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Concise Synthesis of Chromene/Chromane-Type Aryne Precursors and Their Applications

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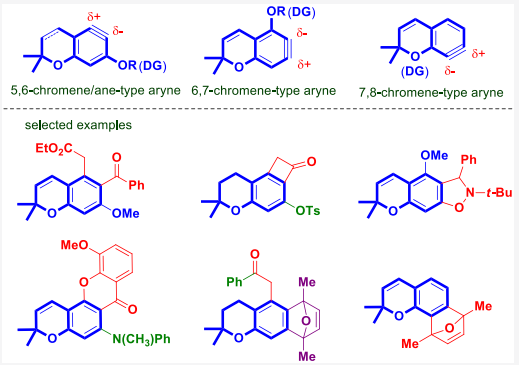
ABSTRACT: The gram-scale synthesis of 5,6-, 6,7-, and 7,8-chromene/chromane-type aryne precursors and their applications in regioselective transformation to other functional derivatives is reported. Chromene/chromane-type arynes are generated under mild conditions, which can further undergo [2 + 2], [3 + 2], and [4 + 2] cycloaddition reactions, nucleophilic addition reactions, and σ-insertion reactions to produce structurally novel substituted chromenes and chromanes. The excellent regioselectivity of the reaction is facilitated by the oxygen-containing guiding groups at the *ortho*-position of the triple bond, which can be removed or switched to other functional groups including alkenyl, aryl, heteroaryl, and arylamino groups.



INTRODUCTION

Arynes are a class of powerful building blocks, which are widely applicable in organic syntheses. In the past two decades, aryne-based synthetic methodologies have been rapidly developed.[1] Aryne-based synthetic strategies are highly effective in enabling the introduction of multiple functional groups or ring systems to the mother core in one step.[1−3] Arynes have also been used as key synthons to construct a variety of natural products and bioactive compounds.[2,3] The chromene fragment has been found in many bioactive molecules (Figure 1), such as tephrosin (antitumor), calanolide A (anti-HIV), artocarbene (tyrosinase inhibitor), and 5-methyllupinifolinol (antibacterial); thus, it has been recognized as a privileged structure in pharmaceutical research.[4] As a result, we sought to make structurally different chromene-type Kobayashi precursors[5] to achieve the rapid and concise construction of functional chromenes.

Recently, we reported the synthesis of 5,6-chromene-type aryne precursor **1a** (Scheme 1), which was successfully used for the gram-scale total synthesis of five chromene/chromane-containing natural xanthones;[6] the benzyloxy substituent at C-7 was the key to achieving excellent regioselectivity control. This method was also envisioned to be amenable to the synthesis of other multisubstituted chromenes. However, the presence of the fixed triple bond and a single guiding group on arynes hampers its extension toward the construction of a more diverse range of functional derivatives. As a consequence, we envisaged the preparation of 6,7- and 7,8-chromene-type aryne precursors, in which oxygen-containing functional groups are present to serve as regioselectivity-controlling groups.[7] Herein, we report the gram-scale synthesis of 5,6-,

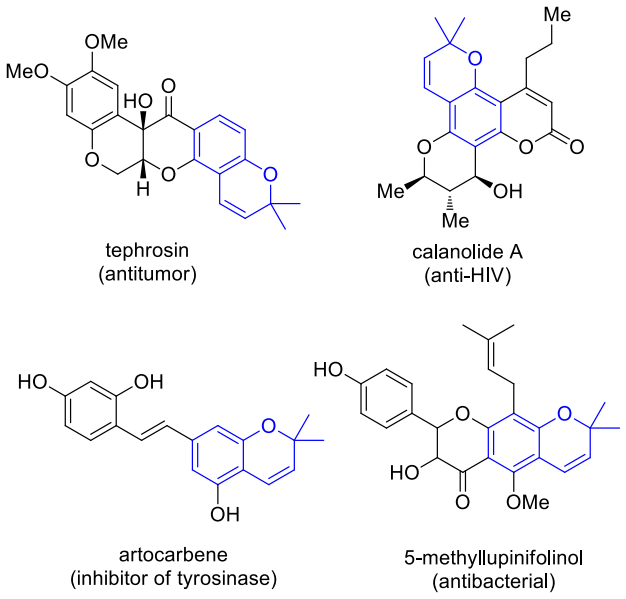


Figure 1. Representative natural chromenes.

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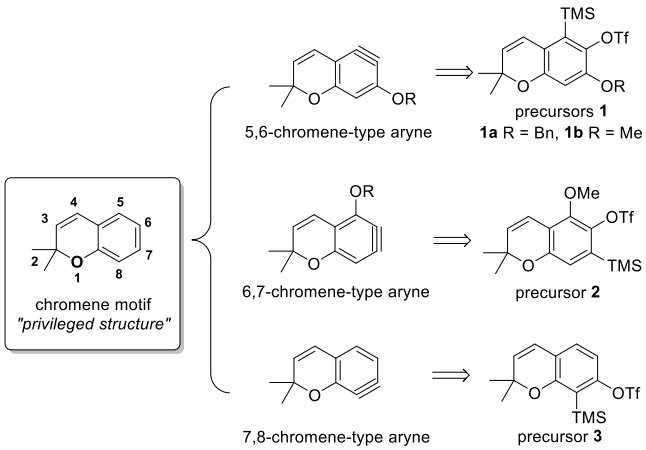
Scheme 1. Design of Chromene-Type Aryne Precursors

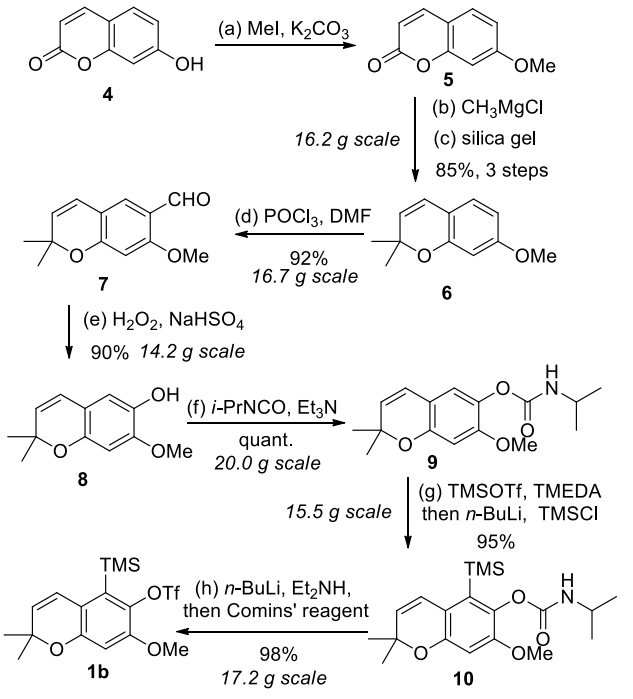


6,7-, and 7,8-chromene/chromane-type Kobayashi aryne precursors and their structural transformation to other functional derivatives in a regioselective manner. We determined that in addition to alkoxy groups, methoxymethyl ether, benzoate, and sulfonate groups can also be used as guiding groups for regioselectivity control.

RESULTS AND DISCUSSION

As shown in Scheme 2, the synthesis of 5,6-chromene-type aryne precursor **1b** was initiated by methylation of

Scheme 2. Gram-Scale Synthesis of 5,6-Chromene-Type Kobayashi Precursor 1b



umbelliferone **4** (Scheme 2). Methyl ether **5** was then converted to chromene **6** in 85% yield by the Grignard reaction followed by acid-promoted ring closure. Subsequently, a Vilsmeier–Haack reaction gave aldehyde **7** in 92% yield. Oxidation of aldehyde **7** with H_2O_2 afforded phenol **8** in 90% yield, which then reacted with isopropyl isocyanate to produce carbamate **9** in quantitative yield. Then, a tetramethylsilane (TMS) group was introduced to obtain silyl carbamate **10** in 95% yield.[8] Treatment of silyl carbamate **10** with *n*-BuLi/Et_2NH and Comins' reagent afforded precursor **1b** in 98% yield. The synthetic approach can be used to effectively prepare decagram quantities of the 5,6-chromene-type aryne precursor.

With precursor **1b** in hand, we then examined its reactivity in different types of chemical reactions. As shown in Scheme 3, the reaction of **1b** with 2,5-dimethylfuran in the presence of CsF led to the Diels–Alder addition product **11** in 96% yield, suggesting that 5,6-chromene-type aryne had been generated in situ. Subsequently, the amenability of precursor **1b** to nucleophilic addition, σ-bond insertion, and dipolar cycloaddition reactions was tested. Use of *N*-methylaniline as a nucleophile,[9] diarylamine **12** was obtained in quantitative yield. Direct acyl-alkylation of 5,6-chromene-type aryne with ethyl benzoylacetate gave diaryl ketone **13** in 71% yield.[10] This achieves difunctionalization of chromene. In addition, the reaction between precursor **1b** and methyl salicylate[11] and ethyl diazoacetate[12] produced xanthone **14** and 1*H*-indazole **15** in 69 and 76% yields, respectively. These compounds are envisioned to be of pharmacological value due to the presence of bioactive groups on arynes. In addition, the dipolar cycloaddition reaction between precursor **1b** and *N*-*tert*-butyl-α-phenylnitrone gave dihydrobenzo isoxazole **16** in 72% yield.[13] Noteworthily, the methoxy group in the precursor showed an excellent capacity for regioselectivity control of the reaction with no regioisomers isolated.

We then turned our attention to the synthesis of biologically interesting xanthones starting from precursors **1a** and **1b**[11] (Scheme 4). Cyclization of salicylate **17** with precursor **1a** in the presence of CsF gave xanthone **18** in 62% yield. Due to the presence of an *ortho*-carbonyl group, $MgBr_2{\cdot}Et_2O$ was employed to remove the benzyl group without compromising the double bond, producing **19** in 85% yield, and the formal total synthesis of 6-deoxyisojacareubin (**20**) was accomplished.[14] The synthesis of di-*O*-methyllorostemin[15] was also achieved. Pinnick oxidation and esterification of a known compound **21** gave trifluoroethyl ester **22** in quantitative yield over two steps. Subsequently, hydrogenation afforded salicylate **23** in 97% yield, which then underwent cyclization with precursor **1b** in the presence of CsF. This produced di-*O*-methyllorostemin (**24**) in 68% yield. Gram-scale preparation of 6-deoxyisojacareubin and di-*O*-methyllorostemin was also achieved using our precursor developed according to the above synthetic routes.

Next, we expanded the scope of the regioselective-controlling group in the precursor developed (Scheme 5). Xanthone **19** was selected as the model substrate. Propargylation of **19** using 3-chloro-3-methyl-1-butyn (**25**) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and a catalytic amount of $CuCl_2$ afforded propargylic ether **26** in 44% yield with 35% of xanthone **19** being recovered. Compound **26** then underwent a tandem Claisen rearrangement/cyclization to furnish chromene **27** in 95% yield, which suggests that C-8 functionalization of the precursor is feasible to producing more substituted aryne derivatives.

We then extended the structural transformation of xanthone **19** to other functional derivatives. As shown in Scheme 6, xanthone **19** could be converted to triflate **28** in an excellent yield, and a subsequent reduction under Pd-based catalytic conditions gave **29** with the guiding group being quantitatively removed after the xanthone core formation. Encouraged by the

