[24]

The described MOs are the lowest unoccupied orbitals at B3LYP/6-31G(d) level.



SOMO energy of bromoimines and bromoketones.[24]

The described MOs are the lowest unoccupied orbitals at UB3LYP/6-31G(d) level.



3-5. References

(1) Selected recent examples, see: (a) H. B. Hepburn, H. W. Lam, *Angew. Chem. Int. Ed.* **2014**, *53*, 11605. (b) G. Yang, W. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7540. (c) Z. Ling, S. Singh, F. Xie, L. Wu, W.

Zhang, *Chem. Commun.* **2017**, *53*, 5364. (d) X.-F. Xiong, H. Zhang, J. Peng, Y.-C. Chen. *Chem. Eur. J.* **2011**, *17*, 2358. (e) A. G. Kravina, J. Mahatthananchai, J. W. Bode, *Angew. Chem. Int. Ed.* **2012**, *51*, 9433. (f) Q. An, J. Li, J. Shen, N. Butt, D. Liu, Y. Liu, W. Zhang, *Chem. Commun.* **2015**, *51*, 885. (g) Y.-Q. Wang, C.-B. Yu, D.-W. Wang, X.-B. Wang, Y.-G. Zhou, *Org. Lett.* **2008**, *10*, 2071. (h) C. M. Young, D. G. Stark, T. H. West, J. J.-E. Taylor, A. D. Smith, *Angew. Chem. Int. Ed.* **2016**, *55*, 14394. (i) Q. An, J. Shen, N. Butt, D. Liu, Y. Liu, W. Zhang, *Org. Lett.* **2014**, *16*, 4496.

(2) K. D. Green, W. Chen, S. G.-Tsodikova, *ChemMedChem* **2012**, *7*, 73.

(3) B. Song, C.-B. Yu, W.-X. Huang, M.-W. Chen, Y.-G. Zhou, *Org. Lett.* **2015**, *17*, 190.

(4) For selected reviews on visible-light photoredox catalysis, see: (a) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102. (b) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322. (c) T. Koike, M. Akita, *Inorg. Chem. Front.* **2014**, *1*, 562. (d) D. P. Hari, B. König, *Chem. Commun.* **2014**, *50*, 6688. (e) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075.

(5) For selected examples, see: (a) M. S. Kharasch, P. S. Skell, P. Fisher, *J. Am. Chem. Soc*. **1948**, *70*, 1055. (b) D. A. Nicewicz, D. W. C. MacMillan, *Science*, **2008**, *322*, 77. (c) M. Yasuda, K. Kiyokawa, K. Osaki, A. Baba, *Organometallics* **2009,** *28,* 132. (d) M. Neumann, S. Füldner, B. König, K. Zeitler, *Angew. Chem. Int. Ed*. **2011**, *50*, 951. (e) J. D. Nguyen, J. W. Tucker, M. D. Konieczńska, C. R. J. Stephenson, *J. Am. Chem. Soc*. **2011**, *133*, 4160. (f) M. Pirtsch, S. Paria, T. Matsuno, H. Isobe, O. Reiser, *Chem. Eur. J.* **2012**, *18*, 7336. (g) Q. Liu, H. Yi, J. Liu, Y. Yang, X. Zhang, Z. Zeng, A. Lei, *Chem. Eur. J.* **2013**, *19*, 5120. (h) I. Suzuki, N. Esumi, M. Yasuda, A. Baba, *Chem. Lett.* **2015**, *44*, 38.

(6) (a) I. Suzuki, N. Esumi, M. Yasuda, *Asian J. Org. Chem.* **2016**, *5*, 179. (b) N. Esumi, K. Suzuki, Y. Nishimoto, M. Yasuda, *Org. Lett.* **2016**, *18*, 5704.

(7) α-Bromo cyclic *N*-sulfonylimines are easily synthesized by the reaction of cyclic *N*-sulfonylimines with pyridinium bromide perbromide. Details of the preparation were shown in Experimental Section.

(8) The reaction via α-iminyl radical cation generated by the radical addition to unsaturated iminium ion has been reported, see: (a) J. J. Murphy, D. Bastida, S. Paria, M. Fagnoni, P. Melchiorre, *Nature* **2016**, 532, 218. (b) A. Bahamonde, J. J. Murphy, M. Savarese, É. Brémond, A. Cavalli, P. Melchiorre, *J. Am. Chem. Soc.* **2017**, *139*, 4559.

(9) The reaction via α-iminyl radical generated by ketoxime has been reported. However, nitrogen atom of the α-iminyl radical is not protected by substituent. Therefore, the introduced imine unit is converted into another functional group, see: (a) L. Ran, Z.-H. Ren, Y.-Y. Wang, Z.-H. Guan, *Green Chem.* **2014**, *16*, 112. (b) J. Ke, Y. Tang, H. Yi, Y. Li, Y. Cheng, C. Liu, A. Lei, *Angew. Chem. Int. Ed.* **2015**, *54*, 6604. (c) H.-B. Yang, N. Selander, *Chem. Eur. J.* **2017**, 23, 1779.

