Peri-Selective Direct Acylmethylation and Amidation of Naphthalene Derivatives Using Iridium and Rhodium Catalysts

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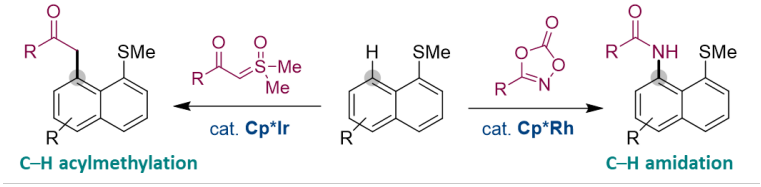
Dedicated to Professor Shinji Murai for his great contribution to the chemistry of catalytic C–H bond activation.



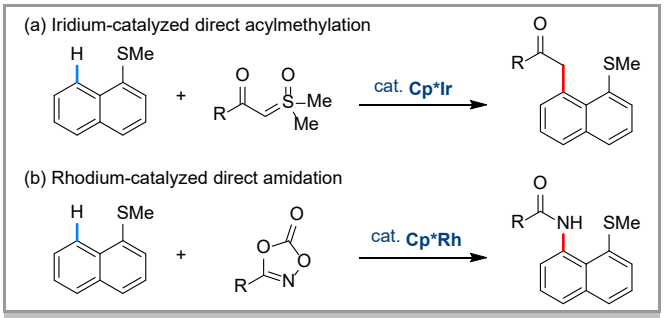
Received:
Accepted:
Published online:
DOI:

Abstract Herein we report an iridium-catalyzed acylmethylation and a rhodium-catalyzed amidation of napthalene derivatives, adopting sulfoxonium ylides and dioxazolones as carbene and nitrene transfer agents, respectively. The use of SMe group as a directing group was key to ensure the *peri*-selective functionalization, and it can be easily removed or diversely transformed to other synthetically useful functionalities after the catalysis.

Key words C-H Activation, Iridium, Rhodium, Alkylation, Amidation

Polycyclic aromatic hydrocarbons as well as heteroarenes have attracted significant attention from the synthetic community during the past decades because of their unique optical and electrochemical properties.[1] In particular, napthalene derivatives have been of key motifs in various binaphthyl-based chiral functional molecules and in numerous bioactive compounds.[2] Owing to their potential applications, strategic synthesis of functionalized naphthalenes has attracted significant attention among the synthetic community. In order to achieve site-selective functionalization of the aromatic core, transition-metal-catalyzed direct C–H bond functionalization has emerged as an effective tool and, particularly, chelation-assisted reactions are among the most powerful methods to introduce functionalities at specific positions.[3]

Insertion reactions of metal-carbenoid species have widely been utilized for the construction of C–C and C–heteroatom bonds.[4] α-Diazo carbonyl compounds, hydrazones, and triazole derivatives have functioned as carbene precursors in this transformation; however, the use of these diazo-based reagents suffers from a potential safety risk of the vigorous release of nitrogen gas under the reaction conditions as well as upon storage. To address this issue, sulfoxonium ylides have been established as alternative carbene sources for the chelation-assisted C–H activation strategy using group 9 metal complexes.[5,6] As demonstrated in pioneering works by Aïssa[5a] and Li[5b] in 2017, the ylide reagents have successfully been applied to the direct acylmethylation under mild reaction conditions, releasing DMSO as the sole byproduct. Meanwhile, transition-metal nitrenoids have also been key active species for direct C–H amination (amidation) reactions.[7] Azides and iminoiodinanes have been used as nitrene precursors in an early stage of this strategy. Because of the intrinsic instability and the handling difficulty of these reagents, new nitrene precursors have become increasingly popular as user-friendly alternatives for the amination over the last several years. In particular, dioxazolone and anthranil derivatives are now recognized as practically valuable nitrene transfer agents in virtue of elegant works by Chang[8] and Li.[9]



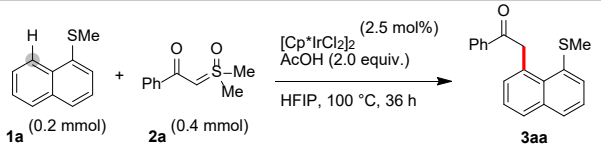
Scheme 1 Schematic representation of the sulfur-directed *peri*-selective C-H functionalization of naphthalenes

Recently, our group have been interested in the use of thioether directing groups for the catalytic C–H activation strategy.[10,11] This reaction system exhibited unique site-selectivity as compared to common carbonyl-based and sp^2-nitrogen directing groups, thereby achieving *peri*-selective direct functionalization[12] over the ortho positions of naphthalene derivatives.[13] Furthermore, C4- and C7-selective C–H functionalization of indoles have also been established based on this concept. Another notable feature of the sulfur directing group is its ease of removal and

transformation into other functionalities after the catalysis. Upon our continuous interest in this research area, we herein report an Ir-catalyzed acylmethylation and a Rh-catalyzed amidation[14] of naphthalenes derivatives (Scheme 1).

At the outset, we conducted an optimization study for the model reaction of 1-(methylthio)naphthalene (**1a**) (0.2 mmol) with 2.0 equiv of a sulfoxonium ylide **2a** (Table 1). Under the standard reaction conditions adopting $[Cp^*IrCl_2]_2$ (2.5 mol%) catalyst and AcOH (2.0 equiv) in HFIP (hexafluoro-2-propanol) solvent, the target *peri*-functionalized napthalene **3aa** was isolated in 85% yield (entry 1). The product was not detected in the absence of the catalyst, and an analogous rhodium complex $[Cp^*RhCl_2]_2$ was not effective (entries 2 and 3). AcOH was found to be essential to the reaction (entry 4), whereas the use of PivOH in place of AcOH resulted in the recovery of **1a** (entry 5). The addition of $AgSbF_6$ (10 mol%) significantly decreased the product yield (entry 6). Slightly lower yield was obtained when the amount of **2a** was reduced to 1.5 equiv (entry 7). Other solvents such as DCE, THF, and TFE (trifluoroethanol) were totally ineffective (entries 8-10). This reaction could be conducted in 1.0 mmol scale to give **3aa** in 84% yield (entry 11).

Table 1 Optimization Study for the Acylmethylation of **1a** with **2a**

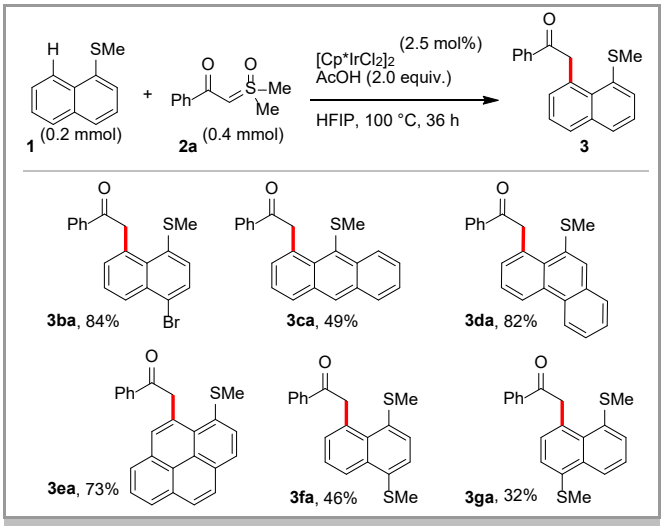


entry	deviation from standard conditions [a]	yield of **3aa** [b]
1	--	85%
2	without $[Cp^*IrCl_2]_2$	n.d.
3	$[Cp^*RhCl_2]_2$ as catalyst	trace
4	without AcOH	n.d.
5	PivOH instead of AcOH	trace
6	with $AgSbF_6$ (10 mol%)	10%
7	1.5 equiv of **2a**	72%
8	DCE as solvent	n.d.
9	THF as solvent	n.d.
10	TFE as solvent	n.d.
11	1.0 mmol scale [c]	84%

