Organic & Biomolecular Chemistry

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Cite this: DOI: 10.1039/c7ob00118e

Efficient synthesis of polymethoxyselenoflavones *via* regioselective direct C–H arylation of selenochromones†

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Received 17th January 2017,
Accepted 13th March 2017

DOI: 10.1039/c7ob00118e

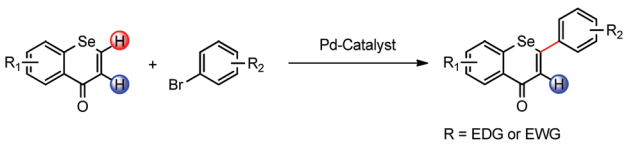
rsc.li/obc

Substantial research has suggested that the configuration and the total number of functional groups on flavones influence their bioactivity. To investigate the changes in the biological activities of selenoflavones in relationship to structural changes, the development of a generally applicable synthetic method was a key. Until now, an efficient pathway for palladium-catalyzed direct arylation with the selenocyclic enone systems is not known in the literature. We herein introduce a simple direct C–H arylation of two difficult coupling partners, selenochromones and electron-rich aryl bromide, affording diverse polymethoxyseleno flavones with great efficiency and high selectivity.

Introduction

Flavones have received intensive attention from medicinal chemists due to their unique structure–activity relationship contributing to beneficial roles in human health including anti-oxidant, anti-inflammatory, anti-cancer, and estrogen-related functions.[1] To investigate the changes in the biological activities of flavones in relationship to structural changes, we considered it worthwhile to substitute the heteroatom in the pyran ring with selenium, since selenium itself could have an effect on mammalian metabolism to prevent cancer, cardiovascular and neurodegenerative diseases.[2] We have recently reported that selenoflavones/selenoflavanones, and selenium substitution along with functional group modifications on benzopyran showed improvements in polarity and lipophilicity.[3] Moreover, *in vitro* and *in vivo* assays indicated more potent anti-oxidant effects, indicating that selenocompounds could be used as promising neuroprotective agents.

Substantial research has suggested that the configuration and the total number of methoxy groups on flavones influence their bioactivity.[4] As part of our ongoing investigation to evaluate diverse selenocompounds, we decided to synthesize polymethoxyselenoflavones (PMSFs). Although Friedel–Crafts acylation was successful in the previous formation of selenoflavones, this synthetic approach was not applicable for PMSFs. Electron-rich aromatic substituents decomposed under various acylation conditions. Until now, a wide range of cyclic substrates have been successfully employed in palladium-catalyzed direct arylations.[5,6] The Pd(0)-catalyzed Heck reaction is one of the most intensively studied methods for C–C bond formation in organic synthesis,[5] and Pd(II)-catalyzed oxidative boron-Heck coupling is also proven to be successful in cyclic enone systems.[6] Despite significant progress in this area, an efficient pathway for palladium-catalyzed direct arylation with the selenocyclic enone systems is not known in the literature. Thus, our group was keen to develop a catalytic process which employed palladium-catalyzed direct arylation of C-2 functionalized selenochromones for the synthesis of PMSFs (Scheme 1).



Scheme 1 A new synthetic approach to PMSFs.

Results and discussion

The traditional Vilsmeier–Haack reaction has been a useful means to introduce the formyl group onto aromatic substrates.[7] Nevertheless, the combination of phosphorus oxychloride, and DMF or *N*-methylformanilide with the starting aryl bromide gave mixtures of formylated products with no regioselectivity along with demethylation. On the other hand, a Rieche formylation[8] provided a clean and high yielding method for the desired electron-rich aromatic aldehyde **7** from

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† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C spectral data. See DOI: 10.1039/c7ob00118e

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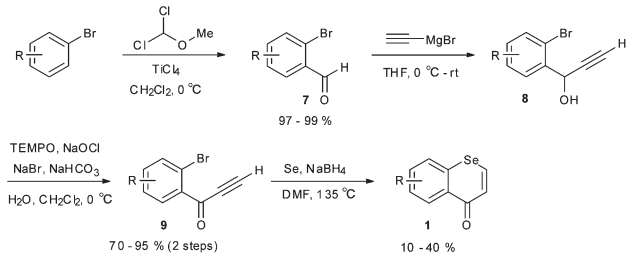


Scheme 2 Synthesis of key intermediate **1**.

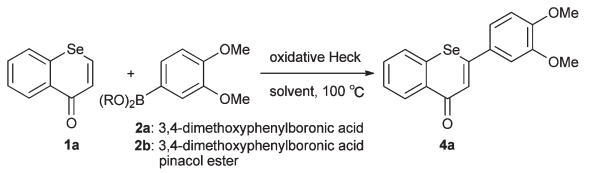
commercially available aryl substrates (Scheme 2). A routine Grignard reaction followed by TEMPO oxidation[9] gave the desired cyclization precursor. Other mild oxidants such as manganese oxide and Dess–Martin periodinane were also tested, but TEMPO gave the best results. An *in situ* method for generating selenides, utilizing selenium and sodium borohydride in DMF, was used in the synthesis of selenochromones **1**.[10] However, only moderate yields of cyclic enones were obtained due to the fact that the precise temperature and equivalent controls needed for the reaction could not be achieved.