(10) See Experimental Section in the section of cyclic voltammetry measurement.

(11) Redox potential of erythrosine B* was calculated by reference to the reported papers, see Experimental Section; a) X.-F. Zhang, I. Zhang, L. Liu, *Photochem. Photobiol.* **2010**, *86*, 492–498; b)

Y. Nishimura, H. Sakuragi, K. Tokumaru, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2887–2893.

(12) Details of luminescence quenching studies were shown in Experimential Section.

(13) Details of the experimental proca periodic “on/off” light event, and the obtained results did not support a radical chain mechanism.

(14) The ATRA reaction was carried out under irradiation by blue LED for 1 h, and then, the reaction mixture was further stirred in the dark for 12 h. In this case, only 12% yield of the desired product was obtained. This result supported that the contribution of the radical chain mechanism to this reaction was small.

(15) (a) Y.-Q.Wang, C.-B. Yu, D.-W. Wang, X.-B. Wang, Y.-G. Zhou, *Org. Lett.* **2008**, *10*, 2071. (b) B. Song, C.-B. Yu, W.-X. Huang, M.-W. Chen, Y.-G. Zhou, *Org. Lett.* **2015**, *17*, 190.

(16) N. D. Kimpe, R. Verhé, L. D. Buyck, L. Moens, N. Schamp, *Synthesis* **1982**, 43.

(17) **2d**: N. Esumi, K. Suzuki, Y. Nishimoto, M. Yasuda, *Org. Lett.* **2016**, *18*, 5704. **2f**: S. Balduzzi, M. A. Brook, M. J. McGlinchey, *Organometallics* **2005**, *24*, 2617. **2g**: T. Carofiglo, D. Marton, G. Tagliavini, *Organometallics* **1992**, *11*, 2961.

(18) Y. Nishimura, H. Sakuragi, K. Tokumaru, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2887.

(19) X.-F. Zhang, I. Zhang, L. Liu, *Photochem. Photobiol.* **2010**, *86*, 492.

(20) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075.

(21) C. K. Prier, D. W. C. MacMillan, *Chem. Sci.* **2014**, *5*, 4173.

(22) Turro, N. J. *Modern Molecular Photochemistry*, Benjamin/Cummings: Menlo Park, CA, 1978.

(23) T. Wada, H. Maki, T. Imamoto, H. Yuki, Y. Miyazato, *Chem. Commun.* **2013***, 49,* 4394.

(24) Gaussian 03, Revision C.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

Conclusion

This research investigates the development of carbon–carbon bond formation by using α-heteroatom-substituted carbonyl derivatives by a photoredox or Lewis acid catalyst. In particular, I investigated the synthetic methods of 1,5-diketones or 1,4-diketones by utilizing carbonyl methyl anion (enolate) and carbonyl methyl radical (α-carbonyl radical). Through this study, I have developed i) the method of the generation of tin enolate by the combination of tin additive and Lewis acid ii) the synthetic strategy for the synthesis of 1,4-diketones by enolate and haloketones iii) new α-iminyl radical precursors; cyclic α-bromo *N*-sulfonyl imines which act as effective electron-deficient radicals to react with various radical acceptors. The results obtained from the present work are summarized as follows.

Chapter 1

The *anti*-selective direct Michael addition of α-alkoxy ketones to enones by cooperative catalysis of $Sm(OTf)_3$ and Bu_3SnOMe was accomplished. The *anti*-selectivity can be rationalized by the following factors: i) the stereo-controlled generation of tin enolate accelerated by the chelation of α-alkoxy ketones to samarium methoxide, which is generated by the transmetalation between $Sm(OTf)_3$ and Bu_3SnOMe, ii) the eight-membered chelated transition state involving tin enolate and enone. This study created the new strategy for the generation of tin enolates by catalytic amount of tin additive.

Chapter 2

The synthetic method of 1,4-diketones from silyl enol ethers and bromoketones catalyzed by an organic dye under visible-light irradiation was developed. The combination of eosin Y and triethanolamine effectively produced α-carbonyl radicals from α-haloketones. The use of silyl enol ether, which has low nucleophilicity, were important for the halo-selective reaction. Although 1,4-diketones are generally synthesized from aldehyde and unsaturated ketones by Stetter reaction, this reaction provides a new option for the synthesis of 1,4-diketones which are difficult to obtain by the Stetter reaction.

Chapter 3

The generation of α-iminyl radicals from α-bromo cyclic *N*-sulfonylimines and the application to coupling with various radical acceptors using a photoredox catalyst was attained. The key for the radical generation was the incorporation of a sulfonyl group into an imine moiety, which facilitated a single-electron reduction from the photoredox catalyst and stabilized the α-iminyl radical. The radical reacted with allyl boron or with allylation reagents, silyl enol ethers and allenyl stannane to give the corresponding coupling products. Furthermore, atom transfer radical addition (ATRA) to olefin proceeded to provide the ATRA product. Generation of α-iminyl radicals from haloimines has never been reported to date. These α-iminyl radical precursors are expected to be applied for various radical reactions, as well as, polymerization initiators in material chemistry.