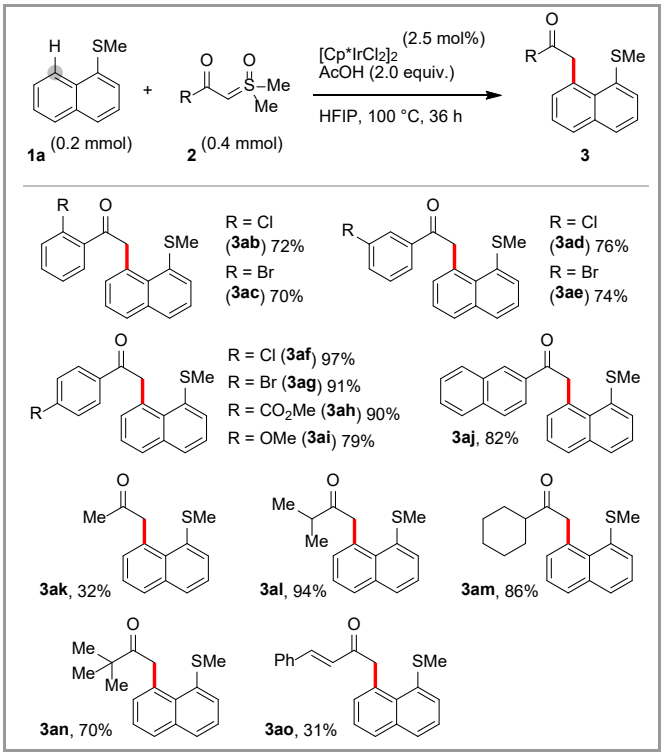
[a] Standard conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $[Cp^*IrCl_2]_2$ (2.5 mol%), AcOH (0.4 mmol), HFIP (1.0 mL), 100 °C, 36 h. [b] Isolated yield. [c] **1a** (1.0 mmol), **2a** (2.0 mmol), $[Cp^*IrCl_2]_2$ (2.5 mol%), AcOH (2.0 mmol), HFIP (5.0 mL), 100 °C, 36 h. HFIP = hexafluoroisopropanol, TFE = trifluoroethanol, DCE = 1,2-dichloroethane, n.d. = not detected.

With the optimized conditions in hand, we examined the direct acylmethylation for a series of aromatic compounds **1** adopting **2a** as a representative carbene precursor (Scheme 2). Bromo substituent of **1b** was tolerated to provide a 1,4,8-trisubstitued naphthalene **3ba** in 84% yield. The present reaction system was also applicable to anthracene (**1c**), phenanthrene (**1d**), and pyrene (**1e**) analogues, giving the corresponding coupling products **3ca** (49%), **3da** (82%), and **3ea** (73%), respectively. The connectivity of **3ea** was unambiguously determined by the X-ray crystallographic analysis. Interestingly, this protocol tends to trigger mono C–H functionalization even in the presence of two SMe directing groups within the substrate. No double C–H activation was observed for the reaction of **1f** and **1g**, producing **3fa** and **3ga** in moderate yields.

Next, we evaluated the scope of sulfoxonium ylides (Scheme 3). Various ylides bearing aromatic (**2b**–**2j**), aliphatic (**2k**–**2n**), and alkenyl (**2o**) groups were synthesized to test the reaction with **1a** under the optimal conditions. Functional groups such as chloro (**2b**, **2d**, **2f**), bromo (**2c**, **2e**, **2g**), ester (**2h**), and alkoxy (**2i**) group were all compatible to deliver the corresponding coupling products in high to excellent yields. The substitution position at the benzene ring did not exert much effect on the reactivity. 2-Napthyl ylide (**2j**) was also highly productive. Although acetyl ylide (**2k**) somewhat decrease the yield, sulfoxonium ylides with secondary alkyl (**2l**, **2m**) and tertiary alkyl (**2n**) groups reacted smoothly. An enone moiety could be installed directly onto the aromatic core adopting the alkenyl ylide **2o**.



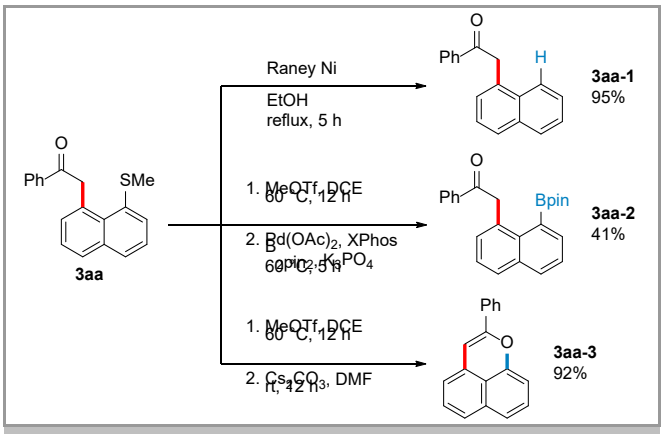
Scheme 2 Scope of Aromatic Compounds



Scheme 3 Scope of Sulfoxonium Ylides

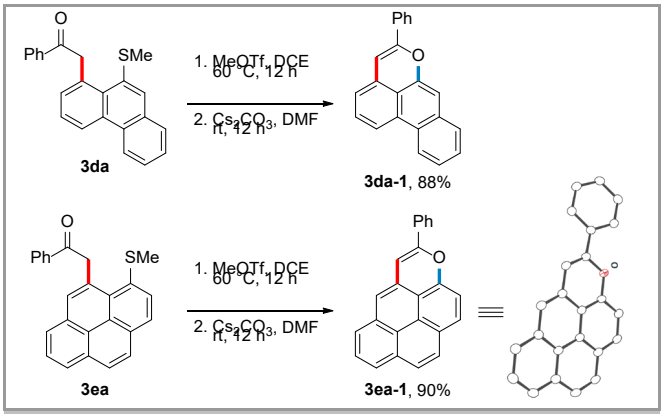
Recently, ease of removal and conversion into other functional groups of the directing group has been utmost important in transition metal catalysis (Scheme 4).[15] It is thus notable that the

SMe directing group of **3aa** was cleanly removed upon treatment with Raney Ni to afford **3aa-1** in 95% yield. Alternatively, a one-pot methylation and Pd-catalyzed borylation[16] was utilized to synthesize the corresponding boronic ester **3aa-2**. During the study, we found that the sulfonium intermediate underwent intramolecular cyclization under basic conditions to form a benzo[*de*]chromene **3aa-3** in 92% yield, unexpectedly.[17]