Selenochromone **1a** and 3,4-dimethoxyphenylboronic acid **2a** were selected as the model substrates to screen reaction conditions, and to investigate the feasibility of a Pd(II)-catalyzed oxidative boron-Heck coupling reaction. It seemed to be a promising method for Heck type coupling on selenocyclic systems, since palladium-catalyzed 1,4-addition of arylboronic acids to electron-deficient systems was well reported.[11]

Previous studies showed that the best Lewis acid for similar transformation was $Fe(OTf)_3$.[11c] Therefore, we used $Fe(OTf)_3$ as the co-catalyst of choice in our screening of reaction conditions. The DDQ/KNO_2 catalytic system was employed for the dehydrogenation process. Another oxidative boron-Heck method, base- and ligand-free $Pd(II)^{2+}$ systems, was also considered with the use of $Pd(OAc)_2$ and trifluoromethanesulfonic acid in DMSO.[11d] 5-Nitro-1,10-phenanthroline and 3,4-dimethoxyphenylboronic acid pinacol ester were tested in order to screen appropriate ligands.[11e] Temperatures from 60 °C to 100 °C were tested in all cases (Table 1). Despite our initial optimism, however, all oxidative boron-Heck conditions failed to produce selenoflavones and selenoflavanones. Issues related to electrophilic attack of arylpalladium and its subsequent migration could be a plausible explanation for this problem.[12]

Cyclic enones are considered to be challenging substrates for Pd(0)-catalyzed Heck conditions, since the unfavorable *syn* β-H elimination step in the traditional Heck pathway often generates conjugate addition products instead.[13] Indeed, PMSFs have never been synthesized because of their synthetic difficulties; consequently, biological studies have not been carried out. Nonetheless, our next aim was to efficiently and selectively control the synthesis of PMSFs by changing variables in the Heck reaction. To investigate the feasibility of Pd(0)-catalyzed Heck coupling, we started with Fagnou direct arylation conditions[5b] by utilizing palladium acetate,

Table 1 Screening for oxidative boron-Heck reaction[a]

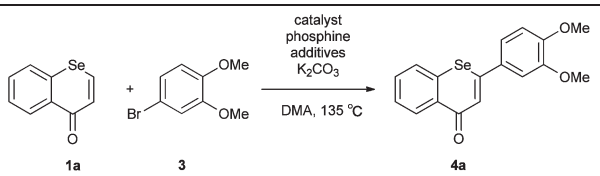


Entry	Aryl	Ligand	Lewis acid	Solvent	Yield[b] (%)
1[c]	**2a**	—	$Fe(OTf)_3$	PivOH	0
2[c]	**2a**	—	$Fe(OTf)_3$	DMSO	0
3[d]	**2a**	—	—	DMSO	Trace
4[e]	**2a**	5-Nitro-phen	—	DMSO	Trace
5[e]	**2b**	5-Nitro-phen	—	DMSO	Trace

[a] Reaction conditions: selenochromone **1a** (0.1 mmol), **2** (0.3 mmol), catalyst (40 mol%), ligand (80 mol%), oxidant (40 mol%), Lewis acid (20 mol%), solvent (0.1 M), 100 °C. [b] Isolated yields. [c] $Pd(OAc)_2$ (40 mol%), DDQ/KNO_2 (40 mol%), $Fe(OTf)_3$ (20 mol%), 24 h. [d] $Pd(OAc)_2$ (40 mol%), TfOH (80 mol%), O_2, 72 h. [e] $Pd(TFA)_2$ (40 mol%), 5-nitro-1,10-phenanthroline (80 mol%), O_2, 48 h.

phosphoniumtetrafluoroborate salt (PCy_3HBF_4), pivalic acid, and potassium carbonate in DMA. Selenochromone **1a** and 1,2-dimethoxy-4-bromobenzene **3** were selected as model compounds, but only 5% of the desired coupling product was obtained under the initial conditions (entry 1, Table 2). Several references suggested that the use of phosphonium salts as additives might enhance the reactivity of Heck coupling,[5h,14] and further addition of tri-*tert*-butylphosphonium hydrogen tetrafluoroborate ($P(t\text{-}Bu)_3HBF_4$) to the Fagnou conditions significantly improved the product yield to 30% (entry 4, Table 2). To find a suitable catalytic system, various palladium and phosphine ligands were screened. Allowing the reaction

Table 2 Reaction optimization of direct C–H arylation[a]



Entry	Catalyst	Ligand	Additives	Yield[b] (%)
1[c]	$Pd(OAc)_2$	PCy_3HBF_4	PivOH	<5
2[c]	$Pd(OAc)_2$	PCy_3HBF_4	$P^tBu_3HBF_4$	22
3[c]	$Pd(OAc)_2$	PCy_3HBF_4	PivOH/$P^tBu_3HBF_4$	25
4	$Pd(OAc)_2$	PCy_3HBF_4	PivOH/$P^tBu_3HBF_4$	30
5	$Pd(PPh_3)_2Cl_2$	PCy_3HBF_4	PivOH/$P^tBu_3HBF_4$	7
6	$Pd(PPh_3)_4$	PCy_3HBF_4	PivOH/$P^tBu_3HBF_4$	6
7	$Pd(PhCN)_2Cl_2$	PCy_3HBF_4	PivOH/$P^tBu_3HBF_4$	21
8	$Pd(OAc)_2$	XPhos	PivOH/$P^tBu_3HBF_4$	46
9	$Pd(OAc)_2$	SPhos	PivOH/$P^tBu_3HBF_4$	43
10	$Pd(OAc)_2$	RuPhos	PivOH/$P^tBu_3HBF_4$	45
11	$Pd(OAc)_2$	*t*BuXPhos	PivOH/$P^tBu_3HBF_4$	18

[a] Reaction conditions: selenochromone **1a** (0.1 mmol), aryl bromide **3** (0.2 mmol), catalyst (40 mol%), ligand (80 mol%), acid additive (1.5 equiv.), phosphine additive (80 mol%), K_2CO_3 (3 equiv.), DMA (0.1 M), 135 °C, 15 h. [b] Isolated yields. [c] 12 h.