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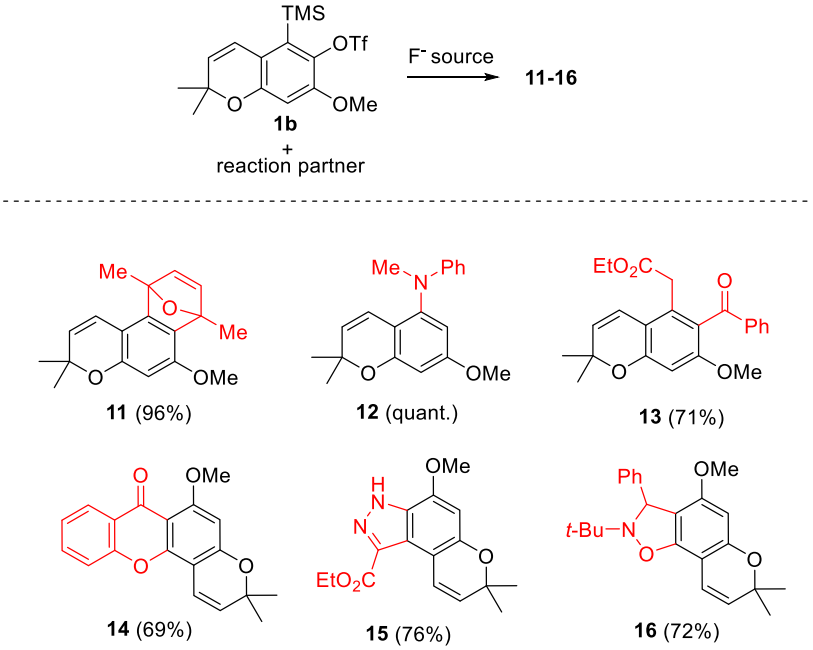
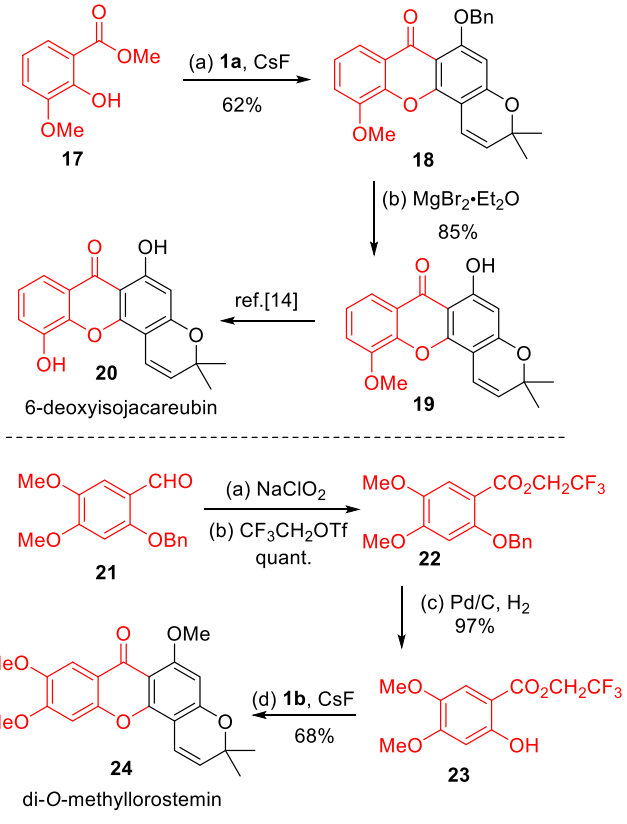
Scheme 3. Reactions of Precursor 1b and Different Partners



Scheme 4. Synthesis of 6-Deoxyisojacareubin and di-*O*-Methyllorostemin



above results, we sought to modify the guiding group by Pd-catalyzed reactions to obtain other substituted chromene products. Styrene **30** was obtained by Suzuki coupling in 97% yield. Other coupling reactions under similar conditions have also proven successful; phenyl, pyridyl, and thienyl groups were introduced to the precursor with excellent yields. In addition, a C−N bond could also be constructed successfully to produce amine **34** in moderate yield under Pd-based catalytic conditions. These results suggest that the different regio-controlling groups introduced to the precursor can be used to expand the structural variety of substituted chromene compounds bearing alkenyl, aryl, heteroaryl, and arylamino groups.

As shown in Scheme 7, 6,7-chromene-type aryne precursor **2** was also prepared. Salicylaldehyde **37** was prepared according to previous procedures,[16] and the following methylation and oxidation gave phenol **38** in 99% yield. This compound was then converted to 6,7-chromene-type aryne precursor **2** by a similar procedure to that of precursor **1** involving carbamation, *ortho*-silylation, and triflation. With precursor **2** in hand, we then showed that it could be used to undergo the Diels−Alder reaction, nucleophilic addition reaction, and dipolar cyclo-addition reaction, giving the corresponding products in an excellent yield. It is worth noting that the desired products **41**−**43** were obtained regioselectively.

Superior to other precursors (Schemes 2 and 7), the presence of an alkoxy group at the *ortho*-position of 7,8-chromene-type aryne serves as a guiding group to control regioselectivity (Scheme 8). We started with the preparation of silyl ether **45** according to Erhardt's procedure.[17] Subsequently, desilylation and carbamation reactions furnished carbamate **46** in 98% yield. Carbamate facilitated a silylation at C-8 over C-6 position, and the expected 8-silyl carbamate **47** was obtained in 83% yield using *sec*-BuLi as the lithiation reagent. Cleavage of the carbamate and triflation of the resulting phenol gave 7,8-chromene-type aryne precursor **3** in 3.3 g, and the following trapping experiments produced the corresponding products **48**−**50** in good to excellent yields with no regioisomers isolated.

Next, the synthesis of chromane-type aryne precursors was carried out to achieve the concise construction of multifunctional chromane fragments instead of the use of the chromene reduction approach. We also investigated the use of other oxygen-containing functional groups for regioselectivity control (Scheme 9). The hydrogenation of precursor **1a** reduced both

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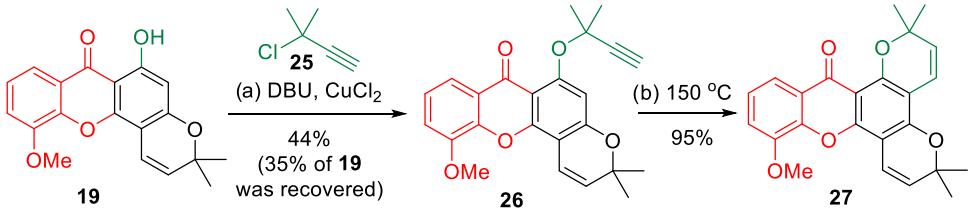
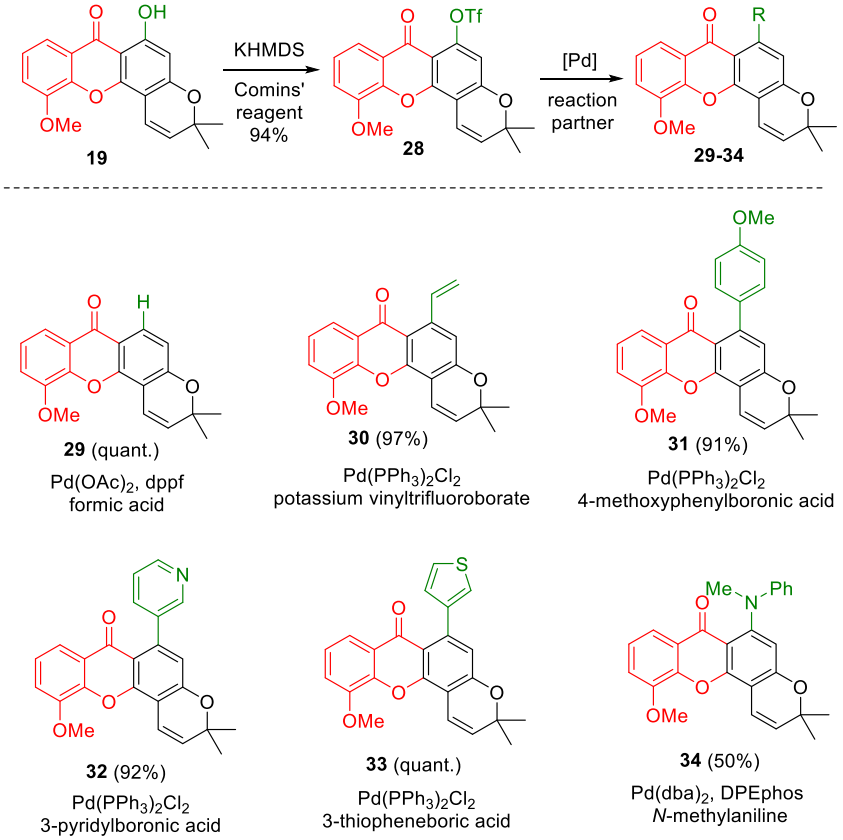
Scheme 5. Elaboration of Xanthone 19



Scheme 6. Synthesis and Pd-Catalyzed Derivatization of Triflate 28



the double bond and the benzyloxy group, and the resulting phenol was used as a general starting substrate of the chromane-type aryne precursors with oxygen-containing functional groups. Accordingly, precursors **51**, **52**, and **53** were successfully prepared in gram-scale. These compounds were further used to undergo 1,3-dipolar cycloaddition reactions, nucleophilic addition reactions, and [2 + 2] cycloaddition reactions, producing the corresponding products **54**−**56** in good yields and with excellent regioselectivity. These results suggest that in addition to alkoxy groups, methoxymethyl ether, benzoate, and sulfonate groups can also serve as excellent regioselectivity-controlling groups in aryne-based reactions. However, olefin and alkane substitution at the *ortho*-position of the aryne triple bond showed a limited capacity for regioselectivity control.

Encouraged by the above results, we sought the use of the OTf group to serve as both a guiding group to control regioselectivity and a leaving group to generate aryne, thereby achieving 1,2,3-trifunctionalization of chromane. Inspired by the methodologies developed by Li[18] and Hosoya,[19] we envisioned that the development of domino aryne precursors[20] is of significant value for organic synthesis (Scheme 10). To our delight, the domino chromane-type precursor was prepared according to the procedure described in Scheme 9. Bistriflate **57** was obtained in 96% yield over two steps. This precursor then generated 5,6-chromane-type aryne in the presence of CsF, which underwent a [2 + 2] cycloaddition with 1,1-diethoxyethylene. Following the hydrolysis under acidic conditions, benzocyclobutanone **58** was obtained in 62% yield without the production of regioisomers. Subsequently, treatment of benzocyclobutanone **58** with PhLi produced 6,7-chroman-type aryne, which was then trapped by 2,5-dimethylfuran to give compound **59** in 80% yield. This approach makes possible the migration of the triple bond in chromane-type arynes and the construction of multifunctional chromanes.

CONCLUSIONS

In summary, we have developed a concise and regioselective approach for the synthesis of a variety of multifunctional chromenes/chromanes. Our strategy relies on the generation of chromene/chromane-type arynes from Kobayashi precursors, which can be prepared in gram-scale from commercially available umbelliferone or 2,4-dihydroxybenzaldehyde. Ex-

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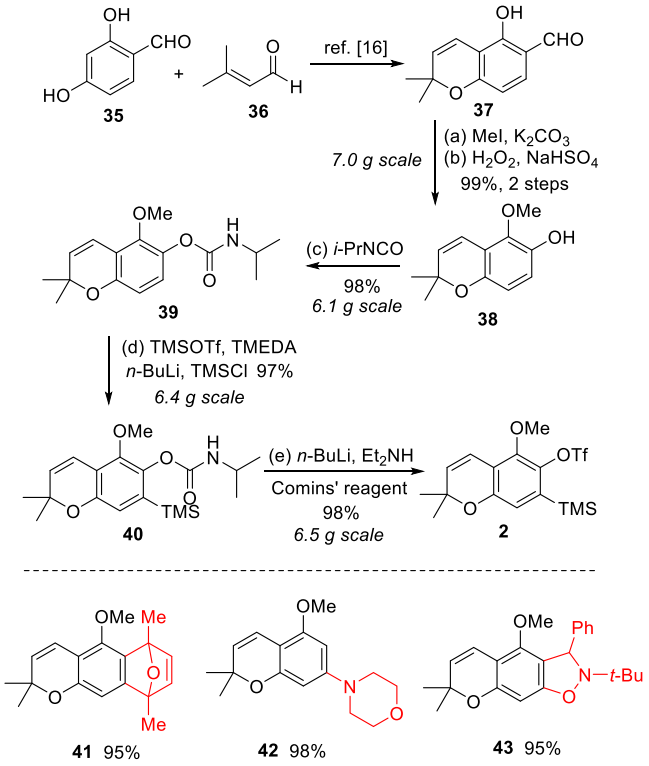
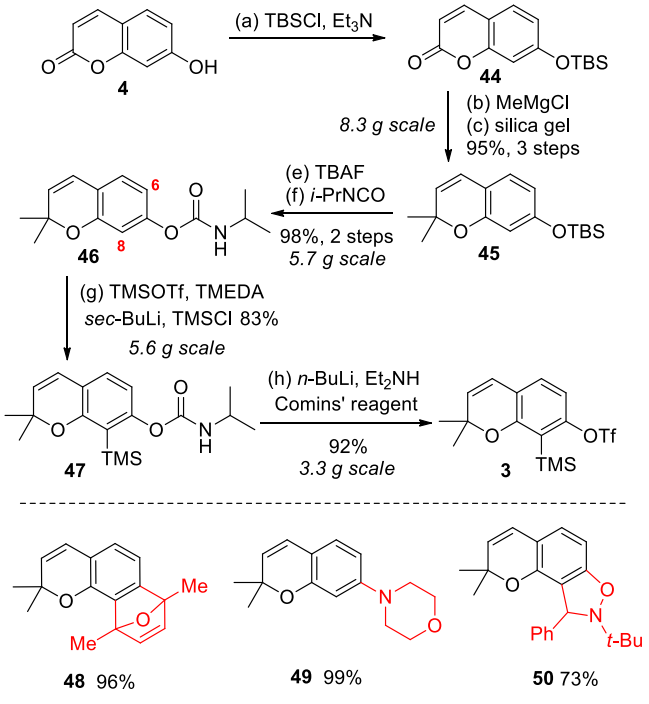
Scheme 7. Gram-Scale Synthesis and Trapping Experiments of the 6,7-Chromene-Type Aryne Precursor