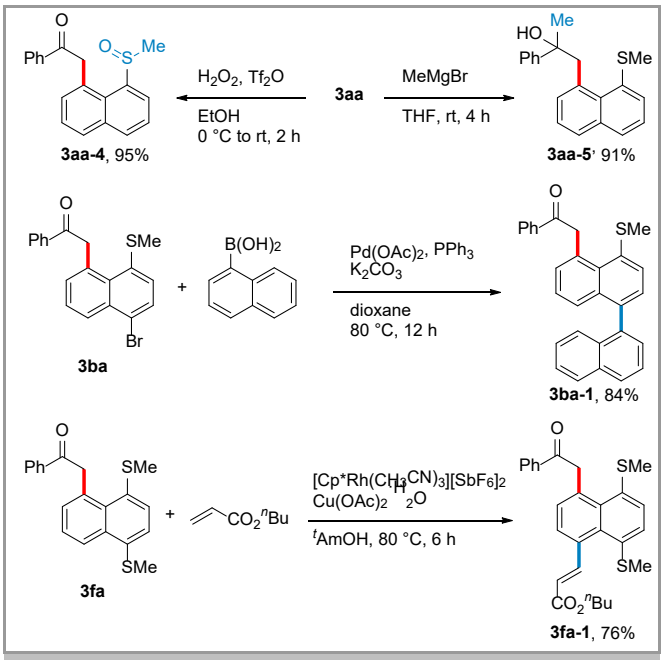
Scheme 4 Removal and Transformation of the Sulfur Directing Group

This base-mediated cyclization was considerably general and successfully converted the phenanthrene (**3da**) and pyrene (**3ea**) variants into the polycyclic chromene derivatives (Scheme 5). The structure of **3ea-1** was confirmed by the X-ray crystallography. These compounds were considerably emissive to exhibit yellow-green fluorescence under UV irradiation with quantum efficiency of 0.22 for **3da-1** and 0.24 for **3ea-1**, respectively (for details, see the Supporting Information).



Scheme 5 Synthesis of Polycyclic Chromene Derivatives

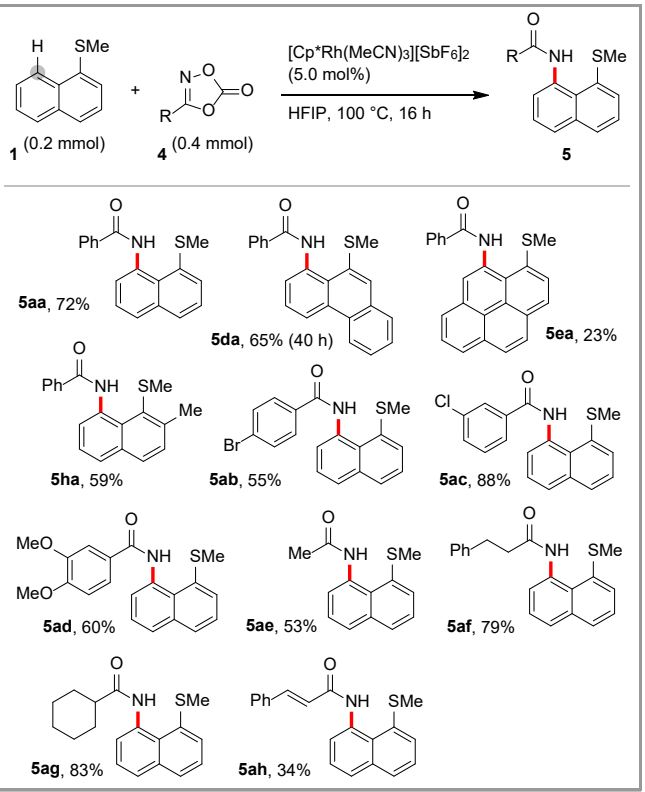
Some additional examples of derivatization are showcased in Scheme 6. The directing group was oxidized to the sulfoxide **3aa-2** in 95% yield by utilizing H_2O_2/Tf_2O system. Addition of a Grignard reagent to the installed carbonyl moiety proceeded smoothly to give the tertiary alcohol **3aa-3** in 91% yield. Such an orthogonal reactivity would be potentially beneficial to the synthesis of unsymmetrically substituted naphthalene derivatives. The palladium-catalyzed coupling of **3ba** with 1-naphthylboronic acid gave a binaphthyl compound **3ba-1**. Since the reaction of **2f** preferentially produced the mono-functionalized product **3fa**, the subsequent C–H alkenylation with butyl acrylate under rhodium catalysis was feasible to afford the doubly functionalized product **3fa-1** in 76% yield.



Scheme 6 Derivatization of the Coupling Products.

To our delight, the sulfur-directed *peri*-selective C–H activation strategy was also applicable to a C–N bond forming reaction through nitrene insertion. According to the seminal work by Chang et al., dioxazolone derivatives **4** were adopted as the nitrene source herein (Scheme 7). Under the optimized reaction conditions using **4a** (2.0 equiv) and $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (5.0 mol%) catalyst in HFIP solvent, **1a** was converted to the target compound **5aa** in 72% isolated yield. In a similar manner, phenanthrene (**1d**), pyrene (**1e**), and 2-methylnaphthalene (**1h**) analogues afforded the corresponding products. We then examined a series of amidating reagents. 3-Aryldioxazolones with bromo (**4b**), chloro (**4c**), and methoxy (**4d**) groups as well as aliphatic dioxazolones (**4e**–**4g**) were successfully utilized to the catalysis, giving **5ab**–**5ag** in moderate to high yields. In addition, a cinnamyl amide **5ah** was obtained in 34% yield as a single isomer.

In summary, we have developed *peri*-selective Ir-catalyzed C–H carbene insertion and Rh-catalyzed C–H nitrene insertion reactions with the aid of thioether directing group. The use of α-carbonyl sulfoxonium ylides and oxazolones was a key factor in achieving the direct functionalization of napthalene derivatives as well as related higher aromatic hydrocarbons. An interesting feature is that the sulfur directing group can be easily removed or transformed after the catalysis. Additionally, the carbene insertion reaction was utilized to the construction of densely fused chromene derivatives via the base-mediated cyclization.



Scheme 7 Scope of Direct Amidation

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General: All manipulations were performed under N_2 using standard Schlenk techniques unless otherwise noted. *N,N*-dimethylformamide (DMF) and 1,4-dioxane were dried and deoxygenated by a Glass Counter Solvent Dispending System (Nikko Hansen & Co., Ltd.). Dichloroethane (DCE) and *tert*-AmOH were distilled from CaH_2. Tetrahydrofuran (THF) and ethanol were purchased as dehydrated solvent and used as received. Aryl sulfides **1** were prepared according to the literature procedures.[10a,10c] Sulfoxonium ylides were prepared according to the literature procedure.[5,18] Amidating reagents **4** were prepared according to the literature procedure.[8,19]

Measurements: Nuclear magnetic resonance spectra were recorded on Bruker AVANCE III 400 spectrometer operating at 400 MHz (^{1}H NMR) and at 100 MHz (^{13}C NMR) in 5 mm NMR tubes. ^{1}H NMR chemical shifts were reported in ppm relative to the resonance of TMS (δ 0.00) or the residual solvent signals at δ 7.26 for $CDCl_3$. ^{13}C NMR chemical shifts were reported in ppm relative to the residual solvent signals at δ 77.2 for $CDCl_3$. High resolution mass spectra (HRMS) were recorded by APCI-TOF. Preparative gel permeation chromatography (GPC) was conducted with Showa Denko H-2001/H-2002 column. Absorption and fluorescence spectra were recorded on JASCO V-750 and JASCO FP-8500 spectrometers. Quantum efficiency was determined using an integration sphere system. Single crystals of **3ea** (CCDC 2027648) and **3ea-1** (CCDC 2027649) suitable for the analysis were obtained by slow evaporation from $CHCl_3$ solutions. The structures were refined by full-matrix least-squares method using SHELXL-2016/6.[20] Hydrogen atoms were included in the refinement on calculated positions riding on their carrier atoms. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Iridium-catalyzed direct acylmethylation (Scheme 2 and 3)

To an oven dried screw-top tube were added aryl sulfide **1** (0.2 mmol, 1.0 equiv), sulfoxonium ylide **2** (0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (2.5 mol%), AcOH (0.4 mmol, 2.0 equiv), and HFIP (1.0 mL). The mixture was heated for 36 h at 100 °C under N_2 with an oil bath. After cooling to room temperature, the resulting mixture was filtered through a pad of silica gel eluting with chloroform. Volatiles were removed under reduced pressure, and the crude material was purified by silica gel column.