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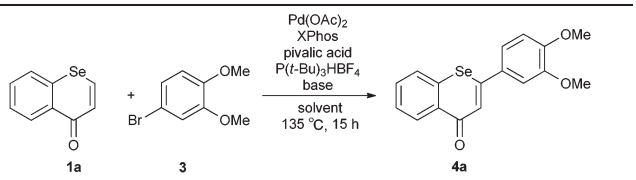
mixture to stir for 15 h resulted in full consumption of the starting material, and a combination of $Pd(OAc)_2$, X-Phos, and the additives afforded the selenoflavone in 46% (entry 8, Table 2). The reactivity of the direct C–H arylation was also found to be very dependent on the base employed, since a noteworthy increase in activity was observed with Cs_2CO_3 in DMA (entry 1, Table 3). With further optimal equivalent screening, 60% of selenoflavone **4a** was obtained (entry 7, Table 3).

Under our optimized reaction conditions (20 mol% of Pd $(OAc)_2$, 40 mol% of XPhos, 40 mol% of $P^tBu_3HBF_4$, 1.5 equiv. of pivalic acid, 3 equiv. of Cs_2CO_3, DMA (0.1 M), 135 °C), the coupling reactions between a variety of aryl bromides and selenochromones were examined to investigate the scope and limitations of the developed method, as well as to exploit diverse selenocompounds (Table 4). The reaction was compatible with a range of electron-rich and electron-deficient aryl bromides, furnishing C-2 substituted Heck coupling products in moderate to good yields (**4**). The effect of resonance and steric hindrance on the aryl group was briefly evaluated (**4d–4f**) with selenochromone **1a**, and steric hindrance at the *ortho*-position gave the lowest yield (**4f**, 35%). Surprisingly, our palladium-catalyzed direct C–H arylation provided good results with different electron-rich aryl bromides. It is contrary to what would be expected since electron-rich aryl halides are considered to be poor substrates in a conventional Heck reaction.[13b,15] In addition, the catalyst system reported in this work does not seem to discriminate between electron-rich and electron-deficient aryl bromides unlike other Heck reaction protocols developed by Pabba and coworkers.[5h] Although different numbers of methoxy groups varying from zero to three on selenochromone provided the desired selenoflavones (**4–6**) with a slight reduction in yield, a similar tendency was well reported with the increase of donating groups.[5a,f,h] Overall, our data indicate the versatility of the use of aryl bromide substrates in direct C–H arylation of selenocyclic enone systems.

The mechanism of palladium-catalyzed direct C–H arylation is well studied in other literature studies.[5g,16] Taken together with the results of our study, a plausible reaction mechanism *via* a concerted metalation–deprotonation (CMD)

Table 3 Solvent and base screening[a]

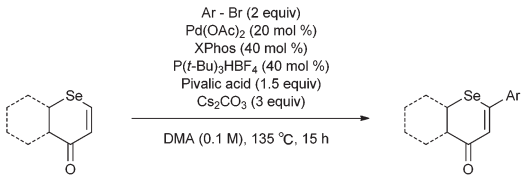


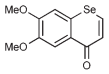
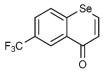
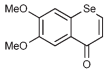
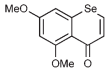
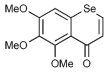
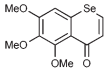
1a 3 4a

Entry	Base (equiv.)	Solvent	Yield[b] (%)
1	Cs_2CO_3 (3)	DMA	58
2	Na_2CO_3 (3)	DMA	16
3	Cs_2CO_3 (3)	DMSO	47
4	Cs_2CO_3 (3)	Acetonitrile	29
5	Cs_2CO_3 (3)	Dioxane	12
6	Cs_2CO_3 (2)	DMA	47
7[c]	Cs_2CO_3 (3)	DMA	60

[a] Reaction conditions: selenochromone **1a** (0.1 mmol), aryl bromide **3** (0.2 mmol), $Pd(OAc)_2$ (40 mol%), XPhos (80 mol%), pivalic acid (1.5 equiv.), $P(t\text{-}Bu)_3HBF_4$ (80 mol%), base (3 equiv.), solvent (0.1 M), 135 °C, 15 h. [b] Isolated yields. [c] $Pd(OAc)_2$ (20 mol%), XPhos (40 mol%), $P(t\text{-}Bu)_3HBF_4$ (40 mol%), pivalic acid (1.5 equiv.).

Table 4 Scope and limitations of a direct C–H arylation of selenochromones



Entry	Selenochromone	Aryl bromide		Product	Yield (%)
1			R = 3,4-diOMe	**4a**	60
2			R = 3,4,5-triOMe	**4b**	55
3			R = 3,5-diOMe	**4c**	65
4			R = 4-OMe	**4d**	56
5			R = 3-OMe	**4e**	67
6			R = 2-OMe	**4f**	35
7			R = 4-Me	**4g**	74
8			R = 4-*t*Bu	**4h**	60
9			R = 4-Cl	**4i**	52
10			R = 4-F	**4j**	58
11			R = 4-CF_3	**4k**	61
12			R = 4-NO_2	**4l**	48
13			R = 4-CN	**4m**	39
14				**4n**	63
15				**4o**	45
16				**4p**	34
17				**5a**	80
18				**5b**	52
19				**5c**	75
20				**5d**	42
21				**5e**	55
22				**6a**	60
23				**6b**	38
24				**6c**	40
25				**6d**	30

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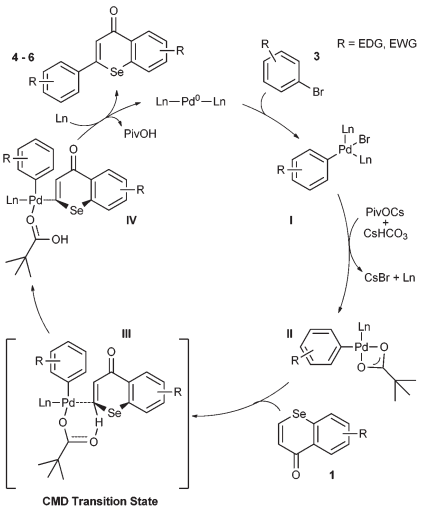

Scheme 3 Proposed mechanism for the direct C–H arylation of selenocyclic enones.

pathway is illustrated in Scheme 3. The catalytic cycle starts with the oxidative addition of aryl bromide to Pd(0) to form the intermediate bromide **I**, which then undergoes an anion exchange of a pivalate. With the employment of suitable directing groups, one of the carboxylate oxygens may be able to displace and coordinate to the palladium metal center. This species (**II**) can then react with selenochromones **1**, resulting in a biarylpalladium(II) intermediate **III** through a concerted deprotonation–palladation. Reductive elimination will eventually furnish the 2-arylated coupling products **4–6** and regenerate the catalysts.