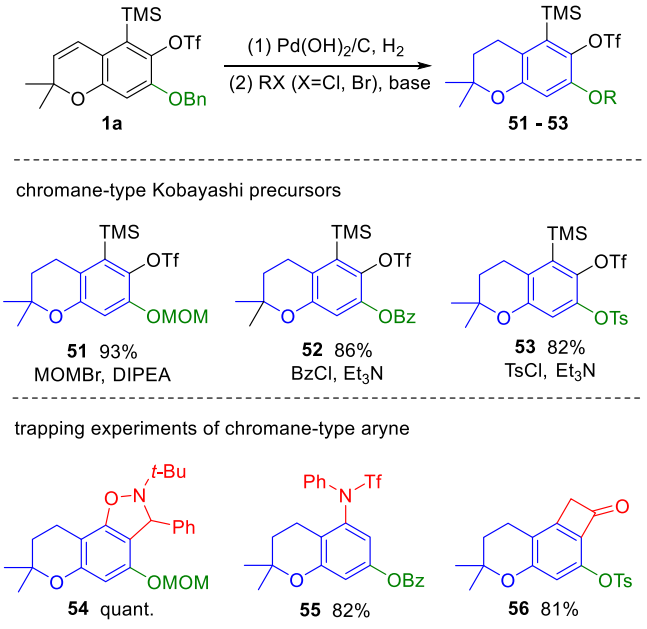


Scheme 8. Gram-Scale Synthesis and Trapping Experiments of the 7,8-Chromene-Type Aryne Precursor

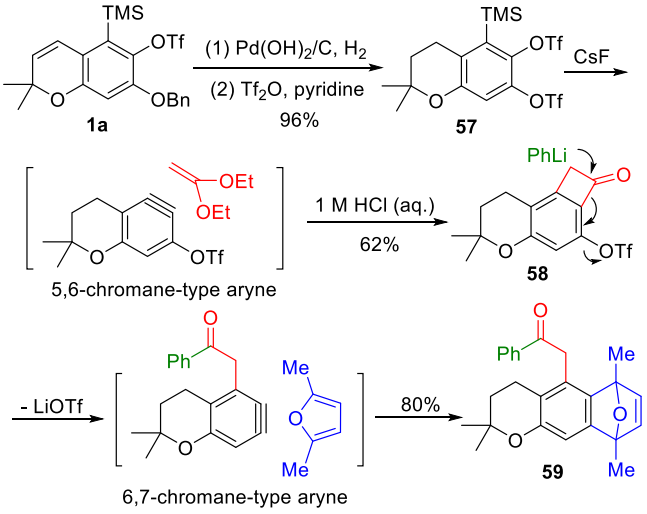


cellent regioselectivity control was achieved in a number of aryne-involved reactions, thanks to the presence of guiding groups including alkoxy groups, methoxymethyl ether, benzoate, and sulfonate groups. Importantly, the regioselectivity-controlling groups can be easily removed or switched to other functional groups including alkenyl, aryl, heteroaryl, and

Scheme 9. Synthesis and Trapping Experiments of the Chromane-Type Aryne Precursor



Scheme 10. Synthesis of Domino Chromane-Type Aryne Precursor 57 and Its Applications



arylamino groups. In addition, a trisubstituted chromane, which is unprecedented to achieve by previous methods, was also constructed through a domino chromane-type aryne approach. Our approach reported here provides a concise strategy for the synthesis of bioactive molecules, that is, converting bioactive fragments to widely applicable aryne equivalents. Applications of chromene/chromane-type arynes in the synthesis of other complex molecules are currently underway in our laboratories.

EXPERIMENTAL SECTION

General Information. Unless otherwise mentioned, all reactions were carried out in a nitrogen atmosphere with dry solvents under anhydrous conditions. Anhydrous solvents were distilled prior to use: tetrahydrofuran (THF), Et_2O, methyl *tert*-butyl ether (MTBE), and toluene were distilled from sodium-benzophenone; MeCN was distilled from P_2O_5; CH_2Cl_2, Et_3N, and *N*,*N*-diisopropylethylamine (DIPEA) were distilled from CaH_2; and acetone was distilled from

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Drierite and stored under a nitrogen atmosphere. Petroleum ether refers to the fraction with the boiling point in the range of 60−90 °C. Reagents of the highest commercial quality were purchased and used without further purification unless otherwise stated.

The reactions under conventional heating were carried out in an oil bath. Reactions were monitored by thin-layer chromatography (TLC) on silica gel using UV light as the visualizing agent or $KMnO_4$ and heat as developing agents. Flash column chromatography uses silica gel (300−400 mesh) supplied by Tsingtao Haiyang Chemicals (China).

NMR spectra were recorded on Bruker III 400 (^{1}H 400 MHz, $^{13}C\{^1H\}$ 101 MHz) or Ascend 600 (^{1}H 600 MHz, $^{13}C\{^1H\}$ 151 MHz). TMS was used as the internal standard for ^{1}H NMR (0.00 ppm), and the solvent signal was used as a reference for $^{13}C\{^1H\}$ NMR ($CDCl_3$, 77.00 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectrometry data were obtained using a XEVO G2 TOF using ESI (electrospray ionization) or a Waters GCT Premier using EI (electron impact). IR spectra were measured on an FT-IR spectrometer. Melting points were recorded without correction.

Synthesis of Compound ***6***. Iodomethane (7.47 mL, 120.0 mmol) was added to a stirred mixture of 7-hydroxycoumarin (16.20 g, 100.0 mmol) and anhydrous potassium carbonate (20.73 g, 150.0 mmol) in acetone (200 mL). The reaction mixture was heated to reflux for 4 h. Upon cooling, water was added. Acetone was removed *in vacuo*, and the residue was dissolved in water and extracted with EtOAc (200 mL × 3). The organic phase was combined, washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and crude compound **3** was obtained as a khaki solid, which was used without further purification. A small sample of crude compound **5** was further purified by column chromatography (4/1 PE/EtOAc) to give analytically pure compound **5**.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 9.6 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 6.85 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.81 (d, J = 2.4 Hz, 1H), 6.25 (d, J = 9.6 Hz, 1H), 3.88 (s, 3H). Spectral data match those previously reported.[21]

Methyl magnesium chloride (3 M in THF, 100.0 mL, 300.0 mmol) was added dropwise to a solution of compound **5** in THF (450 mL) at 0 °C. The resulting brown solution was stirred at room temperature for 24 h. Saturated NH_4Cl was added, and the layers were separated. The aqueous layer was extracted with ether (180 mL × 3). The organic layers were combined and washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated to give an off-white solid, which was used immediately in the next step.

The solid was dissolved in toluene (400 mL), and silica gel was added to the solution (40.00 g). The reaction mixture was heated under gentle reflux for 12 h. Upon cooling to room temperature, the reaction was filtered, and the silica gel was washed extensively with EtOAc. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (PE) to give compound **6** (16.21 g, 85% yield, 3 steps) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (d, J = 8.4 Hz, 1H), 6.40 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 6.37 (d, J = 2.4 Hz, 1H), 6.27 (d, J = 9.6 Hz, 1H), 5.47 (d, J = 9.6 Hz, 1H), 3.76 (s, 3H), 1.42 (s, 6H). Spectral data match those previously reported.[22]

Synthesis of Compound ***7***. Phosphorus oxychloride (23.1 mL, 247.9 mmol) was added dropwise to a flask containing *N*,*N*-dimethylformamide (DMF, 16.6 mL, 214.8 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 20 min followed by the addition of compound **6** (15.72 g, 82.63 mmol) in DMF (83 mL). The ice bath was removed, and the reaction mixture was stirred at 60 °C for 4 h. The solution gradually turned to deep burgundy. Upon cooling, the reaction solution was poured slowly into the ice−water with vigorous stirring; then, EtOAc (200 mL) was added. The layers were separated, and the aqueous layer was extracted with EtOAc (200 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (10/1 PE/EtOAc) to give compound **5** (16.67 g, 92% yield) as a pale yellow solid. Mp 70.9−71.0 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.26 (s, 1H), 7.49 (s, 1H), 6.37 (s, 1H), 6.30 (d, J = 10.0 Hz, 1H), 5.56 (d, J = 10.0 Hz, 1H), 3.88 (s, 3H), 1.46 (s, 6H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 187.9, 163.6, 160.2, 128.6, 126.5, 120.9, 118.5, 114.1, 99.3, 78.0, 55.6, 28.4. IR (KBr): ν_{max} 3046, 2968, 2871, 1663, 1608, 1430, 1293, 1208, 1119, 1013, 836, 757 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{13}H_{14}O_3^+$ 218.0937, found 218.0939.

Synthesis of Compound ***8***. Compound **7** (16.67 g, 76.38 mmol) was dissolved in MeOH (230 mL) and stirred under an ice−water bath. H_2O_2 (30 wt % in water, 9.55 mL) was added dropwise; then, $NaHSO_4{\cdot}H_2O$ (1.58 g, 11.46 mmol) was added in one portion. The solution was stirred under an ice−water bath for 12 h. After the reaction was confirmed by TLC, saturated $NaHSO_3$ (aq.) was added to quench the reaction. Methanol was removed *in vacuo*, and the residue was dissolved in water and extracted with EtOAc (160 mL × 3). The organic phase was combined, washed with brine, and dried over anhydrous Na_2SO_4. After the solvent was removed, the residue was purified by flash column chromatography (15/1 PE/EtOAc) to obtain compound **8** (14.15 g, 90%) as a white crystal. Mp 72.9−73.7 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.57 (s, 1H), 6.39 (s, 1H), 6.22 (d, J = 10.0 Hz, 1H), 5.48 (d, J = 10.0 Hz, 1H), 5.20 (brs, 1H), 3.83 (s, 3H), 1.40 (s, 6H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 146.7, 146.4, 139.4, 128.6, 122.0, 114.0, 111.6, 100.2, 75.8, 55.9, 27.5 IR (KBr): ν_{max} 3397, 2974, 2928, 1623, 1504, 1357, 1292, 1133, 1012, 869, 839 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{14}O_3^+$ 206.0937, found 206.0938.

Synthesis of Compound ***9***. To a round-bottomed flask were added compound **8** (14.15 g, 68.61 mmol) and CH_2Cl_2 (300 mL), followed by isopropyl isocyanate (20.2 mL, 205.8 mmol) and triethylamine (2.86 mL, 20.58 mmol). The clear mixture was stirred at room temperature for 24 h, at which time the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography (3/1 PE/CH_2Cl_2) to obtain compound **9** (19.99 g, quant.) as a white solid. Mp 107.1−107.6 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73 (s, 1H), 6.43 (s, 1H), 6.21 (d, J = 10.0 Hz, 1H), 5.47 (d, J = 10.0 Hz, 1H), 4.89 (d, J = 6.8 Hz, 1H), 3.92−3.83 (m, 1H), 3.79 (s, 3H), 1.42 (s, 6H), 1.22 (d, J = 6.8 Hz, 6H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.8, 152.0, 151.1, 133.3, 128.2, 121.5, 120.5, 113.5, 101.1, 76.4, 56.0, 43.5, 27.9, 22.8 IR (KBr): ν_{max} 3402, 2972, 1743, 1621, 1502, 1363, 1321, 1294, 1200, 1152, 1125, 1010 HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{16}H_{21}NNaO_4^+$ 314.1363, found 314.1369.

Synthesis of Compound ***10***. Carbamate **9** (13.00 g, 44.62 mmol) was taken in MTBE (450 mL) and cooled to 0 °C under N_2. TMEDA (9.37 mL, 62.47 mmol) was added, followed by slow addition of TMSOTf (9.69 mL, 53.55 mmol). The reaction mixture was stirred at 0 °C for 5 min and then at room temperature for 30 min. The second portion of TMEDA (23.4 mL, 156.2 mmol) was added, and the reaction mixture was cooled to −78 °C. *n*-BuLi (2.5 M in hexane, 62.5 mL, 156.2 mmol) was added dropwise, after which the mixture was stirred at the same temperature for 3 h. TMSCl (39.6 mL, 312.3 mmol) was added, and the mixture was stirred for an additional 30 min, then warmed to room temperature slowly, and stirred for 4 h. The reaction mixture was then quenched by the addition of 1 M HCl (aq.) and stirred for 30 min. The aqueous layer was extracted with EtOAc (250 mL × 3), and the combined organic extract was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (3/1 PE/CH_2Cl_2) to obtain compound **10** (15.46 g, 95%) as a white solid. Mp 119.5−120.0 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (d, J = 10.0 Hz, 1H), 6.46 (s, 1H), 5.48 (d, J = 10.0 Hz, 1H), 4.78 (d, J = 7.6 Hz, 1H), 3.95−3.84 (m, 1H), 3.77 (s, 3H), 1.41 (s, 6H), 1.21 (d, J = 6.4 Hz, 6H), 0.34 (s, 9H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.9, 151.7, 151.5, 138.4, 129.6, 127.2, 122.5, 117.8, 102.7, 75.0, 55.9, 43.3, 27.5, 22.9, 1.8 IR (KBr): ν_{max} 3314, 2973, 1708, 1594, 1430, 1246, 1199, 868, 838 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{30}NO_4Si^+$ 364.1939, found 364.1944.