2-(8-(Methylthio)naphthalen-1-yl)-1-phenylethan-1-one (3aa)

White solid (50 mg, 85%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 127-129 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11-8.13 (m, 2H), 7.81 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.56-7.62 (m, 1H), 7.49-7.54 (m, 3H), 7.43 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.38 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.30 (dd, *J* = 7.0, 1.3 Hz, 1H), 5.23 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.3, 137.4, 135.9, 135.0, 132.7, 132.3, 132.3, 131.9, 129.9, 129.5, 128.6, 128.6, 128.2, 125.5, 125.2, 48.5, 20.9.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{17}OS$: 293.0995; found: 293.0961.

2-(5-Bromo-8-(methylthio)naphthalen-1-yl)-1-phenylethan-1-one (3ba)

Pale yellow solid (63 mg, 84%) (R_f = 0.5, hexane/EtOAc = 4/1); mp 134-136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (dd, *J* = 8.6, 1.3 Hz, 1H), 8.01-8.12 (m, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.59-7.63 (m, 1H), 7.50-7.57 (m, 3H), 7.35 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 5.22 (s, 2H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.9, 137.1, 135.6, 133.6, 133.4, 133.3, 132.8, 132.4, 129.5, 129.2, 128.6, 128.6, 128.1, 126.8, 122.8, 48.2. 20.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}BrOS$: 371.0100; found: 371.0101.

2-(9-(Methylthio)anthracen-1-yl)-1-phenylethan-1-one (3ca)

Green gummy oil (34 mg, 49%) (R_f = 0.4, hexane/EtOAc = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89-8.91 (m, 1H), 8.51 (s, 1H), 8.17-8.19 (m, 2H), 7.98-8.01 (m, 2H), 7.48-7.64 (m, 5H), 7.43 (dd, *J* = 8.2, 6.8 Hz, 1H), 7.37-7.39 (m, 1H), 5.27 (s, 2H), 2.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 137.8, 135.0, 133.7, 133.6, 133.4, 132.6, 132.2, 131.5, 130.8, 130.2, 130.1, 128.8, 128.6, 128.0, 127.2, 127.1, 125.4, 124.5, 49.8, 22.8.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}OS$: 343.1151; found: 343.1155.

2-(10-(Methylthio)phenanthren-1-yl)-1-phenylethan-1-one (3da)

Yellow solid (56 mg, 82%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 150-152 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76-8.78 (m, 1H), 8.64-8.66 (m, 1H), 8.12-8.14 (m, 2H), 7.76-7.78 (m, 1H), 7.73 (s, 1H), 7.57-7.65 (m, 4H), 7.50-7.55 (m, 2H), 7.42 (dd, *J* = 7.1, 1.1 Hz, 1H), 5.26 (s, 2H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.3, 137.3, 133.6, 133.0, 132.7, 132.4, 131.3, 130.8, 129.9, 129.4, 128.6, 128.2, 127.3, 126.9, 126.6, 126.2, 123.1, 123.0, 48.6, 20.4.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}OS$: 343.1151; found: 343.1160.

2-(3-(Methylthio)pyren-4-yl)-1-phenylethan-1-one (3ea)

Pale yellow solid (54 mg, 73%) (R_f = 0.5, hexane/EtOAc = 4/1); mp 181-183 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14-8.17 (m, 3H), 8.03-8.09 (m, 4H), 7.95-8.00 (m, 2H), 7.87 (s, 1H), 7.60-7.64 (m, 1H), 7.52-7.56 (m, 2H), 5.31 (s, 2H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7, 137.5, 133.7, 132.6, 132.5, 131.3, 131.0, 130.8, 130.7, 130.5, 128.6, 128.1, 127.6, 127.1, 126.9, 126.1, 125.6, 125.1, 124.5, 49.3, 21.9.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}OS$: 367.1151; found: 367.1155.

2-(5,8-Bis(methylthio)naphthalen-1-yl)-1-phenylethan-1-one (3fa)

Orange solid (31 mg, 46%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 121-123 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (dd, *J* = 8.6, 1.2 Hz, 1H), 8.10-8.12 (m, 2H), 7.57-7.62 (m, 1H), 7.48-7.53 (m, 4H), 7.32-7.35 (m, 2H), 5.22 (s, 2H), 2.56 (s, 3H), 2.26 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.5, 21.4, 48.6, 123.5, 125.3, 125.7, 128.1, 128.5, 130.5, 132.4, 132.4, 132.6, 132.7, 133.6, 136.3, 137.3, 196.0.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}OS_2$: 339.0872; found: 339.0874.

2-(4,8-Bis(methylthio)naphthalen-1-yl)-1-phenylethan-1-one (3ga)

Yellow solid (22 mg, 32%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 128-130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.10-8.12 (m, 2H), 7.55-7.62 (m, 2H), 7.49-7.53 (m, 2H), 7.44 (dd, *J* = 8.4, 7.4 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 5.18 (s, 2H), 2.57 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 137.4, 136.6, 135.7, 133.7, 132.7, 132.6, 132.0, 130.4, 129.5, 128.6, 128.1, 125.4, 124.4, 123.6, 48.5, 21.0, 16.5.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}OS_2$: 339.0872; found: 339.0874.

1-(2-Chlorophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ab)

Pale yellow solid (47 mg, 72%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 132-134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80-7.83 (m, 2H), 7.74 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.51 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.43-7.49 (m, 2H), 7.34-7.43 (m, 4H), 5.25 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.5, 138.7, 135.8, 134.9, 132.5, 132.0, 131.6, 131.5, 131.1, 130.8, 129.9, 129.6, 129.1, 128.4, 126.7, 125.5, 125.2, 52.2, 20.3.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}ClOS$: 327.0605; found: 327.0611.

1-(2-Bromophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ac)

Yellow solid (52 mg, 70%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 117-119 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.73-7.78 (m, 2H), 7.67 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.51 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.45 (dd, *J* = 8.0, 7.0 Hz, 1H), 7.36-7.43 (m, 3H), 7.29-7.33 (m, 1H), 5.24 (s, 2H), 2.49 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 140.8, 135.8, 135.0, 134.0, 132.4, 132.1, 131.5, 130.9, 129.6, 129.4, 129.0, 128.4, 127.2, 125.5, 125.2, 119.6, 51.7, 20.4.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}BrOS$: 371.0100; found: 371.0078.