Conclusions

In conclusion, a simple palladium-catalyzed direct C–H arylation of various electron-rich selenochromones has been accomplished with a broad range of aryl bromides. This regioselective direct C–H arylation allows the synthesis of a large set of various 2-arylated analogues for the selenocyclic enone systems, which could be utilized as promising candidates in medicinal chemistry. Additional investigations on broadening the scope of the reaction, as well as biological studies, are currently ongoing.

Experimental

General experimental methods

In the preparation of selenochromones, all reactions were performed in oven-dried glassware with magnetic stirring under an inert atmosphere of dry nitrogen. All palladium coupling reactions were carried out in dried reaction vessels with sealed Teflon screw caps under dry nitrogen, unless otherwise specified. CH_2Cl_2 and THF used for the reaction were liquid chromatography grade reagents and were redistilled from calcium hydride and sodium benzophenone ketyl, respectively. The commercially available reagents were used as received without additional purification. Reactions were monitored by analytical thin-layer chromatography on 0.25 mm silica plates (F-254). Visualization was accomplished under UV light at 254 nm. Flash chromatography was performed on silica gel (40–63 mesh) by using a standard technique. NMR spectra (^1H and ^{13}C) were obtained on 400 MHz NMR spectrometer systems using $CDCl_3$ solvents. Chemical shifts (δ) are reported in parts per million (ppm); tetramethylsilane with the residual solvent resonance as the internal standard ($CDCl_3$ δ: 7.260). ^1H NMR data are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (J) are quoted in hertz (Hz). HRMS data were determined on a Q-TOF LC/MS analyzer with electrospray ionization (ESI). The major signals are quoted in m/z with the relative intensity in parentheses.

General procedure for Rieche formylation (7)

A magnetically stirred solution of dichloromethyl methyl ether (40 mmol) and $TiCl_4$ (48 mmol) in anhyd. CH_2Cl_2 (75 mL) was treated with a solution of commercially available aryl bromide (20 mmol) in anhyd. CH_2Cl_2 (25 mL) at 0 °C. The reaction mixture was stirred at r.t. for 4 h. After the addition of cold 5% aq. HCl (20 mL) at 0 °C, the stirring was continued for 15 min. The organic layer was then separated and the aqueous solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with 5% aq. $NaHCO_3$ (80 mL) and brine (80 mL), dried ($MgSO_4$), and concentrated under reduced pressure to get bromobenzaldehydes **7**.

2-Bromo-4,5-dimethoxybenzaldehyde (7b). The title compound was prepared from commercially available aryl bromide (4 g, 18.43 mmol). The precipitated solid was filtered off, washed with hexane and dried under vacuum to obtain a white solid **7b** (4.4 g, 17.95 mmol, 97% yield), mp 148–150 °C. The compound was used for the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.41 (s, 1H), 7.06 (s, 1H), 3.96 (s, 1H), 3.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8, 154.5, 148.9, 126.5, 120.4, 115.5, 110.4, 56.5, 56.2; HRMS (ESI-QTOF) calcd for $C_9H_9BrO_3$ 244.9813 ($[M + H]^+$), found 244.9812.

2-Bromo-4,6-dimethoxybenzaldehyde (7c). The title compound was prepared from commercially available aryl bromide (4 g, 18.43 mmol). The precipitated solid was filtered off, washed with hexane and dried under vacuum to obtain white solids **7c** and **7ci** (4.4 g, 17.95 mmol, 97% conversion yield, 85 (**7c**) : 15 (**7ci**) regioselectivity). The compounds were used for the next step without further purification. Regioisomeric compounds were separated by flash chromatography after the Grignard reaction.

6-Bromo-2,3,4-trimethoxybenzaldehyde (7d). The title compound was prepared from commercially available aryl bromide (5 g, 20.23 mmol). Flash chromatography (hexane/EtOAc = 5 : 1) on silica gel gave **7d** as a yellow solid (5.5 g, 20 mmol, 99% yield), mp 51–52 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 10.24

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(s, 1H), 6.97 (s, 1H), 3.96 (s, 3H), 3.94 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 157.8, 156.9, 141.9, 121.5, 119.6, 113.4, 62.4, 61.0, 56.4; HRMS (ESI-QTOF) calcd for $C_{10}H_{11}BrO_4$ 296.9739 ($[M + Na]^+$), found 296.9738.

General procedure for Grignard reaction (8)

A magnetically stirred solution of aldehyde **7** (18 mmol) in dry tetrahydrofuran (THF, 90 mL) was treated with a solution of ethynylmagnesium bromide in THF (0.5 M solution, 23.4 mmol) at 0 °C. The solution was stirred at 0 °C for 0.5 h and then warmed to r.t. and stirred for another 4 h. Saturated aqueous ammonium chloride solution (50 mL) was added, and the mixture was evaporated *in vacuo* and separated between ethyl acetate (100 mL) and saturated ammonium chloride solution. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo* to obtain pure compounds **8**, which were used for the next step without further purification.

1-(2-Bromophenyl)prop-2-yn-1-ol (8a). The title compound was prepared from commercially available bromobenzaldehyde **7a** (4 g, 21.6 mmol). The yellow liquid compound **8a** was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 5.74 (s, 1H), 3.46 (d, J = 3.6 Hz, 1H), 2.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 133.0, 130.1, 128.5, 127.9, 122.7, 82.4, 75.0, 63.9; HRMS (ESI-QTOF) calcd for C_9H_7BrO 210.9759 ($[M + H]^+$), found 192.9649 ($[M - OH]^+$).