Synthesis of Compound ***1b***. To a solution of silyl carbamate **10** (15.46 g, 42.53 mmol) in THF (425 mL) at −78 °C was added a

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solution of *n*-BuLi (2.5 M in hexane, 23.80 mL, 59.54 mmol) dropwise over 1.5 h. Et_2NH (6.60 mL, 63.80 mmol) was added, and the resulting mixture was stirred at −78 °C for 30 min and then allowed to warm to room temperature over 30 min. Next, Comins' reagent (23.38 g, 59.54 mmol) was added. The mixture was allowed to stir for 16 h at room temperature. Aqueous $NaHCO_3$ (5%, 50 mL) was added, and the mixture was extracted with EtOAc (300 mL × 3). The combined organic layers were washed with brine and dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (PE) afforded compound **1b** (17.17 g, 98%) as a white solid. Mp 45.6−45.7 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.49 (d, J = 10.0 Hz, 1H), 6.48 (s, 1H), 5.55 (d, J = 10.0 Hz, 1H), 3.80 (s, 3H), 1.42 (s, 6H), 0.43 (s, 9H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 153.4, 151.0, 136.7, 132.0, 127.8, 122.4, 118.9 (q, $J_{C\text{-}F}$ = 321.4 Hz), 118.7, 102.8, 75.6, 55.6, 27.4, 1.6 IR (KBr): ν_{max} 2976, 1596, 1410, 1316, 1200, 1160, 1130, 921, 864, 843 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{16}H_{22}F_3O_5SSi^+$ 411.0904, found 411.0908.

Synthesis of Compound ***11***. To a stirred solution of silyltriflate **1b** (1.64 g, 4.00 mmol) and 2,5-dimethylfuran (1.27 mL, 12.0 mmol) in MeCN (20 mL) was added CsF (1.82 g, 12.0 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (150/1 PE/EtOAc) to afford compound **11** (1.09 g, 96%) as pale yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84 (d, J = 5.6 Hz, 1H), 6.72 (d, J = 5.6 Hz, 1H), 6.58 (d, J = 10.0 Hz, 1H), 6.08 (s, 1H), 5.55 (d, J = 10.0 Hz, 1H), 3.72 (s, 3H), 1.98 (s, 3H), 1.96 (s, 3H), 1.41 (s, 3H), 1.38 (s, 3H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 153.1, 152.5, 150.7, 147.8, 145.7, 130.2, 129.1, 118.0, 110.1, 97.8, 89.6, 88.8, 75.5, 55.4, 27.9, 27.4, 18.3, 17.2 IR (KBr): ν_{max} 2976, 2935, 1613, 1477, 1441, 1303, 1197, 1135, 1017, 729 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{21}O_3^+$ 285.1485, found 285.1492.

Synthesis of Compound ***12***. To a stirred solution of silyltriflate **1b** (410.5 mg, 1.00 mmol) and *N*-methylaniline (160.7 mg, 1.50 mmol) in MeCN (5 mL) was added CsF (455.7 mg, 3.00 mmol). The mixture was stirred at room temperature for 18 h and then filtered over silica gel (EtOAc eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (200/1 PE/EtOAc) to afford compound **12** (295.0 mg, quant.) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.16 (m, 2H), 6.74 (t, J = 7.2 Hz, 1H), 6.66 (d, J = 8.0 Hz, 2H), 6.32 (d, J = 2.4 Hz, 1H), 6.27 (d, J = 2.4 Hz, 1H), 6.22 (d, J = 10.0 Hz, 1H), 5.42 (d, J = 10.0 Hz, 1H), 3.73 (s, 3H), 3.22 (s, 3H), 1.42 (s, 6H)

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 161.0, 155.3, 149.3, 145.5, 128.9, 127.9, 118.7, 117.5, 113.9, 112.6, 105.4, 100.1, 76.0, 55.3, 39.9, 27.7 IR (neat): ν_{max} 2975, 1608, 1568, 1500, 1315, 1298, 1197, 1146, 1114, 1042, 751, 694 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{19}H_{21}NO_2^+$ 295.1567, found 295.1571.

Synthesis of Compound ***13***. To a stirred solution of silyltriflate **1b** (591.1 mg, 1.44 mmol) and ethyl benzoylacetate (230.7 mg, 1.20 mmol) in MeCN (6 mL) was added CsF (437.5 mg, 2.88 mmol). The solution was stirred at 80 °C for 1 h and then cooled to room temperature. The mixture was extracted with brine. The aqueous layer was back-extracted with EtOAc (10 mL × 3). The organics were combined and dried over Na_2SO_4. After filtration, the residue was concentrated under reduced pressure and purified by flash chromatography (20/1 PE/EtOAc) to afford compound **13** (325.9 mg, 71%) as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 6.45 (d, J = 10.0 Hz, 1H), 6.41 (s, 1H), 5.61 (d, J = 10.0 Hz, 1H), 3.91 (q, J = 7.2 Hz, 2H), 3.60 (s, 3H), 3.58 (s, 2H), 1.46 (s, 6H), 1.01 (t, J = 7.2 Hz, 3H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 197.5, 170.3, 157.8, 155.4, 138.4, 133.0, 129.5, 129.2, 129.0, 128.2, 122.6, 118.6, 114.2, 99.3, 76.3, 60.8, 55.6, 34.5, 27.8, 13.9 IR (KBr): ν_{max} 2975, 1730, 1662, 1594, 1472, 1446, 1313, 1196, 1124, 1026, 711, 687 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{24}O_5^+$ 380.1618, found 380.1627.

Synthesis of Compound ***14***. To a stirred solution of silyltriflate **1b** (492.6 mg, 1.20 mmol) and methyl salicylate (152.2 mg, 1.00 mmol) in MeCN (10 mL) was added CsF (607.6 mg, 4.00 mmol). The solution was stirred at 65 °C for 24 h, then cooled to room temperature, and filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (5/1 PE/CH_2Cl_2) to afford xanthone **14** (212.1 mg, 69%) as a pale yellow solid.

Mp 196.9−197.6 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.64−7.59 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 6.88 (d, J = 10.0 Hz, 1H), 6.30 (s, 1H), 5.60 (d, J = 10.0 Hz, 1H), 3.98 (s, 3H), 1.50 (s, 6H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 175.4, 161.7, 158.8, 154.6, 153.7, 133.6, 127.0, 126.7, 123.8, 122.8, 116.8, 115.4, 106.9, 102.2, 95.5, 78.1, 56.3, 28.2 IR (KBr): ν_{max} 2970, 1724, 1654, 1629, 1489, 1465, 1423, 1383, 1357, 1304, 1087, 754 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{17}O_4^+$ 309.1121, found 309.1125.

Synthesis of Compound ***15***. Ethyl diazoacetate (171.1 mg, 1.50 mmol) was added to a solution of silyltriflate **1b** (738.9 mg, 1.80 mmol), KF (261.5 mg, 4.25 mmol), and 18-crown-6 (1.39 g, 5.25 mmol) in THF (7.2 mL) under a N_2 atmosphere. The reaction mixture was stirred at room temperature for 18 h, then filtered through a short pad of Celite, and eluted with EtOAc. The filtrate was concentrated, and the residue was purified by chromatography (7/1 PE/EtOAc) to afford compound **15** (343.5 mg, 76%) as a white solid. Mp 182.6−182.9 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.31 (brs, 1H), 7.68 (d, J = 10.0 Hz, 1H), 6.41 (s, 1H), 5.52 (d, J = 10.0 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 1.46 (s, 6H), 1.41 (t, J = 7.2 Hz, 3H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 162.9, 150.5, 145.2, 125.9, 121.1, 120.3, 104.9, 99.2, 75.9, 61.1, 55.7, 27.3, 14.2 IR (KBr): ν_{max} 3158, 2971, 2933, 1712, 1593, 1433, 1295, 1262, 1201, 1135, 1102, 1035, 984, 762 cm^{-1} HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{16}H_{18}N_2NaO_4^+$ 325.1159, found 325.1163.

Synthesis of Compound ***16***. *N-tert*-butyl-α-phenylnitrone (177.2 mg, 1.00 mmol) was added to a solution of silyltriflate **1b** (656.8 mg, 1.60 mmol) and CsF (607.6 mg, 4.00 mmol) in THF (20 mL) under a N_2 atmosphere. The solution was stirred at 65 °C for 16 h, then cooled to room temperature, and filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (20/1 PE/EtOAc) to afford compound **16** (264.2 mg, 72%) as a white solid. Mp 158.8−159.8 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 2H), 7.21 (t, J = 7.2 Hz, 1H), 6.44 (d, J = 10.0 Hz, 1H), 5.91 (s, 1H), 5.52 (s, 1H), 5.43 (d, J = 10.0 Hz, 1H), 3.61 (s, 3H), 1.44 (s, 3H), 1.41 (s, 3H), 1.17 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.1, 154.9, 154.5, 143.2, 128.2, 127.4, 127.0, 126.1, 116.5, 108.6, 96.9, 92.8, 76.6, 64.9, 61.4, 55.4, 28.0, 27.6, 25.4 IR (KBr): ν_{max} 2971, 2932, 1637, 1589, 1495, 1454, 1360, 1333, 1197, 1119, 1010, 773, 711, 699, 578 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{27}NO_3^+$ 365.1985, found 365.1994.

Synthesis of Compound ***18***. CsF (9.11 g, 60.00 mmol), salicylate (2.87 g, 15.75 mmol), and precursor **1b** (7.30 g, 15.00 mmol) in freshly distilled THF (300 mL) were stirred at 65 °C for 24 h. The reaction mixture was allowed to cool to room temperature, diluted with EtOAc (500 mL), and washed with brine (100 mL × 2). The aqueous layer was re-extracted with diethyl ether (100 mL × 3). The organic layers were combined, dried with Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (15/1 PE/EtOAc) to give compound **18** (3.84 g, 62%) as a pale yellow solid. Mp 196.5−196.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, J = 8.0, 1.6 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 6.95 (d, J = 10.0 Hz, 1H), 6.37 (s, 1H), 5.59 (d, J = 10.0 Hz, 1H), 5.24 (s, 2H), 3.99 (s, 3H), 1.49 (s, 6H) ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 175.2, 160.4, 158.6, 153.5, 148.2, 145.0, 136.3, 128.5, 127.6, 127.0, 126.6, 123.8, 123.1, 117.5, 115.5, 114.5, 107.1, 102.8, 97.0, 78.1, 70.6, 56.3, 28.1 IR (KBr): ν_{max} 3055, 2974, 2950, 2838, 1653, 1633, 1588,

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1569, 1452, 1392, 1150, 1120, 753, 732 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{26}H_{23}O_5^+$ 415.1540, found 415.1542.

Synthesis of Compound ***19***. Magnesium bromide etherate (3.78 g, 14.6 mmol) was added portionwise to a solution of compound **18** (4.04 g, 9.75 mmol) in toluene/ether (20/1, 205 mL). After the mixture was stirred at 60 °C for 8 h, it was cooled to 0 °C and quenched with 1 M aqueous. The aqueous phase was extracted with EtOAc (100 mL × 3), and the combined organic phase was washed with water and brine and dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash column chromatography (3/1 PE/CH_2Cl_2) to give compound **19** (2.68 g, 85%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ 12.92 (s, 1H), 7.75 (dd, J = 7.2 Hz, 1.6 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.19 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 6.87 (d, J = 10.0 Hz, 1H), 6.25 (s, 1H), 5.60 (d, J = 10.0 Hz, 1H), 3.99 (s, 3H), 1.49 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 180.7, 162.9, 160.8, 151.5, 148.4, 146.0, 127.0, 123.5, 121.2, 116.5, 115.6, 115.1, 103.6, 101.3, 99.2, 78.2, 56.3, 28.2 IR (KBr): ν_{max} 3439, 2976, 2928, 1648, 1578, 1498, 1274, 1151, 1118, 752 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$calcd for $C_{19}H_{17}O_5^+$ 325.1071, found 325.1075.

Synthesis of Compound ***22***. To a stirred solution of compound **21** (3.80 g, 13.96 mmol) and 2,3-dimethyl-2-butene (13.7 mL, 139.6 mmol) in *t*-BuOH/THF (1/1, 56 mL) was added dropwise 80% $NaClO_2$ (3.16 g, 27.91 mmol) in 27.91 mL of 2 M NaH_2PO_4 (aq.). After being stirred at room temperature for 1 h, the mixture was quenched with 10% $NaHSO_3$ (aq.), then concentrated *in vacuo*, and diluted with EtOAc (40 mL). The mixture was extracted with EtOAc (60 mL × 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude acid, which was used without further purification.