1-(3-Chlorophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ad)

Pale yellow solid (50 mg, 76%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 146-148 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 1.8 Hz, 1H), 7.98-8.00 (m, 1H), 7.83 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.76 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.56-7.59 (m, 1H), 7.53 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.37-7.47 (m, 3H), 7.28 (dd, *J* = 7.0, 1.3 Hz, 1H), 5.16 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 139.0, 135.8, 134.8, 134.7, 132.6, 132.4, 132.1, 131.2, 130.2, 129.9, 129.6, 128.7, 128.2, 126.2, 125.5, 125.2, 48.5, 21.0.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}ClOS$: 327.0605; found: 327.0618.

1-(3-Bromophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ae)

Yellow solid (55 mg, 74%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 148-150 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (t, *J* = 1.8 Hz, 1H), 8.02-8.05 (m, 1H), 7.83 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.71-7.73 (m, 1H), 7.52 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.37-7.46 (m, 3H), 7.28 (dd, *J* = 7.0, 1.3 Hz, 1H), 5.16 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 139.2, 135.8, 135.5, 134.7, 132.4, 132.1, 131.2, 131.1, 130.2, 129.7, 128.8, 126.7, 125.5, 125.3, 122.9, 48.5, 21.0.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}BrOS$: 371.0100; found 371.0083.

1-(4-Chlorophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3af)

Yellow solid (64 mg, 97%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 164-166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04-8.07 (m, 2H), 7.83 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.47-7.53 (m, 3H), 7.37-7.46 (m, 2H), 7.28 (dd, *J* = 7.0, 1.2 Hz, 1H), 5.16 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 139.0, 135.8, 135.7, 134.7, 132.3, 132.1, 131.4, 129.9, 129.6, 129.5, 128.8, 128.7, 125.4, 125.2, 48.3, 20.8.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}ClOS$: 327.0605; found: 327.0627.

1-(4-Bromophenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ag)

Yellow solid (68 mg, 91%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 167-169 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96-7.99 (m, 2H), 7.82 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.63-7.67 (m, 2H), 7.51 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.37-7.46 (m, 2H), 7.28 (dd, *J* = 7.0, 1.2 Hz, 1H), 5.15 (s, 2H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0, 136.1, 135.8, 134.7, 132.3, 132.1, 131.8, 131.4, 130.0, 129.7, 129.6, 128.7, 127.7, 125.4, 125.2, 48.3, 20.8.

HRMS (APCI):

m/z $[M+H]^+$ calcd for $C_{19}H_{16}BrOS$: 371.0100; found: 371.0128.

Methyl 4-(2-(8-(methylthio)naphthalen-1-yl)acetyl)benzoate (3ah)

Yellow solid (63 mg, 90%) (R_f = 0.3, hexane/EtOAc = 4/1); mp 123-125 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14-8.19 (m, 4H), 7.83 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.51 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.37-7.46 (m, 2H), 7.30 (dd, *J* = 7.0, 1.3 Hz, 1H), 5.20 (s, 2H), 3.97 (s, 3H), 2.27 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 166.3, 140.7, 135.8, 134.6, 133.5, 132.4, 132.1, 131.3, 130.2, 129.8, 129.6, 128.7, 128.0, 125.5, 125.2, 52.4, 48.7, 20.9.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}O_3S$: 351.1049; found: 351.1030.

1-(4-Methoxyphenyl)-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3ai)

White solid (51 mg, 79%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 123-125 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08-8.11 (m, 2H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.35-7.44 (m, 2H), 7.28 (d, *J* = 7.0 Hz, 1H), 6.96-7.00 (m, 2H), 5.19 (s, 2H), 3.89 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 163.1, 135.8, 135.1, 132.3, 132.2, 132.1, 130.4, 130.3, 129.5, 129.3, 128.4, 125.4, 125.1, 113.7, 55.4, 48.1, 20.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}O_2S$: 323.1100; found 323.1111.

2-(8-(Methylthio)naphthalen-1-yl)-1-(naphthalen-2-yl)ethan-1-one (3aj)

Yellow solid (56 mg, 82%) (R_f = 0.4, hexane/EtOAc = 5/1); mp 134-136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.69 (bs, 1H), 8.20 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.92-7.97 (m, 2H), 7.85 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.57-7.65 (m, 2H), 7.52 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.47 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.38-7.42 (m, 1H), 7.35 (dd, *J* = 7.0, 1.3 Hz, 1H), 5.37 (s, 2H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.1, 135.8, 135.4, 135.0, 134.7, 132.6, 132.4, 132.2, 131.9, 129.7, 129.5, 129.4, 128.5, 128.3, 128.1, 127.7, 126.6, 125.5, 125.2, 124.2, 48.5, 20.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}OS$: 343.1151; found 343.1170.

1-(8-(Methylthio)naphthalen-1-yl)propan-2-one (3ak)

White semisolid (15 mg, 32%) (R_f = 0.4, 20% hexane/EtOAc = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.72 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.50 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.36-7.43 (m, 2H), 7.22 (dd, *J* = 7.0, 1.3 Hz, 1H), 4.61 (s, 2H), 2.45 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.6, 135.8, 134.9, 132.2, 131.9, 131.7, 129.5, 129.1, 128.4, 125.5, 125.2, 53.2, 29.7, 20.4.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{14}H_{15}OS$: 231.0838; found: 231.0831.

3-Methyl-1-(8-(methylthio)naphthalen-1-yl)butan-2-one (3al)

Colorless semisolid (49 mg, 94%) (R_f = 0.4, hexane/EtOAc = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.71 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.35-7.42 (m, 2H), 7.21 (dd, *J* = 7.0, 1.3 Hz, 1H), 4.71 (s, 2H), 2.86-2.97 (m, 1H), 2.46 (s, 3H), 1.23 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 211.3, 135.8, 135.0, 132.1, 132.1, 131.9, 129.3, 128.8, 128.3, 125.4, 125.1, 50.4, 40.3, 20.3, 18.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{16}H_{19}OS$: 259.1151; found: 259.1134.

1-Cyclohexyl-2-(8-(methylthio)naphthalen-1-yl)ethan-1-one (3am)

Pale yellow solid (51 mg, 86%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 53-55 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.71 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.34-7.41 (m, 2H), 7.19 (dd, *J* = 7.0, 1.3 Hz, 1H), 4.70 (s, 2H), 2.62-2.69 (m, 1H), 2.45 (s, 3H), 1.98-2.05 (m, 2H), 1.80-1.86 (m, 2H), 1.67-1.72 (m, 1H), 1.43-1.53 (m, 2H), 1.22-1.37 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.5, 135.7, 135.0, 132.1, 132.0, 131.9, 129.2, 128.9, 128.3, 125.4, 125.1, 50.5, 50.3, 28.9, 25.9, 25.8, 20.3.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{23}OS$: 299.1464; found: 299.1473.

3,3-Dimethyl-1-(8-(methylthio)naphthalen-1-yl)butan-2-one (3an)

Colorless semisolid (39 mg, 70%) (R_f = 0.4, hexane/EtOAc = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.71 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.49 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.34-7.41 (m, 2H), 7.15 (dd, *J* = 7.0, 1.3 Hz, 1H), 4.84 (s, 2H), 2.45 (s, 3H), 1.33 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.8, 135.8, 135.0, 132.5, 132.4, 131.6, 129.2, 129.1, 128.4, 125.3, 125.0, 46.9, 44.0, 27.3, 20.3.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{17}H_{21}OS$: 273.1308; found: 273.1306.