1-(2-Bromo-4,5-dimethoxyphenyl)prop-2-yn-1-ol (8b). The title compound was prepared from bromobenzaldehyde **7b** (4.4 g, 17.95 mmol). The precipitated solid was filtered off, washed with hexane and dried under vacuum to obtain a white solid **8b**, mp 105–106 °C. The compound was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.01 (s, 1H), 5.76 (s, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 2.67 (s, 1H), 2.50 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 148.8, 131.2, 115.5, 112.8, 111.0, 82.9, 74.9, 63.9, 56.4, 56.2; HRMS (ESI-QTOF) calcd for 270.9970 ($[M + H]^+$), found 252.9866 ($[M - OH]^+$).

1-(2-Bromo-4,6-dimethoxyphenyl)prop-2-yn-1-ol (8c). The title compound was prepared from crude bromobenzaldehyde **7c** (4.4 g, 17.95 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **8c** as an off-white solid (4.14 g, 15.27 mmol, 85% yield), mp 84–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.46 (s, 1H), 5.86 (d, J = 11.2 Hz, 1H), 3.93 (s, 1H), 3.89 (s, 3H), 3.77 (s, 3H), 2.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 159.0, 123.0, 121.0, 109.5, 99.4, 83.5, 72.2, 62.4, 56.1, 55.6; HRMS (ESI-QTOF) calcd for $C_{11}H_{11}BrO_3$ 270.9970 ($[M + H]^+$), found 252.9866 ($[M - OH]^+$).

1-(6-Bromo-2,3,4-trimethoxyphenyl)prop-2-yn-1-ol (8d). The title compound was prepared from bromobenzaldehyde **7d** (5.5 g, 20 mmol). The yellow liquid compound **8d** was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 5.74 (dd, J = 10.8, 2.0 Hz, 1H), 4.10 (s, 1H), 4.07 (s, 3H), 3.85 (d, J = 2.0 Hz, 6H), 2.61 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.7, 142.0, 126.6, 115.5, 111.7, 84.2, 72.9, 62.9, 61.7, 60.7, 56.2; HRMS (ESI-QTOF) calcd for $C_{12}H_{13}BrO_4$ 301.0075 ($[M + H]^+$), found 282.9966 ($[M - OH]^+$).

1-(2-Bromo-4-methylphenyl)prop-2-yn-1-ol (8e). The title compound was prepared from commercially available bromobenzaldehyde (1 g, 5 mmol). The yellow liquid compound **8e** was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.9 Hz, 1H), 7.36 (s, 1H), 7.13 (d, J = 7.8 Hz, 1H), 5.72 (d, J = 3.5 Hz, 1H), 2.96 (d, J = 5.4 Hz, 1H), 2.62 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 135.9, 133.3, 128.6, 128.2, 122.3, 82.6, 74.8, 63.6, 20.7; HRMS (ESI-QTOF) calcd for $C_{10}H_9BrO$ 224.9915 ($[M + H]^+$), found 206.9808 ($[M - OH]^+$).

1-(2-Bromo-5-fluorophenyl)prop-2-yn-1-ol (8f). The title compound was prepared from commercially available bromobenzaldehyde (2 g, 9.85 mmol). The yellow liquid compound **8f** was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.5, 4.6 Hz, 2H), 6.93 (td, J = 8.5, 3.0 Hz, 1H), 5.71 (dd, J = 5.1, 2.0 Hz, 1H), 2.97 (d, J = 5.2 Hz, 1H), 2.67 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (d, J = 247.7 Hz), 141.0 (d, J = 7.1 Hz), 134.2 (d, J = 7.9 Hz), 117.2 (d, J = 22.6 Hz), 116.4 (d, J = 3.3 Hz), 115.7 (d, J = 24.5 Hz), 81.8, 75.3, 63.5; HRMS (ESI-QTOF) calcd for C_9H_6BrFO 228.9664 ($[M + H]^+$), found 210.9559 ($[M - OH]^+$).

1-(2-Bromo-5-(trifluoromethyl)phenyl)prop-2-yn-1-ol (8g). The title compound was prepared from commercially available bromobenzaldehyde (1 g, 3.95 mmol). The white solid compound **8g** was used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.46 (d, J = 8.3 Hz, 1H), 5.80 (dd, J = 5.1, 2.1 Hz, 1H), 2.72–2.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 133.6, 130.4 (q, J = 33.2 Hz), 126.6 (q, J = 3.7 Hz), 126.4 (q, J = 1.4 Hz), 125.3 (q, J = 3.8 Hz), 123.6 (q, J = 272.5 Hz), 81.5, 75.7, 63.5; HRMS (ESI-QTOF) calcd for $C_{10}H_6BrF_3O$ 278.9632 ($[M + H]^+$), found 260.9529 ($[M - OH]^+$).

General procedure for TEMPO oxidation (9)

To a stirred solution of NaBr (18 mmol), $NaHCO_3$ (36 mmol), TEMPO (0.9 mmol), and secondary alcohol **8** (18 mmol) in CH_2Cl_2 (90 mL) was added the solution of NaOCl (12%, 54 mmol) at 0 °C. The reaction mixture was vigorously stirred at 0 °C and monitored by TLC. After the oxidation was complete, the organic layer was separated and the aqueous solution was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed with brine (90 mL), dried ($MgSO_4$), and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel to give products **9**.