Cesium carbonate (4.55 g, 13.96 mmol) was added to a solution of crude acid in anhydrous MeCN (140 mL). The resulting mixture was stirred at room temperature for 20 min, and then, 2,2,2-trifluoroethyl trifluoromethanesulfonate (2.11 mL, 14.66 mmol) was added. The reaction mixture was stirred for 4 h at room temperature and filtered through Celite. The filtrate was concentrated *in vacuo*, and the residue was purified by chromatography (15/1 PE/CH_2Cl_2) to afford compound **22** (5.32 g, quant.) as a white solid. Mp 58.5−59.7 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 7.2 Hz, 2H), 7.43 (s, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.33−7.29 (m, 1H), 6.54 (s, 1H), 5.15 (s, 2H), 4.66 (q, J = 8.4 Hz, 2H), 3.87 (s, 3H), 3.86 (s, 3H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.6, 155.3, 154.2, 142.9, 136.4, 128.5, 127.9, 127.1, 123.2 (q, $J_{C\text{-}F}$ = 277.4 Hz), 114.2, 109.3, 99.7, 72.0, 60.3 (q, $J_{C\text{-}F}$ = 36.7 Hz), 56.2, 55.9 IR (KBr): ν_{max} 2943, 1704, 1610, 1518, 1463, 1272, 1158, 1023, 962 cm^{-1} HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{18}H_{17}F_3NaO_5^+$ 393.0920, found 393.0925.

Synthesis of Compound ***23***. To a solution of compound **22** (4.95 g, 13.37 mmol) in MeOH (67 mL) and EtOAc (67 mL) was added Pd/C (20%, 356.0 mg). The mixture was placed under an atmosphere of hydrogen, stirred for 2 h at room temperature, and then filtered over Celite (EtOAc eluent). Evaporation of the solvent under reduced pressure gave compound **23** (3.65 g, 97%) as a white solid. *Note that the residue was pure enough to be characterized and can be used directly in the following reaction*. Mp 117.3−117.7 °C ^1H NMR (400 MHz, $CDCl_3$): δ 10.28 (s, 1H), 7.20 (s, 1H), 6.50 (s, 1H), 4.71 (q, J = 8.4 Hz, 2H), 3.92 (s, 3H), 3.86 (s, 3H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 167.9, 159.0, 156.8, 142.5, 122.9 (q, $J_{C\text{-}F}$ = 277.5 Hz), 110.1, 101.6, 100.2, 60.4 (q, $J_{C\text{-}F}$ = 36.1 Hz), 56.3, 56.1 IR (KBr): ν_{max} 3211, 2975, 1680, 1627, 1519, 1371, 1163, 1023, 990 cm^{-1} HRMS-ESI (m/z): $[M - H]^-$ calcd for $C_{11}H_{10}F_3O_5^-$ 279.0486, found 279.0482.

Synthesis of Compound ***24***. CsF (6.08 g, 40.00 mmol), salicylate (2.80 g, 10.00 mmol), and precursor **1b** (4.93 g, 12.00 mmol) in freshly distilled THF (100 mL) were stirred at 65 °C for 24 h. The reaction mixture was allowed to cool to room temperature, diluted with EtOAc (250 mL), and washed with brine (80 mL × 3). The aqueous layer was re-extracted with EtOAc (120 mL × 3). The organic layers were combined, dried with Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by recrystallization (EtOAc/CH_2Cl_2) to give compound **24** (2.50 g, 68%) as a pale pink solid. Mp 272.4−273.7 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.63 (s, 1H), 6.85 (d, J = 10.0 Hz, 1H), 6.82 (s, 1H), 6.29 (s, 1H), 5.59 (d, J = 10.0 Hz, 1H), 3.99 (s, 3H), 3.97 (s, 6H), 1.50 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 174.6, 161.5, 158.1, 154.2, 153.7, 150.5, 146.4, 126.9, 115.8, 115.4, 106.5, 105.7, 102.1, 98.9, 95.5, 77.9, 56.3, 56.2, 56.2, 28.2 IR (KBr): ν_{max} 2964, 1633, 1509, 1482, 1426, 1386, 1355, 1274, 1118, 1006, 821, 781 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{21}H_{21}O_6^+$ 369.1333, found 369.1339.

Synthesis of Compound ***26***. To a solution of xanthone **19** (960 mg, 2.96 mmol) in acetonitrile (20 mL) were added 3-chloro-3-methylbutyne (0.40 mL, 3.55 mmol) and DBU (0.53 mL, 3.55 mmol) followed by $CuCl_2$ (8.0 mg, 0.06 mmol). The resulting mixture was stirred for 4 h at 60 °C, then, additional 3-chloro-3-methylbutyne (0.27 mL, 2.37 mmol) and DBU (0.35 mL, 2.37 mmol) were added, and the mixture was stirred for 30 h at 60 °C before cooled to room temperature. Then, 20 mL of H_2O and 10 mL of EtOAc were added. After separating both layers, the aqueous layer was extracted with EtOAc (20 mL × 3). The combined organic layers were dried with Na_2SO_4, and the solvent was evaporated under reduced pressure. Purification of the residue by flash column chromatography provided compound **26** (505.1 mg, 44%) as a white solid, and compound **19** (333.4 mg, 35%) was recovered. Mp 137.0−138.2 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.14 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.04 (s, 1H), 6.97 (d, J = 10.0 Hz, 1H), 5.64 (d, J = 10.0 Hz, 1H), 3.99 (s, 3H), 2.65 (s, 1H), 1.83 (s, 6H), 1.50 (s, 6H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 175.3, 157.8, 157.6, 153.1, 148.3, 145.1, 127.8, 123.8, 123.1, 117.6, 115.6, 114.5, 109.8, 104.5, 104.3, 85.9, 78.0, 74.3, 74.1, 56.4, 29.2, 28.2 IR (KBr): ν_{max} 3244, 2974, 1638, 1563, 1429, 1367, 1289, 1270, 1121, 1094, 965 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{24}H_{23}O_5^+$ 391.1540, found 391.1544.

Synthesis of Compound ***27***. Compound **26** (375.0 mg, 0.96 mmol) was dissolved in dry DMF (14.4 mL), and the mixture was stirred at 150 °C for 1 h before cooled to room temperature. EtOAc (80 mL) was added and then washed with brine several times to remove DMF. The organic layers were dried with Na_2SO_4, and the solvent was evaporated under reduced pressure. Purification of the residue by flash column chromatography (8/1 PE/EtOAc) provided compound **27** (356.7 mg, 95%) as a yellow foam. Mp 168.5−169.6 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.13 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.95 (d, J = 10.0 Hz, 1H), 6.59 (d, J = 10.0 Hz, 1H), 5.62 (d, J = 10.0 Hz, 1H), 5.59 (d, J = 10.0 Hz, 1H), 3.98 (s, 3H), 1.57 (s, 6H), 1.50 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 175.2, 155.3, 153.4, 152.4, 148.2, 145.2, 127.7, 126.9, 123.7, 123.1, 117.6, 115.8, 115.7, 114.6, 106.7, 106.4, 102.2, 78.1, 77.8, 56.4, 28.2, 28.0 IR (KBr): ν_{max} 1640, 1596, 1573, 1492, 1355, 1266, 1142, 1124, 991, 758, 707 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{24}H_{23}O_5^+$ 391.1540, found 391.1546.

Synthesis of Compound ***28***. To a solution of xanthone **19** (973.0 mg, 3.00 mmol) in anhydrous THF (18 mL) at −20 °C was added a solution of KHMDS (1 M in THF, 4.50 mL, 4.50 mmol) dropwise over 10 min. The resulting mixture was stirred at −20 °C for 30 min, then Comins' reagent (1.77 g, 4.50 mmol) was added, and the mixture was allowed to warm to room temperature over 30 min and stirred for 24 h before being quenched with 5% $NaHCO_3$ (aq.). The organic layer was separated, and then, the aqueous layer was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (50/1 PE/EtOAc) gave triflate **28** (1.28 g, 94%) as a white solid. Mp 155.6−156.8 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.20 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.96 (d J = 10.0 Hz, 1H), 6.65 (s, 1H), 5.87 (d J = 10.0 Hz, 1H), 3.99 (s, 3H), 1.53 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 174.4, 157.5, 152.3, 148.4, 147.5, 145.3, 130.7, 124.0, 122.6, 118.8 (q, J = 322.0 Hz), 117.4, 115.5, 114.6, 109.9, 109.4, 108.1, 79.2, 56.3, 28.3 IR (KBr): ν_{max} 1661, 1646, 1620, 1593,

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1455, 1349, 1239, 1204, 1088, 956, 937, 759 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$calcd for $C_{20}H_{16}F_3O_7S^+$ 457.0563, found 457.0568.

Synthesis of Compound ***29***. Triflate **28** (547.7 mg, 1.20 mmol), $Pd(OAc)_2$ (13.5 mg, 0.06 mmol), and dppf (36.6 mg, 0.066 mmol) were dissolved in anhydrous THF (7.8 mL), Et_3N (1.25 mL, 9.00 mmol), and HCOOH (0.38 mL, 10.20 mmol), and the mixture was stirred for 1 h at 60 °C in a closed round-bottomed flask. The reaction was quenched with saturated aqueous NH_4Cl solution, and the mixture was extracted with EtOAc (15 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (20/1 PE/EtOAc) gave xanthone **29** (370.0 mg, quant.) as a pale yellow solid. Mp 184.7−185.7 °C ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.8 Hz, 1H), 7.85 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 7.19 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.01 (d, J = 10.0 Hz, 1H), 6.82 (d, J = 8.8 Hz, 1H), 5.73 (d, J = 10.0 Hz, 1H), 4.00 (s, 3H), 1.51 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.4, 158.5, 152.0, 148.7, 146.3, 129.7, 127.1, 123.3, 122.5, 117.4, 115.5, 115.4, 115.1, 114.1, 109.3, 77.9, 56.4, 28.1 IR (KBr): ν_{max} 1641, 1583, 1438, 1354, 1112, 1065, 976, 940, 747 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{17}O_4^+$ 309.1121, found 309.1126.

Synthesis of Compound ***30***. To a Schlenk flask were added triflate **28** (273.8 mg, 0.60 mmol), potassium vinyltrifluoroborate (241.1 mg, 1.80 mmol), and $(Ph_3P)_2PdCl_2$ (21.1 mg, 0.03 mmol). The flask was degassed with N_2 three times, then Na_2CO_3 (2 M aqueous, 1.20 mL, 2.40 mmol) and dioxane (15 mL) were added to the flask, and then stirred for 18 h at 100 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and washed with water. The mixture was extracted with EtOAc (25 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (3/1 PE/CH_2Cl_2) afforded compound **30** (194.5 mg, 97%) as a white solid. Mp 197.6−198.6 °C ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, J = 17.2 Hz, 10.8 Hz, 1H), 7.81 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.15 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.01 (d, J = 10.0 Hz, 1H), 6.90 (s, 1H), 5.45 (d, J = 10.0 Hz, 1H), 5.58 (dd, J = 17.2 Hz, 1.6 Hz, 1H), 5.40 (dd, J = 10.8 Hz, 1.6 Hz, 1H), 3.99 (s, 3H), 1.51 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 177.6, 157.2, 152.8, 148.4, 145.4, 142.1, 137.3, 129.7, 123.5, 123.2, 117.5, 116.5, 115.6, 114.7, 112.9, 112.4, 109.1, 77.8, 56.3, 28.2 IR (KBr): ν_{max} 2970, 1635, 1586, 1557, 1492, 1375, 1352, 1269, 1167, 1090, 951, 758, 725 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{21}H_{19}O_4^+$ 335.1278, found 335.1284.

Synthesis of Compound ***31***. To an oven-dried Schlenk flask were added triflate **28** (547.7 mg, 1.20 mmol), 4-methoxyphenylboronic acid (437.6 mg, 2.88 mmol), KF (460.2 mg, 7.92 mmol), and $(Ph_3P)_2PdCl_2$ (84.2 mg, 0.12 mmol). The flask was degassed with N_2 three times, and dry toluene (16 mL) was added to the flask and stirred for 6 h at 100 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and washed with water. The mixture was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (6/1 PE/EtOAc) afforded compound **31** (455.1 mg, 91%) as a pale yellow solid. Mp 188.8−189.2 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.6 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.21−7.14 (m, 2H), 7.07 (d, J = 10.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.65 (s, 1H), 5.74 (d, J = 10.4 Hz, 1H), 4.01 (s, 3H), 3.86 (s, 3H), 1.52 (s, 6H) $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 176.1, 158.8, 156.7, 153.1, 148.3, 145.4, 144.7, 134.0, 129.6, 129.6, 123.5, 123.2, 117.7, 117.2, 115.6, 114.7, 113.1, 112.9, 108.7, 77.9, 56.4, 55.2, 28.3 IR (KBr): ν_{max} 2956, 2836, 1606, 1599, 1511, 1284, 1253, 1115, 1092, 834, 757 cm^{-1}.

HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{26}H_{23}O_5^+$ 415.1540, found 415.1546.

Synthesis of Compound ***32***. To a Schlenk flask were added triflate **28** (273.8 mg, 0.60 mmol), 3-pyridylboronic acid (221.3 mg, 1.80 mmol), and $(Ph_3P)_2PdCl_2$ (21.1 mg, 0.03 mmol). The flask was degassed with N_2 three times; then, Na_2CO_3 (2 M aqueous, 1.20 mL, 2.40 mmol) and dioxane (15 mL) were added to the flask and stirred for 16 h at 100 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and washed with water. The mixture was extracted with EtOAc (25 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (3/1 PE/EtOAc) afforded compound **32** (212.6 mg, 92%) as a pale yellow solid.