(*E*)-1-(8-(Methylthio)naphthalen-1-yl)-4-phenylbut-3-en-2-one (3ao)

Yellow solid (20 mg, 31%) (R_f = 0.3, hexane/EtOAc = 4/1); mp 144-146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.74 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.55-7.60 (m, 2H), 7.52 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.37-7.45 (m, 5H), 7.29 (dd, *J* = 7.0, 1.3 Hz, 1H), 6.95 (d, *J* = 16.1 Hz, 1H), 4.88 (s, 2H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 141.8, 135.8, 135.0, 134.8, 132.3, 132.1, 131.7, 130.2, 129.5, 128.9, 128.5, 128.3, 126.1, 125.5, 125.2, 51.0, 20.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}OS$: 319.1151; found: 319.1168.

Directing group removal under reductive conditions (Scheme 4)

To a solution of **3aa** (30 mg, 0.10 mmol) in 5.0 mL ethanol in a round-bottom flask was added Raney Ni (excess) and refluxed for 12 h. Upon completion of the reaction, the mixture was cooled to room temperature and filtered through a small pad of silica gel. The filtrate was concentrated in vacuo, and the residue was purified by silica gel chromatography to afford **3aa-1**.

2-(Naphthalen-1-yl)-1-phenylethan-1-one (3aa-1)[21]

White solid (24 mg, 95%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 104-106 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08-8.10 (m, 2H), 7.85-7.89 (m, 2H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.57-7.61 (m, 1H), 7.47-7.52 (m, 4H), 7.43 (dd, *J* = 8.2, 7.0 Hz, 1H), 7.35-7.37 (m, 1H), 4.75 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 136.7, 133.9, 133.3, 132.2, 131.3, 128.8, 128.7, 128.5, 128.0, 127.9, 126.3, 125.7, 125.5, 123.8, 43.1.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{18}H_{15}O$: 247.1117; found: 247.1117.

Palladium-catalyzed borylation (Scheme 4)

To a Schlenk tube were added **3aa** (30 mg, 0.10 mmol), 1,2-dichloroethane (2.0 mL), and MeOTf (16 μL, 0.14 mmol). The mixture was stirred for 12 h at 60 °C. After the completion of the reaction as indicated by TLC, all volatiles were removed under a reduced pressure. Then, bis(pinacolato)diboron (51 mg, 0.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), XPhos (2.4 mg, 0.005 mmol), K_3PO_4 (26 mg, 0.12 mmol), and THF (2.0 mL) were introduced to the tube and stirred for 5 h at 60 °C. Upon completion of the reaction, the mixture was cooled to room temperature and filtered through a pad of silica gel. The filtrate was concentrated and the residue was purified by silica gel chromatography to afford **3aa-2**.

1-Phenyl-2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)naphthalen-1-yl)ethan-1-one (3aa-2)

Pale yellow oil (12 mg, 41%) (R_f = 0.4, hexane/EtOAc = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90-7.95 (m, 3H), 7.85 (dd, *J* = 6.9, 1.4 Hz, 1H), 7.74 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.46-7.52 (m, 2H), 7.31-7.39 (m, 3H), 7.21-7.23 (m, 1H), 4.88 (s, 2H), 1.31 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.3, 136.5, 134.4, 134.0, 133.1, 132.5, 131.6, 128.8, 128.6, 127.9, 125.3, 124.7, 84.3, 45.1, 24.7.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{26}BO_3$: 373.1970; found: 373.1975.

Chromane synthesis through base-mediated cyclization (Scheme 4 and 5)

To a Schlenk tube were added **3** (0.10 mmol), 1,2-dichloroethane (2.0 mL), and MeOTf (16 μL, 0.14 mmol). The mixture was stirred for 12 h at 60 °C. After the completion of the reaction as indicated by TLC, all volatiles were removed under a reduced pressure. The sulfonium salt was dissolved in DMF (0.5 mL), and this solution was added to another Schlenk tube charged with Cs_2CO_3 (49 mg, 0.15 mmol) and DMF (1.0 mL). The mixture was stirred at room temperature for 12 h. The resulting mixture was extracted with ethyl acetate, and the combined organic layer was dried over Na_2SO_4, concentrated under a reduced pressure, and purified by silica gel column chromatography.

2-Phenylbenzo[*de*]chromene (3aa-3)

Yellow solid (23 mg, 92%) (R_f = 0.4, hexane/EtOAc = 5/1); mp 81-83 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76-7.79 (m, 2H), 7.36-7.45 (m, 3H), 7.33 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.26-7.30 (m, 1H), 7.19-7.23 (m, 2H), 6.85 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.77 (dd, *J* = 7.0, 0.7 Hz, 1H), 6.50 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0, 152.1, 134.8, 133.1, 130.0, 129.1, 128.5, 127.9, 127.5, 124.6, 123.5, 123.2, 119.4, 115.9, 107.1, 103.1.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{18}H_{13}O$: 245.0961; found: 245.0945.

5-Phenyldibenzo[*de,g*]chromene (3da-1)

Pale yellow solid (26 mg, 88%) (R_f = 0.6, hexane/EtOAc = 5/1); mp 136-138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42-8.44 (m, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.82-7.85 (m, 2H), 7.71-7.74 (m, 1H), 7.39-7.54 (m, 6H), 7.13 (s, 1H), 7.07 (d, J = 7.3 Hz, 1H), 6.54 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 150.8, 133.6, 133.0, 131.4, 130.2, 129.2, 128.5, 128.4, 127.3, 127.2, 126.0, 124.7, 124.1, 122.7, 122.3, 120.1, 119.4, 104.5, 102.0.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{15}O$: 295.1117; found: 295.1108.

4-Phenylphenaleno[2,1,9-*def*]chromene (3ea-1)

Greenish yellow solid (27 mg, 90%) (R_f = 0.6, hexane/EtOAc = 5/1); mp 176-178 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.5 Hz, 1H), 7.84-7.87 (m, 2H), 7.72-7.81 (m, 5H), 7.41-7.51 (m, 4H), 7.15 (s, 1H), 6.66 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 150.3, 133.8, 133.2, 132.3, 129.2, 128.6, 126.8, 126.5, 126.0, 125.9, 125.6, 125.1, 124.7, 122.2, 122.0, 118.4, 114.6, 112.3, 104.0.

HRMS (APCI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{15}O$: 319.1117; found: 319.1130.

Oxidation of the SMe group of 3aa (Scheme 6)

To a round-bottom flask were added **3aa** (30 mg, 0.1 mmol) and ethanol (5.0 mL). After cooling to 0 °C, Tf_2O (9.0 μL, 0.05 mmol) and H_2O_2 (30%aq, 23 mg, 0.2 mmol) were subsequently added to the vessel and the mixture was stirred for 5 minutes at this temperature. Then the mixture was allowed to warm to room temperature and stirred for another 2 h. The

reaction was quenched by adding 5.0 mL of water and extracted with ethyl acetate. The combined organic layer were dried over Na_2SO_4, concentrated in vacuo, and the residue was subjected to silica gel column chromatography to give **3aa-4**.