1-(2-Bromophenyl)prop-2-yn-1-one (9a). The title compound was prepared from crude **8a** (4.56 g, 21.6 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 20 : 1 : 2) on silica gel gave **9a** as a yellow solid (4.07 g, 19.47 mmol, 90% yield (2 steps)), mp 49–50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.50–7.35 (m, 2H), 3.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 136.0, 135.2, 133.8, 133.6, 127.4, 121.4, 81.5, 80.8; HRMS (ESI-QTOF) calcd for C_9H_5BrO 208.9602 ($[M + H]^+$), found 208.9604.

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1-(2-Bromo-4,5-dimethoxyphenyl)prop-2-yn-1-one (9b). The title compound was prepared from crude **8b** (4.87 g, 17.95 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **9b** as a white solid (4.39 g, 16.16 mmol, 90% yield (2 steps)), mp 164–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.13 (s, 1H), 3.95 (d, J = 5.6 Hz, 1H), 3.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 153.2, 147.9, 127.8, 117.6, 116.1, 114.5, 81.2, 81.0, 56.5, 56.2; HRMS (ESI-QTOF) calcd for $C_{11}H_9BrO_3$ 268.9813 ($[M + H]^+$), found 268.9808.

1-(2-Bromo-4,6-dimethoxyphenyl)prop-2-yn-1-one (9c). The title compound was prepared from **8c** (4.14 g, 15.27 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **9c** as an off-white solid (2.88 g, 10.70 mmol, 70% yield), mp 55–56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.43 (s, 1H), 3.82 (s, 6H), 3.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 162.4, 159.5, 122.9, 120.5, 110.0, 98.2, 82.3, 79.8, 56.1, 55.8; HRMS (ESIQTOF) calcd for $C_{11}H_9BrO_3$ 268.9813 ($[M + H]^+$), found 268.9810.

1-(6-Bromo-2,3,4-trimethoxyphenyl)prop-2-yn-1-one (9d). The title compound was prepared from crude **8d** (6.02 g, 20 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **9d** as a yellow liquid (5.38 g, 18 mmol, 90% yield (2 steps)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (s, 1H), 3.96 (s, 3H), 3.87 (d, J = 13.2 Hz, 6H), 3.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 155.8, 152.7, 141.5, 127.8, 113.1, 112.3, 82.3, 80.2, 61.9, 60.9, 56.4; HRMS (ESI-QTOF) calcd for $C_{12}H_{11}BrO_4$ 298.9919 ($[M + H]^+$), found 298.9917.

1-(2-Bromo-4-methylphenyl)prop-2-yn-1-one (9e). The title compound was prepared from crude **8e** (1.12 g, 5.0 mmol). Flash chromatography (hexane/EtOAc = 5 : 1) on silica gel gave **9e** as a pale-yellow solid (1.0 g, 4.5 mmol, 90% yield (2 steps)), mp 69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.9 Hz, 1H), 7.51 (s, 1H), 7.24 (d, J = 7.9 Hz, 1H), 3.46 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 145.4, 135.9, 134.2, 132.9, 128.1, 121.5, 81.0, 80.8, 21.2; HRMS (ESI-QTOF) calcd for $C_{10}H_7BrO$ 277.9759 ($[M + H]^+$), found 277.9757.

1-(2-Bromo-5-fluorophenyl)prop-2-yn-1-one (9f). The title compound was prepared from crude **8f** (2.25 g, 9.85 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **9f** as a pale-yellow solid (2.12 g, 9.36 mmol, 95% yield (2 steps)), mp 71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.6, 3.0 Hz, 1H), 7.67 (dd, J = 8.8, 5.0 Hz, 1H), 7.15 (td, J = 8.6, 3.0 Hz, 1H), 3.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1 (d, J = 1.9 Hz), 161.3 (d, J = 249.8 Hz), 137.2 (d, J = 6.2 Hz), 136.6 (d, J = 7.2 Hz), 121.1, 120.3 (d, J = 24.4 Hz), 115.6 (d, J = 3.5 Hz), 82.2, 80.4.

1-(2-Bromo-5-(trifluoromethyl)phenyl)prop-2-yn-1-one (9g). The title compound was prepared from crude **8g** (1.1 g, 3.95 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **9g** as a pale-yellow liquid (1.04 g, 3.75 mmol, 95% yield (2 steps)). Volatile under vacuum.

General procedure for selenochromones (1)

To a stirred solution of NaHSe (1.2 mmol), which was prepared from selenium powder (1.1 mmol) and $NaBH_4$ (1.2 mmol) in anhyd. DMF (10 mL) at 135 °C for 1 h, a solution of **9** (1.0 mmol) in anhyd. DMF (10 mL) was added in one portion and the mixture was stirred for another 1 h. After the addition of water (10 mL), the mixture was filtered to remove remaining selenium. The filtrate was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with water (5 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resulting residue was purified by flash chromatography to give selenochromones **1**.

***4H*-Selenochromen-4-one (1a).** The title compound was prepared from **9a** (0.21 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **1a** as a pale-yellow solid (83.6 mg, 0.4 mmol, 40% yield), mp 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 5.6 Hz, 1H), 8.24 (d, J = 10.8 Hz, 1H), 7.66 (d, J = 5.6 Hz, 1H), 7.58–7.48 (m, 2H), 7.22 (d, J = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.4, 137.8, 136.5, 133.2, 131.4, 130.2, 128.8, 128.4, 127.9; HRMS (ESI-QTOF) calcd for C_9H_6OSe 210.9662 ($[M + H]^+$), found 210.9658.

6,7-Dimethoxy-4*H*-selenochromen-4-one (1b). The title compound was prepared from **9b** (0.27 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **1b** as a pale-yellow solid (80.7 mg, 0.3 mmol, 30% yield), mp 138–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 10.8 Hz, 1H), 8.07 (s, 1H), 7.20 (d, J = 10.4 Hz, 1H), 7.03 (s, 1H), 3.99 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5, 152.4, 149.6, 136.6, 130.1, 127.7, 127.2, 110.3, 109.2, 56.3, 56.2; HRMS (ESI-QTOF) calcd for $C_{11}H_{10}O_3Se$ 270.9873 ($[M + H]^+$), found 270.9871.