Mp 216.3−217.1 °C ^1H NMR (400 MHz, $CDCl_3$): δ 8.62 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.59 (d, J = 1.6 Hz, 1H), 7.72−7.69 (m, 2H), 7.35 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.17 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 7.09 (d, J = 10.0 Hz, 1H), 6.64 (s, 1H), 5.79 (d, J = 10.0 Hz, 1H), 4.03 (s, 3H), 1.54 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.0, 156.9, 153.0, 148.6, 148.4, 148.0, 145.5, 140.6, 137.4, 136.1, 130.1, 123.4, 123.2, 122.2, 117.5, 117.2, 115.4, 114.9, 113.0, 109.6, 78.1, 56.4, 28.3 IR (KBr): ν_{max} 2979, 1638, 1571, 1557, 1492, 1435, 1351, 1304, 1267, 1118, 1097, 942, 760 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{24}H_{20}NO_4^+$ 386.1387, found 386.1393.

Synthesis of Compound ***33***. To a Schlenk flask were added triflate **28** (456.4 mg, 1.00 mmol), 3-thiopheneboronic acid (511.8 mg, 4.00 mmol), and $(Ph_3P)_2PdCl_2$ (70.2 mg, 0.10 mmol). The flask was degassed with N_2 three times; then, Na_2CO_3 (2 M aqueous, 3.00 mL, 6.00 mmol) and dioxane (30 mL) were added to the flask and then stirred for 16 h at 100 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and washed with water. The mixture was extracted with EtOAc (35 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (15/1 PE/EtOAc) afforded compound **33** (390.5 mg, quant.) as a yellow solid. Mp 165.3−166.2 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.33 (dd, J = 5.2 Hz, 3.2 Hz, 1H), 7.24 (dd, J = 3.2 Hz, 1.2 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.17−7.13 (m, 2H), 7.06 (d, J = 10.0 Hz, 1H), 6.73 (s, 1H), 5.75 (d, J = 10.0 Hz, 1H), 4.00 (s, 3H), 1.52 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 176.0, 156.8, 153.0, 148.3, 145.4, 141.9, 139.3, 129.8, 129.6, 123.6, 123.4, 123.3, 121.9, 117.6, 117.2, 115.6, 114.8, 113.4, 109.1, 77.9, 56.4, 28.3 IR (KBr): ν_{max} 2965, 1650, 1584, 1560, 1490, 1351, 1267, 1226, 1156, 1114, 949, 855, 755 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{23}H_{19}O_4S^+$ 391.0999, found 391.1003.

Synthesis of Compound ***34***. To an oven-dried Schlenk tube were added triflate **28** (456.4 mg, 1.00 mmol), DPEPhos (53.9 mg, 0.10 mmol), Cs_2CO_3 (977.5 mg, 3.00 mmol), and $Pd(dba)_2$ (28.8 mg, 0.05 mmol). The flask was degassed with N_2 three times; dry toluene (6 mL) and *N*-methylaniline (163 μL 1.50 mmol) were added to the tube and then stirred for 16 h at 100 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and washed with water. The mixture was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (3/1 PE/CH_2Cl_2) afforded compound **34** (206.7 mg, 50%) as a light yellow solid. Mp 198.0−199.4 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.19−7.11 (m, 4H), 7.03 (d, J = 10.0 Hz, 1H), 6.78−6.72 (m, 3H), 6.68 (s, 1H), 5.71 (d, J = 10.0 Hz, 1H), 3.99 (s, 3H), 3.31 (s, 3H), 1.50 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 174.2, 158.0, 153.9, 149.3, 149.0, 148.3, 145.2, 129.0, 128.7, 123.4, 123.1, 118.2, 117.6, 115.6, 114.8, 114.6, 113.2, 112.4, 107.2, 78.0, 56.4, 40.2, 28.3 IR (KBr): ν_{max} 2971, 1640, 1584, 1597, 1491, 1375, 1297, 1270, 1192, 1088, 949, 761 cm^{-1} HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{26}H_{24}NO_4^+$ 414.1700, found 414.1706.

Synthesis of Compound ***38***. To a stirred solution of phenol **37** (6.99 g, 34.23 mmol) in DMF (68 mL) were sequentially added anhydrous K_2CO_3 (9.46 g, 68.45 mmol) and MeI (2.34 mL, 37.65 mmol) at room temperature. The reaction mixture was allowed to stir for 4 h before it was diluted with water (100 mL). The resulting mixture was extracted with EtOAc (60 mL × 3). The combined organic phases were washed with water and brine and dried over

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anhydrous Na_2SO_4. After filtration and removal of the solvent *in vacuo*, the crude methyl ether was used immediately in the next step.

The crude methyl ether was dissolved in MeOH (100 mL) and stirred at room temperature. H_2O_2 (30 wt % in water, 4.28 mL) was added dropwise; then, $NaHSO_4{\cdot}H_2O$ (709.0 mg, 5.14 mmol) was added in one portion. The solution was stirred for 48 h. After the reaction was confirmed by TLC, saturated $NaHSO_3$ (aq.) was added to quench the reaction. Methanol was removed *in vacuo*, and the residue was dissolved in water and extracted with EtOAc (60 mL × 3). The organic phase was combined, washed with brine, and dried over anhydrous Na_2SO_4. After the solvent was removed, the residue was purified by flash column chromatography (50/1 PE/EtOAc) to obtain compound **38** (7.05 g, 99%) as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.72 (d, J = 8.8 Hz, 1H), 6.55 (d, J = 10.0 Hz, 1H), 6.50 (d, J = 8.8 Hz, 1H), 5.69 (d, J = 10.0 Hz, 1H), 5.27 (brs, 1H), 3.81 (s, 3H), 1.41 (s, 6H) Spectral data match those previously reported.[23]

Synthesis of Compound ***39***. To a round-bottomed flask were added compound **38** (4.39 g, 21.29 mmol) and CH_2Cl_2 (85 mL), followed by isopropyl isocyanate (2.51 mL, 25.55 mmol) and triethylamine (888 μL, 6.387 mmol). The clear mixture was stirred at room temperature for 24 h, at which time the reaction mixture was concentrated *in vacuo*; the residue was purified by flash column chromatography (2/1 PE/CH_2Cl_2) to obtain compound **39** (6.09 g, 98%) as a white solid. Mp 126.4−126.8 °C ^{1}H NMR (400 MHz, $CDCl_3$): 6.84 (d, J = 8.8 Hz, 1H), 6.59 (d, J = 10.0 Hz, 1H), 6.52 (d, J = 8.8 Hz, 1H), 5.64 (d, J = 10.0 Hz, 1H), 4.98 (d, J = 7.6 Hz, 1H), 3.92−3.86 (m, 1H), 3.80 (s, 3H), 1.42 (s, 6H), 1.22 (d, J = 6.4 Hz, 6H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.8, 150.9, 147.7, 137.1, 130.6, 123.0, 116.8, 115.5, 111.7, 75.8, 61.7, 43.5, 27.7, 22.8 IR (ATR): ν_{max} 3307, 2967, 1742, 1710, 1538, 1474, 1371, 1236, 1211, 1115, 1043, 930, 829 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{16}H_{21}NO_4^+$ 291.1465, found 291.1468.

Synthesis of Compound ***40***. Carbamate **39** (5.28 g, 18.12 mmol) was taken in MTBE (110 mL) and cooled to 0 °C under N_2. TMEDA (3.26 mL, 21.74 mmol) was added, followed by slow addition of TMSOTf (3.61 mL, 19.93 mmol). The reaction mixture was stirred at 0 °C for 5 min and then at room temperature for 30 min. The second portion of TMEDA (8.15 mL, 54.36 mmol) was added, and the reaction mixture was cooled to −78 °C. *n*-BuLi (2.5 M in hexane, 21.74 mL, 54.36 mmol) was added dropwise, after which the mixture was stirred at the same temperature for 3 h. TMSCl (11.49 mL, 90.60 mmol) was added, and the mixture was stirred for an additional 30 min, then warmed to room temperature slowly, and stirred for 4 h. The reaction mixture was then quenched by the addition of 1 M HCl (aq.) and stirred for 30 min. The aqueous layer was extracted with EtOAc (60 mL × 3), and the combined organic extract dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1/1 PE/CH_2Cl_2) to obtain compound **40** (6.41 g, 97%) as a white solid. Mp 121.7−123.0 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.62 (s, 1H), 6.57 (d, J = 10.0 Hz, 1H), 5.64 (d, J = 10.0 Hz, 1H), 4.87 (d, J = 8.0 Hz, 1H), 3.95−3.91 (m, 1H), 3.78 (s, 3H), 1.43 (s, 6H), 1.23 (d, J = 6.8 Hz, 6H), 0.24 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.7, 150.4, 147.6, 141.6, 133.7, 130.9, 117.0, 116.6, 116.5, 75.8, 61.8, 43.4, 27.9, 23.0, −1.1 IR (ATR): ν_{max} 3327, 2967, 1702, 1547, 1403, 1366, 1300, 1243, 1162, 1049, 951, 868, 837 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{19}H_{29}NO_4Si^+$ 363.1860, found 363.1871.

Synthesis of Compound ***2***. To a solution of silyl carbamate **40** (5.84 g, 16.07 mmol) in THF (130 mL) at −78 °C was added a solution of *n*-BuLi (2.5 M in hexane, 9.00 mL, 22.50 mmol) dropwise over 30 min. Et_2NH (2.49 mL, 24.11 mmol) was added, and the resulting mixture was stirred at −78 °C for 30 min and then allowed to warm to room temperature over 30 min. Next, Comins' reagent (8.83 g, 22.49 mmol) was added. The mixture was allowed to stir for 16 h at room temperature. Aqueous $NaHCO_3$ (5%, 40 mL) was added, and the mixture was extracted with EtOAc (60 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (PE) afforded compound **2** (6.45 g, 98%) as a white solid. Mp 69.6−70.2 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.67 (s, 1H), 6.56 (d, J = 10.0 Hz, 1H), 5.72 (d, J = 10.0 Hz, 1H), 3.78 (s, 3H), 1.45 (s, 6H), 0.36 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3, 146.9, 140.4, 134.7, 131.9, 118.7 (q, $J_{C\text{-}F}$ = 320.5 Hz), 117.9, 116.9, 116.2, 76.6, 62.4, 27.9, −0.4 IR (ATR): ν_{max} 2981, 1547, 1412, 1368, 1301, 1209, 1117, 1090, 1005, 972, 838, 788, 746 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{16}H_{21}F_3O_5SSi^+$ 410.0826, found 410.0829.

Synthesis of Compound ***41***. To a stirred solution of silyltriflate **2** (492.6 mg, 1.20 mmol) and 2,5-dimethylfuran (637 μL, 6.00 mmol) in MeCN (12 mL) was added CsF (546.8 mg, 3.60 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (60/1 PE/EtOAc) to afford compound **41** (325.4 mg, 95%) as pale yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 (d, J = 5.6 Hz, 1H), 6.69 (d, J = 5.6 Hz, 1H), 6.49 (s, 1H), 6.46 (d, J = 9.6 Hz, 1H), 5.53 (d, J = 9.6 Hz, 1H), 3.73 (s, 3H), 2.02 (s, 3H), 1.82 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.4, 152.1, 149.4, 147.0, 145.9, 133.5, 128.6, 117.0, 111.2, 105.8, 88.7, 88.5, 75.9, 63.0, 27.9, 27.2, 16.8, 15.2 IR (KBr): ν_{max} 2975, 2934, 1619, 1579, 1426, 1381, 1361, 1305, 1137, 1119, 1072, 1007, 859, 723 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{18}H_{21}O_3^+$ 284.1407, found 284.1411.

Synthesis of Compound ***42***. To a stirred solution of silyltriflate **2** (492.6 mg, 1.20 mmol) and morpholine (314 μL, 3.60 mmol) in MeCN (12 mL) was added CsF (546.8 mg, 3.60 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (30/1 PE/EtOAc) to afford compound **42** (323.6 mg, 98%) as a white solid. Mp 107.2−107.5 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.57 (d, J = 10.0 Hz, 1H), 6.02 (d, J = 2.0 Hz, 1H), 5.99 (d, J = 2.0 Hz, 1H), 5.41 (d, J = 10.0 Hz, 1H), 3.83 (t, J = 4.8 Hz, 4H), 3.80 (s, 3H), 3.15 (t, J = 4.8 Hz, 4H), 1.40 (s, 6H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.0, 154.5, 152.4, 125.8, 116.6, 103.6, 96.4, 91.5, 76.0, 66.8, 55.4, 49.1, 27.8 IR (KBr): ν_{max} 3054, 1633, 1564, 1504, 1443, 1427, 1246, 1212, 1179, 1164, 1115, 1102, 978, 821, 767 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{16}H_{21}NO_3^+$ 275.1516, found 275.1518.