2-(8-(Methylsulfinyl)naphthalen-1-yl)-1-phenylethan-1-one (3aa-4)

White solid (30 mg, 95%) (R_f = 0.4, hexane/EtOAc = 1/1); mp 188-190 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (dd, *J* = 7.4, 1.4 Hz, 1H), 8.07-8.10 (m, 2H), 8.04 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.91 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.66-7.70 (m, 1H), 7.61-7.66 (m, 1H), 7.49-7.55 (m, 3H), 7.35-7.37 (m, 1H), 5.19 (d, *J* = 18.6 Hz, 1H), 4.70 (d, *J* = 18.6 Hz, 1H), 2.52 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.1, 144.0, 136.3, 135.2, 133.5, 133.2, 132.9, 129.4, 129.3, 129.0, 128.9, 128.1, 126.0, 125.4, 123.7, 47.9, 45.5.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{19}H_{17}O_2S$: 309.0944; found: 309.0929.

Grignard reaction of 3aa (Scheme xx)

To an ice-cold solution of solution of **3aa** (30 mg, 0.1 mmol) in THF (5.0 mL) was added MeMgBr (45 µl, 0.13 mmol), and the mixture was stirred at room temperature for 4 h. The reaction was quenched by adding NH_4Claq, extracted with ethyl acetate. The combined organic layer were dried over Na_2SO_4, concentrated in vacuo, and the residue was subjected to silica gel column chromatography to give **3aa-5**.

1-(8-(Methylthio)naphthalen-1-yl)-2-phenylpropan-2-ol (3aa-5)

Yellow semisolid (29 mg, 91%) (R_f = 0.4, hexane/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.44-7.47 (m, 2H), 7.42 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.27-7.37 (m, 4H), 7.21-7.26 (m, 1H), 7.06 (dd, *J* = 7.2, 1.4 Hz, 1H), 4.45 (d, *J* = 14.6 Hz, 1H), 3.93 (d, *J* = 14.6 Hz, 1H), 2.55 (s, 3H), 3.13 (s, 1H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 135.8, 134.8, 134.0, 132.6, 132.4, 129.1, 128.1, 127.9, 126.6, 126.3, 125.0, 124.9, 124.6, 75.2, 49.1, 29.4, 18.6; HRMS (APCI) *m/z*: [M-H_2O+H]$^+$ Calcd for $C_{20}H_{19}S$ 291.1202; Found 291.1202.

Suzuki-Miyaura coupling reaction of 3ba (Scheme 6)

To a Schlenk tube were added **3ba** (37 mg, 0.10 mmol), 1-naphthylboronic acid (34 mg, 0.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), PPh_3 (2.6 mg, 0.005 mmol), K_2CO_3 (27 mg, 0.2 mmol), and 1,4-dioxane (2.0 mL). The mixture was stirred for 8 h at 80 °C. After cooling to room temperature, the mixture was filtered through a pad of silica gel. The filtrate was concentrated and the residue was purified by silica gel chromatography to give **3ba-1**.

2-(4-(Methylthio)-[1,1'-binaphthalen]-5-yl)-1-phenylethan-1-one (3ba-1)

White solid (37 mg, 89%) (R_f = 0.4, hexane/EtOAc = 4/1); mp 145-147 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17-8.19 (m, 2H), 7.94-7.97 (m, 2H), 7.58-7.65 (m, 3H), 7.53-7.57 (m, 2H), 7.47-7.51 (m, 2H), 7.39-7.44 (m, 3H), 7.28-7.34 (m, 2H), 7.23 (dd, *J* = 8.3, 7.0 Hz, 1H), 5.35 (d, *J* = 18.4 Hz, 1H), 5.26 (d, *J* = 18.4 Hz, 1H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.3, 138.8, 138.2, 137.4, 135.1, 134.8, 133.4, 132.8, 132.7, 132.4, 132.3, 131.9, 128.7, 128.6, 128.2, 128.1, 127.9, 127.8, 127.4, 126.6, 126.0, 125.8, 125.5, 125.4, 48.8, 20.7.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{29}H_{23}OS$: 419.1464; found: 419.1463.

Rhodium-catalyzed direct alkenylation of 3fa (Scheme 6)

To an oven dried screw-top tube were added **3fa** (34 mg, 0.1 mmol, 1.0 equiv), butyl acrylate (29 µL, 0.4 mmol, 2.0 equiv), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4.0 mol%), $Cu(OAc)_2{\cdot}H_2O$ (40 mg, 0.4 mmol, 2.0 equiv), and *tert*-AmOH (1.0 mL). The mixture was heated for 6 h at 100 °C under N_2 with an oil bath. After cooling to room temperature, the resulting mixture was filtered through a pad of silica gel eluting with chloroform. The filtrate was concentrated and the residue was subjected to silica gel column.

Butyl (*E*)-3-(5,8-bis(methylthio)-4-(2-oxo-2-phenylethyl)naphthalen-1-yl)acrylate (3fa-1)

Deep yellow solid (35 mg, 75%) (R_f = 0.6, hexane/EtOAc = 5/1); mp 96-98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 15.4 Hz, 1H), 8.08-8.10 (m, 2H), 7.58-7.62 (m, 1H), 7.49-7.53 (m, 3H), 7.44-7.46 (m, 2H), 7.26-7.28 (m, 1H), 6.21 (d, *J* = 15.4 Hz, 1H), 5.17 (s, 2H), 4.24 (t, *J* = 6.6 Hz, 2H), 2.39 (s, 3H), 2.26 (s, 3H), 1.68-1.75 (m, 2H), 1.42-1.51 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 167.3, 148.2, 137.2, 135.9, 134.9, 134.1, 134.0, 132.8, 132.1, 129.9, 128.6, 128.3, 128.1, 128.0, 116.2, 64.3, 48.8, 30.8, 21.1, 20.2, 19.2, 13.8.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{27}H_{29}O_3S_2$: 465.1553; found: 465.1543.

Rhodium-catalyzed direct amidation (Scheme 7)

To an oven dried screw-top tube were added aryl sulfide **1** (0.2 mmol, 1.0 equiv), amidating reagent **4** (0.4 mmol, 2.0 equiv), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (5.0 mol%), and HFIP (1.0 mL). The mixture was heated for 16 h at 100 °C under N_2 with an oil bath. After cooling to room temperature, the resulting mixture was filtered through a pad of silica gel eluting with chloroform. Volatiles were removed under reduced pressure, and the crude material was purified by silica gel column chromatography.

***N*-(8-(methylthio)naphthalen-1-yl)benzamide (5aa)**[14]

Yellow solid (42 mg, 72%) (R_f = 0.3, hexane/EtOAc = 5/1); mp 121-123 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.77 (s, 1H), 8.58 (d, *J* = 7.7 Hz, 1H), 8.09-8.11 (m, 2H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.71 (t, *J* = 7.3 Hz, 2H), 7.51-7.60 (m, 4H), 7.38 (t, *J* = 8.0 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 136.2, 135.4, 134.9, 134.4, 131.8, 130.6, 129.8, 128.8, 127.4, 126.3, 126.2, 125.3, 121.5, 21.5 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{18}H_{16}NOS$: 294.0947; found: 294.0952.

***N*-(10-(methylthio)phenanthren-1-yl)benzamide (5da)**

White solid (45 mg, 65%) (R_f = 0.2, hexane/EtOAc = 5/1); mp 168-170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.28 (s, 1H), 8.61 (t, *J* = 8.0 Hz, 2H), 8.48 (d, *J* = 7.8 Hz, 1H), 8.11 (d, *J* = 6.8 Hz, 2H), 7.91 (s, 1H), 7.78 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.51-7.73 (m, 6H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 135.3, 135.0, 134.1, 133.0, 131.8, 131.0, 130.3, 128.8, 127.8, 127.6, 127.5, 127.3, 127.0, 123.4, 123.2, 123.1, 120.5, 20.5 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{22}H_{18}NOS$: 344.1104; found: 344.1094.