5,7-Dimethoxy-4*H*-selenochromen-4-one (1c). The title compound was prepared from **9c** (0.27 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **1c** as a pale-yellow solid (80.7 mg, 0.3 mmol, 30% yield), mp 154–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 10.8 Hz, 1H), 7.03 (d, J = 10.8 Hz, 1H), 6.67 (s, 1H), 6.50 (s, 1H), 3.90 (d, J = 22.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5, 163.8, 161.8, 141.0, 132.1, 130.9, 117.7, 103.2, 99.3, 56.3, 55.6; HRMS (ESI-QTOF) calcd for $C_{11}H_{10}O_3Se$ 270.9873 ($[M + H]^+$), found 270.9874.

5,6,7-Trimethoxy-4*H*-selenochromen-4-one (1d). The title compound was prepared from **9d** (0.30 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **1d** as a pale-yellow solid (53.85 mg, 0.18 mmol, 18% yield), mp 86–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 10.8 Hz, 1H), 7.05 (d, J = 10.4 Hz, 1H), 6.88 (s, 1H), 3.93 (d, J = 14.0 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.2, 156.7, 156.0, 143.1, 133.7, 133.0, 129.8, 122.3, 106.1, 61.9, 61.3, 56.2; HRMS (ESI-QTOF) calcd for $C_{12}H_{12}O_4Se$ 300.9979 ($[M + H]^+$), found 300.9984.

7-Methyl-4*H*-selenochromen-4-one (1e). The title compound was prepared from **9e** (0.22 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **1e** as a pale-yellow solid (12.94 mg, 0.26 mmol, 26% yield), mp 90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 8.3 Hz, 1H), 8.19 (d, J = 10.6 Hz, 1H), 7.45 (s, 1H), 7.32 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 10.6 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz,

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$CDCl_3$) δ 181.3, 142.2, 137.3, 136.6, 130.8, 130.0, 129.4, 128.6, 128.4, 21.4.

6-Fluoro-4*H*-selenochromen-4-one (1f). The title compound was prepared from **9f** (0.23 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **1f** as a pale-yellow solid (22.7 mg, 0.1 mmol, 10% yield), mp 130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34–8.25 (m, 2H), 7.67 (dd, J = 8.7, 5.0 Hz, 1H), 7.33 (td, J = 8.6, 2.9 Hz, 1H), 7.23 (d, J = 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5 (d, J = 2.3 Hz), 162.4 (d, J = 249.0 Hz), 138.0, 134.9 (d, J = 6.5 Hz), 131.2 (d, J = 2.8 Hz), 130.6 (d, J = 7.3 Hz), 127.5, 120.1 (d, J = 23.7 Hz), 115.9 (d, J = 22.7 Hz); HRMS (ESI-QTOF) calcd for C_9H_5FOSe 228.9568 ($[M + H]^+$), found 228.9562.

6-(Trifluoromethyl)-4*H*-chromen-4-one (1g). The title compound was prepared from **9g** (0.28 g, 1.0 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **1g** as a pale-yellow solid (27.7 mg, 0.1 mmol, 10% yield), mp 96–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.26 (d, J = 10.6 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 140.3, 137.8, 133.2, 130.4 (q, J = 33.6 Hz), 130.0, 128.5, 127.4 (q, J = 4.0 Hz), 127.2 (q, J = 3.4 Hz), 123.5 (q, J = 272.4 Hz); HRMS (ESI-QTOF) calcd for $C_{10}H_5F_3OSe$ 300.9355 ($[M + Na]^+$), found 300.9351.

General procedure for Pd-catalyzed direct C–H arylation of selenochromones with aryl bromides (4–6)

To a dried reaction vessel were added $Pd(OAc)_2$ (20 mol%), XPhos (40 mol%), tri-*tert*-butylphosphonium hydrogen tetrafluoroborate (40 mol%), pivalic acid (0.15 mmol), Cs_2CO_3 (0.3 mmol), corresponding aryl halide **3** (0.2 mmol), selenochromone **1** (0.1 mmol), and DMA (0.1 M). The flask was placed in a heating block and heated to 135 °C with constant stirring over 15 h. After completion of the reaction, the resulting mixture was cooled to room temperature, diluted with EtOAc, washed with saturated brine and water, dried over $MgSO_4$, and concentrated. The residue obtained was purified by flash column chromatography over silica gel to give the final products **4–6**.

2-(3,4-Dimethoxyphenyl)-4*H*-selenochromen-4-one (4a). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4a** as a pale-yellow solid (20.71 mg, 0.06 mmol, 60% yield), mp 149–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 6.0 Hz, 1H), 7.68 (d, J = 6.0 Hz, 1H), 7.58–7.48 (m, 2H), 7.35 (s, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.15 (s, 1H), 6.95 (d, J = 8.0 Hz, 1H), 3.95 (d, J = 2.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 153.9, 151.4, 149.6, 136.8, 131.8, 131.6, 130.8, 130.1, 128.3, 127.8, 124.5, 120.1, 111.4, 109.5, 56.1; HRMS (ESI-QTOF) calcd for $C_{17}H_{14}O_3Se$ 347.0186 ($[M + H]^+$), found 347.0187.

2-(3,4,5-Trimethoxyphenyl)-4*H*-selenochromen-4-one (4b). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4b** as a pale-yellow solid (20.64 mg, 0.055 mmol, 55% yield), mp 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 6.8 Hz, 1H), 7.58–7.49 (m, 2H), 7.35 (s, 1H), 6.86 (s, 2H), 3.93 (d, J = 7.6 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 154.2, 153.8, 140.2, 136.8, 133.7, 131.8, 131.7, 130.1, 128.3, 127.9, 125.3, 104.2, 61.0, 56.4; HRMS (ESI-QTOF) calcd for $C_{18}H_{16}O_4Se$ 377.0292 ($[M + H]^+$), found 377.0286.