Synthesis of Compound ***43***. *N-tert*-butyl-α-phenylnitrone (177.2 mg, 1.00 mmol) was added to a solution of silyltriflate **2** (492.6 mg, 1.20 mmol) and CsF (607.6 mg, 4.00 mmol) in THF (20 mL) under a N_2 atmosphere. The solution was stirred at 65 °C for 24 h, then cooled to room temperature, and filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (120/1 PE/EtOAc) to afford compound **43** (345.7 mg, 95%) as a pale yellow syrup. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.27 (m, 4H), 7.26−7.21 (m, 1H) 6.43 (d, J = 10.0 Hz, 1H), 6.12 (s, 1H), 5.59 (s, 1H), 5.42 (d, J = 10.0 Hz, 1H), 3.34 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.18 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 159.1, 155.5, 151.3, 143.5, 128.5, 127.6, 127.4, 126.3, 116.9, 112.8, 107.6, 91.4, 76.3, 65.3, 61.4, 60.6, 28.0, 27.5, 25.4 IR (KBr): ν_{max} 2972, 1611, 1591, 1466, 1454, 1363, 1313, 1213, 1124, 1086, 818, 696 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{23}H_{27}NO_3^+$ 365.1985, found 365.1989.

Synthesis of Compound ***45***. TBSCl (5.43 g, 36.00 mmol) was added to a stirred mixture of 7-hydroxycoumarin **4** (4.86 g, 30.00 mmol) and Et_3N (8.34 mL, 60.00 mmol) in 60 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for 4 h. Saturated NH_4Cl was added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give a light brown solid, which was used without further purification.

Methyl magnesium chloride (3 M in THF, 30.00 mL, 90.00 mmol) was added dropwise to a solution of crude compound **44** in 120 mL of anhydrous THF at 0 °C. The resulting brown solution was stirred at room temperature for 24 h. Saturated NH_4Cl was then added, and

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the layers were separated. The aqueous layer was extracted with EtOAc (80 mL × 3). The organic layers were combined, washed with water and brine, then dried over anhydrous Na_2SO_4, and evaporated to give a yellowish solid that was used in the next step immediately by dissolving it in 120 mL of toluene and adding 15 g of silica gel to the solution. The reaction mixture was heated under reflux for 12 h. The reaction was then cooled to room temperature and filtered. The silica gel was extensively washed with EtOAc. The filtrate was evaporated to give the crude product, which was purified by flash chromatography (PE) to afford compound **45** (8.29 g, 95%, 3 steps) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.82 (d, J = 7.6 Hz, 1H), 6.35−6.31 (m, 2H), 6.27 (d, J = 9.6 Hz, 1H), 5.47 (d, J = 9.6 Hz, 1H), 1.41 (s, 6H), 0.97 (s, 9H), 0.19 (s, 6H) Spectral data match those previously reported.[17]

Synthesis of Compound ***46***. TBAF·3H_2O (7.64 g, 24.20 mmol) was dissolved in THF (90 mL) at room temperature; then, compound **45** (6.39 g, 22.00 mmol) was added. The mixture was allowed to stir at room temperature for 30 min. Water was added to quench the reaction; then, the mixture was concentrated *in vacuo* and diluted with EtOAc (50 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (50 mL × 3). The organic layers were combined, washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated to give crude phenol as a pale yellow solid that was used immediately in the next step.

To a round-bottomed flask was added crude phenol and CH_2Cl_2 (90 mL), followed by isopropyl isocyanate (2.60 mL, 26.40 mmol) and triethylamine (0.92 mL, 6.60 mmol). The clear mixture was stirred at room temperature for 24 h, at which time the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography (3/1 PE/CH_2Cl_2) to obtain compound **46** (5.66 g, 98%) as a white solid. Mp 108.7−109.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92 (d, J = 8.0 Hz, 1H), 6.62 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 6.28 (d, J = 10.0 Hz, 1H), 5.55 (d, J = 10.0 Hz, 1H), 4.93 (d, J = 7.2 Hz, 1H), 3.91−3.81 (m, 1H), 1.41 (s, 6H), 1.20 (d, J = 6.4 Hz, 6H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.5, 153.4, 151.4, 129.7, 126.4, 121.6, 118.4, 113.7, 109.9, 76.3, 43.3, 28.0, 22.8 IR (KBr): ν_{max} 3284, 2973, 1729, 1697, 1533, 1495, 1464, 1238, 1143, 1117, 1026, 989, 867, 822, 661 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{15}H_{19}NO_3^+$ 261.1359, found 261.1362.

Synthesis of Compound ***47***. Carbamate **46** (5.23 g, 20.00 mmol) was taken in MTBE (120 mL) and cooled to 0 °C under N_2. TMEDA (3.60 mL, 24.00 mmol) was added, followed by slow addition of TMSOTf (3.98 mL, 22.00 mmol). The reaction mixture was stirred at 0 °C for 5 min and then at room temperature for 30 min. The second portion of TMEDA (6.60 mL, 44.00 mmol) was added, and the reaction mixture was cooled to −78 °C. Then, *sec*-BuLi (1.0 M in hexane, 44.0 mL, 44.00 mmol) was added dropwise, after which the mixture was stirred at the same temperature for 1 h. TMSCl (12.68 mL, 100.0 mmol) was added, and the mixture was stirred for an additional 30 min, then warmed to room temperature slowly, and stirred for 4 h. The reaction mixture was then quenched by the addition of 1 M HCl (aq.) and stirred for 30 min. The aqueous layer was extracted with EtOAc (80 mL × 3), and the combined organic extract dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (12/4/1 PE/CH_2Cl_2/EtOAc) to obtain compound **47** (5.56 g, 83%) as a white solid. Mp 128.7−129.0 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 8.0 Hz, 1H), 6.25 (d, J = 9.6 Hz, 1H), 5.51 (d, J = 9.6 Hz, 1H), 4.73 (d, J = 8.0 Hz, 1H), 3.95−3.84 (m, 1H), 1.42 (s, 6H), 1.21 (d, J = 6.4 Hz, 6H), 0.30 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.3, 155.6, 153.8, 129.2, 128.0, 122.0, 118.6, 117.6, 114.9, 76.4, 43.3, 28.0, 22.9, 1.1 IR (ATR): ν_{max} 3284, 2971, 1734, 1701, 1536, 1452, 1255, 1244, 1165, 1053, 926, 838, 758 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{18}H_{27}NO_3Si^+$ 333.1755, found 333.1757.

Synthesis of Compound ***3***. To a solution of silyl carbamate **47** (3.11 g, 9.33 mmol) in THF (94 mL) at −78 °C was added a solution of *n*-BuLi (2.5 M in hexane, 5.22 mL, 13.06 mmol) dropwise over 30 min. Et_2NH (1.45 mL, 14.00 mmol) was added, and the resulting mixture was stirred at −78 °C for 30 min and then allowed to warm to room temperature over 30 min. Next, Comins' reagent (5.13 g, 13.06 mmol) was added. The mixture was allowed to stir for 16 h at room temperature. Aqueous $NaHCO_3$ (5%, 30 mL) was added, and the mixture was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (PE) afforded compound **3** (3.25 g, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.27 (d, J = 10.0 Hz, 1H), 5.61 (d, J = 10.0 Hz, 1H), 1.45 (s, 6H), 0.38 (s, 9H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.7, 154.0, 130.9, 128.3, 121.3, 119.9, 119.4, 118.6 (q, $J_{C\text{-}F}$ = 320.9 Hz), 112.4, 77.3, 28.0, 1.0 IR (ATR): ν_{max} 2978, 1575, 1447, 1421, 1408, 1370, 1250, 1218, 1142, 1001, 853, 606 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{15}H_{19}F_3O_4SSi^+$ 380.0720, found 380.0727.

Synthesis of Compound ***48***. To a stirred solution of silyltriflate **3** (456.5 mg, 1.20 mmol) and 2,5-dimethylfuran (637 μL, 6.00 mmol) in MeCN (12 mL) was added CsF (546.8 mg, 3.60 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (40/1 PE/EtOAc) to afford compound **48** (293.6 mg, 96%) as pale yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (d, J = 5.2 Hz, 1H), 6.70 (d, J = 5.2 Hz, 1H), 6.63 (d, J = 7.2 Hz, 1H), 6.58 (d, J = 7.2 Hz, 1H), 6.29 (d, J = 10.0 Hz, 1H), 5.56 (d, J = 10.0 Hz, 1H), 2.02 (s, 3H), 1.83 (s, 3H), 1.44 (s, 3H), 1.39 (s, 3H) ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.2, 146.6, 146.2, 146.0, 136.2, 130.5, 123.4, 122.5, 120.5, 111.3, 88.9, 88.4, 75.9, 28.4, 27.4, 16.9, 15.2 IR (KBr): ν_{max} 2975, 2932, 1622, 1449, 1400, 1342, 1263, 1209, 1131, 988, 859, 823 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{17}H_{18}O_2^+$ 254.1301, found 254.1309.

Synthesis of Compound ***49***. To a stirred solution of silyltriflate **3** (456.5 mg, 1.20 mmol) and morpholine (314 μL, 3.60 mmol) in MeCN (12 mL) was added CsF (546.8 mg, 3.60 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (30/1 PE/EtOAc) to afford compound **49** (290.5 mg, 99%) as a white solid. Mp 84.0−84.9 °C ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.87 (d, J = 7.8 Hz, 1H), 6.46 (dd, J = 7.8 Hz, 1.8 Hz, 1H), 6.36 (d, J = 1.8 Hz, 1H), 6.26 (d, J = 10.8 Hz, 1H), 5.45 (d, J = 10.8 Hz, 1H), 3.83 (t, J = 4.8 Hz, 4H), 3.14 (t, J = 4.8 Hz, 4H), 1.41 (s, 6H).

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.9, 152.2, 127.6, 126.8, 121.8, 113.8, 107.6, 103.3, 76.2, 66.8, 48.9, 28.0 IR (KBr): ν_{max} 2960, 1615, 1552, 1508, 1451, 1354, 1265, 1185, 1112, 1044, 987, 830, 795 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{15}H_{19}NO_2^+$ 245.1410, found 245.1413.

Synthesis of Compound ***50***. *N-tert*-butyl-α-phenylnitrone (177.2 mg, 1.00 mmol) was added to a solution of silyltriflate **3** (456.5 mg, 1.20 mmol) and CsF (607.6 mg, 4.00 mmol) in THF (20 mL) under a N_2 atmosphere. The solution was stirred at 65 °C for 16 h, then cooled to room temperature, and filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (100/1 PE/EtOAc) to afford compound **50** (243.9 mg, 73%) as a white solid. Mp 68.2−68.9 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.31 (d, J = 8.0 Hz, 1H), 6.21 (d, J = 10.0 Hz, 1H), 5.58 (s, 1H), 5.34 (d, J = 10.0 Hz, 1H), 1.34 (s, 3H), 1.18 (s, 9H), 0.80 (s, 3H) ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.4, 148.9, 143.3, 128.0, 127.8, 127.2, 127.0, 127.0, 122.0, 117.0, 115.3, 98.6, 76.4, 64.8, 61.3, 28.3, 26.5, 25.4 IR (KBr): ν_{max} 2970, 1619, 1476, 1453, 1362, 1327, 1294, 1211, 1118, 1085, 1045, 805, 799 cm^{-1} HRMS-EI (m/z): [M]$^+$ calcd for $C_{22}H_{25}NO_2^+$ 335.1880, found 335.1881.

Synthesis of Compound ***51***. To a solution of triflate **1a** (2.92 g, 6.00 mmol) in THF (30 mL) was added 20% $Pd(OH)_2$/C (84.3 mg, 0.12 mmol). The mixture was placed under an atmosphere of hydrogen, stirred for 24 h at room temperature, and then filtered over Celite (EtOAc eluent). After evaporation of the solvent under

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reduced pressure, the crude phenol was obtained as a red solid, which was then dissolved in CH_2Cl_2 (24 mL) and cooled to 0 °C. MOMBr (734 μL, 9.00 mmol) and DIPEA (2.48 mL, 15.00 mmol) were added successively, and the mixture was then warmed to room temperature and stirred for 4 h. Saturated NH_4Cl (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure afforded the crude product, which was further purified by flash chromatography (200/1 PE/EtOAc) to afford compound **51** (2.46 g, 93%) as a colorless syrup. ^1H NMR (400 MHz, $CDCl_3$): δ 6.75 (s, 1H), 5.12 (s, 2H), 3.47 (s, 3H), 2.76 (t, J = 6.8 Hz, 2H), 1.77 (t, J = 6.8 Hz, 2H), 1.33 (s, 6H), 0.45 (s, 9H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 153.7, 147.7, 136.4, 134.0, 119.5, 118.8 (q, $J_{C\text{-}F}$ = 321.4 Hz), 106.6, 95.1, 74.0, 56.3, 32.9, 27.0, 23.8, 2.0 IR (ATR): ν_{max} 2974, 1600, 1569, 1404, 1315, 1200, 1152, 1120, 1060, 993, 924, 839, 599 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{17}H_{25}F_3O_6SSi^+$ 442.1088, found 442.1095.