***N*-(3-(methylthio)pyren-4-yl)benzamide (5ea)**[14]

Yellow solid (14 mg, 19%) (R_f = 0.3, hexane/EtOAc = 5/1); m.p. 157-159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.16 (s, 1H), 9.30 (s, 1H), 8.13-8.24 (m, 5H), 8.07-8.09 (m, 2H), 7.99-8.03 (m, 2H), 7.55-7.61 (m, 3H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 135.6, 134.4, 132.8, 132.1, 131.8, 131.0, 130.8, 128.8, 128.4, 127.5, 127.2, 127.1, 127.1, 126.7, 125.7, 125.6, 125.1, 122.3, 121.2, 22.0 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{24}H_{18}NOS$: 368.1104; found: 368.1100.

***N*-(7-methyl-8-(methylthio)naphthalen-1-yl)benzamide (5ha)**

Brown oil (36 mg, 59%) (R_f = 0.2, hexane/EtOAc = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.78 (s, 1H), 8.70 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.09-8.11 (m, 2H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.49-7.63 (m, 5H), 7.38 (d, *J* = 8.3 Hz, 1H), 2.76 (s, 3H), 2.17 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 143.9, 135.8, 135.0, 134.4, 131.7, 131.0, 128.7, 128.6, 127.3, 126.5, 125.8, 125.7, 125.5, 121.1, 22.8, 20.4.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{19}H_{18}NOS$: 308.1104; found: 308.1105.

4-bromo-*N*-(8-(methylthio)naphthalen-1-yl)benzamide (5ab)[14]

After column chromatography, the crude material was dissolved in EtOAc. Hexane was added to this solution, and the precipitate was corrected, washed with hexane, and dried in vacuo to give the pure product.

White solid (41 mg, 55%) (R_f = 0.3, hexane/EtOAc = 5/1); m.p. 194-196 °C.

^{1}H NMR (400 MHz, $CDCl_3$ and CS_2): δ = 11.81 (s, 1H), 8.55 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.82-7.85 (m, 1H), 7.65-7.73 (m, 4H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$ and CS_2): δ = 164.7, 136.2, 135.1, 134.3, 134.2, 132.0, 130.7, 129.6, 129.0, 126.6, 126.3, 126.3, 125.4, 125.2, 121.4, 21.5.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{18}H_{15}BrNOS$: 372.0052; found: 372.0037.

3-chloro-*N*-(8-(methylthio)naphthalen-1-yl)benzamide (5ac)

White solid (58 mg, 88%) (R_f = 0.4, hexane/EtOAc = 5/1); mp 138-140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.8 (s, 1H), 8.54 (d, *J* = 7.6 Hz, 1H), 8.09 (t, *J* = 1.8 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.83 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.68-7.72 (m, 2H), 7.52-7.56 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 137.3, 136.1, 135.0, 134.9, 134.1, 131.8, 130.6, 130.0, 129.7, 127.9, 126.4, 126.3, 125.4, 125.3, 125.2, 121.5, 21.5.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{18}H_{15}ClNOS$: 328.0557; found: 328.0556.

3,4-dimethoxy-*N*-(8-(methylthio)naphthalen-1-yl)benzamide (5ad)

White solid (42 mg, 60%) (R_f = 0.4, hexane/EtOAc = 1/1); mp 161-163 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.71 (s, 1H), 8.57 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.67-7.72 (m, 4H), 7.53-7.57 (m, 1H), 7.35-7.39 (m, 1H), 6.97 (dd, *J* = 9.0, 1.4 Hz, 1H), 3.99 (d, *J* = 0.9 Hz, 3H), 3.97 (d, *J* = 1.2 Hz, 3H), 2.34 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 152.0, 149.0, 136.2, 134.9, 134.5, 130.6, 129.7, 128.0, 126.3, 125.9, 125.2, 125.2, 121.3, 120.2, 110.7, 110.5, 56.1, 21.5 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{20}H_{20}NO_3S$: 354.1158; found: 354.1166.

***N*-(8-(methylthio)naphthalen-1-yl)acetamide (5ae)**

White solid (24 mg, 53%) (R_f = 0.3, hexane/EtOAc = 1/1); m.p. 134-136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.77 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 2.50 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 136.0, 134.0, 133.1, 130.6, 129.9, 126.2, 126.1, 125.3, 125.0, 121.6, 25.2, 20.9.

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{13}H_{14}NOS$: 232.0791; found: 232.0800.

***N*-(8-(methylthio)naphthalen-1-yl)-3-phenylpropanamide (5af)**[14]

White solid (51 mg, 79%) (R_f = 0.3, hexane/EtOAc = 3/1); mp 117-119 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.95 (s, 1H), 8.39 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.62-7.64 (m, 2H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.29-7.37 (m, 5H), 7.19-7.22 (m, 1H), 3.15 (t, *J* = 7.6 Hz, 2H), 2.81 (t, *J* = 7.9 Hz, 2H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 141.1, 136.0, 134.1, 133.6, 130.4, 130.1, 128.6, 128.5, 126.3, 125.9, 125.3, 124.8, 121.1, 40.3, 31.6, 21.0 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{20}H_{20}NOS$: 322.1260; found: 322.1273.

***N*-(8-(methylthio)naphthalen-1-yl)cyclohexanecarboxamide (5ag)**

White solid (50 mg, 83%) (R_f = 0.4, hexane/EtOAc = 3/1); m.p. 163-165 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.89 (s, 1H), 8.43 (d, *J* = 7.4 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.63 (t, *J* = 9.7 Hz, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 2.48 (s, 3H), 2.34-2.40 (m, 1H), 2.03-2.07 (m, 2H), 1.84-1.89 (m, 2H), 1.62-1.71 (m, 3H), 1.27-1.39 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6, 136.0, 134.4, 133.7, 130.3, 130.2, 126.25, 125.7, 125.2, 124.8, 121.0, 47.6, 29.7, 25.8, 21.3 (1 peak overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{18}H_{22}NOS$: 300.1417; found: 300.1412.

***N*-(8-(methylthio)naphthalen-1-yl)cinnamamide (5ah)**

Yellow solid (22 mg, 34%) (R_f = 0.3, hexane/EtOAc = 5/1); mp 153-155 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.56 (s, 1H), 8.62 (s, 1H), 7.80-7.86 (m, 2H), 7.51-7.71 (m, 5H), 7.36-7.41 (m, 4H), 6.67 (d, *J* = 15.5 Hz, 1H), 2.49 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 142.0, 136.1, 134.9, 134.4, 130.6, 129.9, 128.9, 128.0, 126.3, 126.0, 125.4, 124.7, 121.9, 120.9, 21.6 (2 peaks overlapped).

HRMS (APCI): *m/z* [M+H]$^+$ calcd for $C_{20}H_{18}NOS$: 320.1104; found: 320.1088.

Funding Information

This work was supported by JSPS KAKENHI Grant No. JP 19K15586 (Grant-in-Aid for Young Scientists) to Y.N. and JP 17H06092 (Grant-in-Aid for Specially Promoted Research) to M.M.

Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

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