Synthesis of Compound ***52***. To a solution of triflate **1a** (1.95 g, 4.00 mmol) in THF (20 mL) was added 20% $Pd(OH)_2/C$ (56.2 mg, 0.08 mmol). The mixture was placed under an atmosphere of hydrogen, stirred for 24 h at room temperature, and then filtered over Celite (EtOAc eluent). After evaporation of the solvent under reduced pressure, the crude phenol was obtained as a red solid, which was then dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. BzCl (0.56 mL, 4.80 mmol), Et_3N (0.83 mL, 6.00 mmol), and 4-dimethylaminopyridine (DMAP, 4.9 mg, 0.04 mmol) were added successively, and the mixture was then warmed to room temperature and stirred for 4 h. Saturated $NaHCO_3$ (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was further purified by flash chromatography (120/1 PE/EtOAc) to afford compound **52** (1.74 g, 86%) as a white solid. Mp 88.7−89.3 °C ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 6.77 (s, 1H), 2.86 (t, J = 6.8 Hz, 2H), 1.82 (t, J = 6.8 Hz, 2H), 1.35 (s, 6H), 0.47 (s, 9H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.1, 153.9, 141.4, 136.4, 135.0, 133.9, 130.4, 128.6, 128.5, 125.5, 118.4 (q, $J_{C\text{-}F}$ = 321.4 Hz), 114.3, 74.4, 32.7, 27.2, 24.0, 1.8 IR (ATR): ν_{max} 2977, 1748, 1403, 1259, 1246, 1229, 1198, 1172, 1154, 1120, 1078, 1051, 891, 837, 710, 628 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{22}H_{25}F_3O_6SSi^+$ 502.1088, found 502.1094.

Synthesis of Compound ***53***. To a solution of triflate **1a** (2.92 g, 6.00 mmol) in THF (30 mL) was added 20% $Pd(OH)_2/C$ (84.3 mg, 0.12 mmol). The mixture was placed under an atmosphere of hydrogen, stirred for 24 h at room temperature, and then filtered over Celite (EtOAc eluent). After evaporation of the solvent under reduced pressure, the crude phenol was obtained as a red solid, which was then dissolved in CH_2Cl_2 (24 mL) and cooled to 0 °C. TsCl (1.20 g, 6.30 mmol) and Et_3N (1.25 mL, 9.00 mmol) were added successively, and the mixture was then warmed to room temperature and stirred for 4 h. Saturated $NaHCO_3$ (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was further purified by flash chromatography (80/1 PE/EtOAc) to afford compound **53** (2.71 g, 82%) as a white solid. Mp 102.8−104.1 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 6.85 (s, 1H), 2.79 (t, J = 6.0 Hz, 2H), 2.45 (s, 3H), 1.79 (t, J = 6.0 Hz, 2H), 1.34 (s, 6H), 0.32 (s, 9H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 153.8, 145.8, 139.5, 137.0, 135.4, 131.7, 129.5, 128.8, 126.5, 118.4 (q, $J_{C\text{-}F}$ = 320.9 Hz), 114.7, 74.7, 32.5, 27.1, 23.8, 21.7, 1.6 IR (ATR): ν_{max} 2980, 1598, 1573, 1415, 1381, 1227, 1191, 1175, 1133, 1116, 1064, 884, 833, 810, 645, 548 cm^{-1}.

HRMS-EI (m/z): $[M]^+$ calcd for $C_{22}H_{27}F_3O_7S_2Si^+$ 552.0914, found 552.0922.

Synthesis of Compound ***54***. *N-tert*-butyl-α-phenylnitrone (184.3 mg, 1.04 mmol) was added to a solution of silyltriflate **51** (551.3 mg, 1.25 mmol) and CsF (631.9 mg, 4.16 mmol) in THF (20 mL) under a N_2 atmosphere. The solution was stirred at 65 °C for 48 h, then cooled to room temperature, and filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (60/1 PE/EtOAc) to afford compound **54** (410.2 mg, quant.) as a white solid. Mp 86.7−87.8 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J = 7.2 Hz, 2H), 7.27 (t, J = 7.2 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 6.01 (s, 1H), 5.58 (s, 1H), 4.96 (d, J = 6.4 Hz, 1H), 4.83 (d, J = 6.4 Hz, 1H), 3.07 (s, 3H), 2.68−2.58 (m, 2H), 1.79−1.75 (m, 2H), 1.33 (s, 3H), 1.31 (s, 3H), 1.18 (s, 9H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 156.6, 155.5, 150.7, 143.5, 128.1, 127.6, 126.9, 108.4, 95.5, 95.4, 93.6, 74.5, 65.4, 61.3, 55.7, 32.0, 27.0, 26.4, 25.4, 16.5 IR (ATR): ν_{max} 2976, 1748, 1404, 1229, 1198, 1120, 1077, 1065, 1022, 929, 837, 808, 729 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{24}H_{31}NO_2^+$ 397.2248, found 397.2256.

Synthesis of Compound ***55***. To a stirred solution of silyltriflate **52** (552.8 mg, 1.10 mmol) and trifluoromethanesulfonanilide (225.2 mg, 1.00 mmol) in MeCN (10 mL) was added CsF (455.7 mg, 3.00 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (60/1 PE/EtOAc) to afford compound **55** (414.8 mg, 82%) as a white solid. Mp 66.3−68.6 °C ^1H NMR (400 MHz, $CDCl_3$): δ 8.21−8.19 (m, 2H), 7.65 (tt, J = 7.2 Hz, 1.2 Hz, 1H), 7.55−7.51 (m, 4H), 7.42−7.38 (m, 2H), 7.32 (tt, J = 7.2 Hz, 2.0 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 6.79 (d, J = 2.0 Hz, 1H), 3.01 (brs, 1H), 2.58 (brs, 1H), 1.82−1.77 (m, 2H), 1.33 (s, 3H), 1.23 (s, 3H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.7, 156.0, 149.7, 138.5, 138.0, 133.8, 130.2, 129.4, 129.2, 128.6, 128.2, 126.9, 120.2 (q, $J_{C\text{-}F}$ = 324.6 Hz), 119.3, 114.9, 112.5, 75.0, 31.9, 26.6, 19.0 IR (ATR): ν_{max} 2978, 1737, 1584, 1397, 1245, 1202, 1141, 1117, 1058, 1025, 960, 807, 753, 706, 626 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{25}H_{22}F_3NO_5S^+$ 505.1165, found 505.1169.

Synthesis of Compound ***56***. To a stirred solution of silyltriflate **53** (663.2 mg, 1.20 mmol) and ketene diethyl acetal (238 μL, 1.80 mmol) in MeCN (18 mL) was added CsF (364.6 mg, 2.40 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product as a yellow oil, which was dissolved in 12 mL of acetone and 3.0 mL of 1 M HCl (aq.) and stirred in the dark for 30 min. Saturated $NaHCO_3$ (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was further purified by flash chromatography (7/1 PE/EtOAc) to afford compound **56** (361.3 mg, 81%) as a white solid. Mp 137.1−137.9 °C ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 6.66 (s, 1H), 3.68 (s, 2H), 2.69 (t, J = 6.8 Hz, 2H), 2.44 (s, 3H), 1.84 (t, J = 6.8 Hz, 2H), 1.36 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 180.4, 161.8, 151.3, 145.5, 138.6, 132.2, 130.1, 129.8, 128.5, 115.7, 113.3, 76.7, 49.7, 31.6, 26.8, 21.7, 18.8 IR (ATR): ν_{max} 2988, 1751, 1584, 1482, 1372, 1320, 1193, 1170, 1083, 1035, 956, 808, 764, 665 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{20}H_{20}O_5S^+$ 372.1026, found 372.1034.

Synthesis of Compound ***57***. To a solution of triflate **1a** (4.78 g, 9.72 mmol) in THF (50 mL) was added 20% $Pd(OH)_2/C$ (137.9 mg, 0.196 mmol). The mixture was placed under an atmosphere of hydrogen, stirred for 24 h at room temperature, and then filtered over Celite (EtOAc eluent). After evaporation of the solvent under reduced pressure, the crude phenol was obtained as a red solid, which was then dissolved in CH_2Cl_2 (50 mL) and cooled to −20 °C. Pyridine (3.95 mL, 49.10 mmol) was added and then Tf_2O (2.48 mL, 14.73 mmol) was added dropwise, after which the mixture was stirred at the same temperature for 12 h. Saturated $NaHCO_3$ (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The

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combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was further purified by flash chromatography (150/1 PE/EtOAc) to afford compound **57** (4.98 g, 96%) as a white solid. Mp 42.1−42.7 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (s, 1H), 2.86 (t, J = 6.4 Hz, 2H), 1.83 (t, J = 6.4 Hz, 2H), 1.36 (s, 6H), 0.48 (s, 9H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.1, 139.6, 137.1, 135.3, 128.0, 118.6 (q, J_{C-F} = 320.9 Hz), 118.5 (q, J_{C-F} = 320.9 Hz), 113.1, 75.2, 32.4, 27.1, 23.9, 1.7 IR (ATR): ν_{max} 2977, 1775, 1584, 1422, 1404, 1243, 1209, 1132, 1059, 1022, 855, 805, 710, 655, 596 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{16}H_{20}F_6O_7S_2Si^+$ 530.0318, found 530.0320.

Synthesis of Compound ***58***. To a stirred solution of silyltriflate **57** (3.05 g, 5.75 mmol) and ketene diethyl acetal (910 μL, 6.90 mmol) in MeCN (69 mL) was added CsF (1.75 g, 11.50 mmol). The solution was stirred at room temperature for 12 h and then filtered over silica gel (CH_2Cl_2 eluent). Evaporation under reduced pressure afforded the crude product as a brown oil, which was dissolved in 58 mL of acetone and 15.0 mL of 1 M HCl (aq.) and stirred in the dark for 30 min. Saturated $NaHCO_3$ (aq.) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with EtOAc (60 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was further purified by flash chromatography (40/1 → 30/1 → 20/1 PE/EtOAc) to afford compound **58** (1.25 g, 62%) as a white solid. Mp 78.6−79.2 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (s, 1H), 3.86 (s, 2H), 2.76 (t, J = 6.8 Hz, 2H), 1.89 (t, J = 6.8 Hz, 2H), 1.40 (s, 6H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 179.5, 162.0, 151.8, 137.3, 129.2, 118.6 (q, J_{C-F} = 324.6 Hz), 117.3, 112.1, 77.3, 50.4, 31.4, 26.7, 18.9 IR (ATR): ν_{max} 2987, 1774, 1756, 1421, 1296, 1209, 1153, 1080, 1021, 954, 908, 854, 804, 655, 601 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{13}F_3O_5S^+$ 350.0430, found 350.0432.

Synthesis of Compound ***59***. To a solution of compound **58** (350.0 mg, 1.00 mmol) and 2,5-dimethylfuran (531 μL, 5.00 mmol) dissolved in anhydrous toluene (10 mL) was slowly added PhLi (1.0 M in Et_2O, 1.30 mL, 1.30 mmol) at −78 °C. After stirring for 1 min at the same temperature, the mixture was stirred for 2 h at room temperature, and an aqueous phosphate buffer solution (pH = 7, 15 mL) was added. The mixture was extracted with EtOAc (15 mL × 3), the combined organic extract was washed with brine and dried over Na_2SO_4, and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (20/1 PE/EtOAc) to give compound **59** (300.1 mg, 80%) as a white solid. Mp 108.8−109.9 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 7.6 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 6.84 (d, J = 5.2 Hz, 1H), 6.72 (d, J = 5.2 Hz, 1H), 6.62 (s, 1H), 4.47 (d, J = 18.0 Hz, 1H), 4.38 (d, J = 18.0 Hz, 1H), 2.53 (dt, J = 16.4 Hz, 6.4 Hz, 1H), 2.40 (dt, J = 16.4 Hz, 6.4 Hz, 1H), 1.84 (s, 3H), 1.81 (s, 3H), 1.72 (t, J = 7.2 Hz, 2H), 1.29 (s, 3H), 1.26 (s, 3H) $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 196.7, 152.0, 151.1, 147.0, 145.7, 142.0, 136.7, 133.3, 128.8, 128.0, 126.1, 114.4, 109.0, 89.6, 87.9, 73.2, 37.9, 32.8, 27.0, 26.0, 20.3, 17.6, 15.2 IR (ATR): ν_{max} 2973, 2933, 1679, 1598, 1448, 1432, 1328, 1259, 1214, 1112, 1050, 992, 888, 847, 755, 689 cm^{-1} HRMS-EI (m/z): $[M]^+$ calcd for $C_{25}H_{26}O_3^+$ 374.1876, found 374.1885.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00493.

Copies of ^{1}H NMR spectra for compounds **1b**, **2**, **3**, **5**−**16**, **18**, **19**, **22**−**24**, **26**−**34**, **38**−**43**, and **45**−**49** and copies of $^{13}C\{^1H\}$ NMR spectra for compounds **1b**, **2**, **3**, **7**−**16**, **18**, **19**, **22**−**24**, **26**−**34**, **39**−**43**, and **46**−**59**

(PDF)

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Notes

The authors declare no competing financial interest.

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