2-(3,5-Dimethoxyphenyl)-4*H*-selenochromen-4-one (4c). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4c** as a pale-yellow solid (22.44 mg, 0.065 mmol, 65% yield), mp 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H), 7.58–7.48 (m, 2H), 7.38 (s, 1H), 6.77 (s, 2H), 6.58 (s, 1H), 3.85 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 161.3, 154.1, 140.1, 137.0, 131.9, 131.6, 130.1, 128.3, 127.9, 125.7, 105.0, 102.6, 55.6; HRMS (ESI-QTOF) calcd for $C_{17}H_{14}O_3Se$ 347.0186 ($[M + H]^+$), found 347.0183.

2-(4-Methoxyphenyl)-4*H*-selenochromen-4-one (4d). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4d** as a pale-yellow solid (17.65 mg, 0.056 mmol, 56% yield), mp 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 6.8 Hz, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.56–7.48 (m, 2H), 7.33 (s, 1H), 7.00 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 161.9, 153.9, 136.9, 131.9, 131.6, 130.6, 130.2, 128.4, 127.9, 124.5, 114.8, 55.6; HRMS (ESI-QTOF) calcd for $C_{16}H_{12}O_2Se$ 317.0081 ($[M + H]^+$), found 317.0078.

2-(3-Methoxyphenyl)-4*H*-selenochromen-4-one (4e). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4e** as a pale-yellow solid (21.12 mg, 0.067 mmol, 67% yield), mp 123–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 7.2 Hz, 1H), 7.60–7.48 (m, 2H), 7.43–7.37 (m, 2H), 7.22 (d, J = 7.6 Hz, 1H), 7.16 (s, 1H), 7.04 (d, J = 8.0 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 160.2, 154.0, 139.5, 136.9, 131.8, 131.6, 130.4, 130.1, 128.3, 127.9, 125.7, 119.3, 116.4, 112.2, 55.5; HRMS (ESI-QTOF) calcd for $C_{16}H_{12}O_2Se$ 317.0081 ($[M + H]^+$), found 317.0080.

2-(2-Methoxyphenyl)-4*H*-selenochromen-4-one (4f). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4f** as a pale-yellow solid (11.03 mg, 0.035 mmol, 35% yield), mp 99–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 6.4 Hz, 1H), 7.58–7.38 (m, 4H), 7.32 (s, 1H), 7.03 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 156.2, 150.8, 138.2, 131.4, 131.3, 129.94, 129.85, 128.4, 128.1, 127.5, 126.9, 121.1, 111.7, 55.7; HRMS (ESI-QTOF) calcd for $C_{16}H_{12}O_2Se$ 317.0081 ($[M + H]^+$), found 317.0078.

2-(*p*-Tolyl)-4*H*-selenochromen-4-one (4g). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4g** as a pale-yellow solid (22.14 mg, 0.074 mmol, 74% yield), mp 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 6.8 Hz, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.56–7.48 (m, 4H), 7.36

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(s, 1H), 7.28 (d, J = 7.2 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 154.1, 141.2, 136.9, 135.3, 131.8, 131.5, 130.04, 130.00, 128.3, 127.8, 126.7, 125.0, 21.4; HRMS (ESI-QTOF) calcd for $C_{16}H_{12}OSe$ 301.0131 ($[M + H]^+$), found 301.0134.

2-(4-(*tert*-Butyl)phenyl)-4*H*-selenochromen-4-one (4h). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4h** as a pale-yellow solid (20.48 mg, 0.060 mmol, 60% yield), mp 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 6.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.55–7.48 (m, 4H), 7.38 (s, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 154.3, 154.1, 136.9, 135.2, 131.8, 131.5, 130.1, 128.3, 127.8, 126.6, 126.3, 125.1, 34.9, 31.2; HRMS (ESI-QTOF) calcd for $C_{19}H_{18}OSe$ 343.0601 ($[M + H]^+$), found 343.0598.

2-(4-Chlorophenyl)-4*H*-selenochromen-4-one (4i). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4i** as a pale-yellow solid (16.62 mg, 0.052 mmol, 52% yield), mp 128–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 4.8 Hz, 1H), 7.70 (d, J = 4.3 Hz, 1H), 7.60–7.52 (m, 4H), 7.48 (d, J = 8.2 Hz, 2H), 7.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 152.4, 136.9, 136.60, 136.55, 131.7, 131.6, 130.2, 129.6, 128.3, 128.2, 128.0, 125.9; HRMS (ESI-QTOF) calcd for $C_{15}H_9ClOSe$ 320.9585 ($[M + H]^+$), found 320.9580.

2-(4-Fluorophenyl)-4*H*-selenochromen-4-one (4j). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4j** as a pale-yellow solid (17.58 mg, 0.058 mmol, 58% yield), mp 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.65–7.59 (m, 2H), 7.58–7.49 (m, 2H), 7.31 (s, 1H), 7.18 (t, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 164.2 (d, J = 250.6 Hz), 152.7, 136.6, 134.3 (d, J = 3.3 Hz), 131.7, 131.6, 130.1, 128.9 (d, J = 8.6 Hz), 128.3, 128.0, 125.7, 116.5 (d, J = 21.8 Hz); HRMS (ESI-QTOF) calcd for $C_{15}H_9FOSe$ 304.9881 ($[M + H]^+$), found 304.9878.

2-(4-(Trifluoromethyl)phenyl)-4*H*-selenochromen-4-one (4k). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4k** as a pale-yellow solid (21.55 mg, 0.061 mmol, 61% yield), mp 173–174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.4 Hz, 1H), 7.76 (s, 4H), 7.71 (d, J = 8.16 Hz, 1H), 7.62–7.52 (m, 2H), 7.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 151.9, 141.6, 136.5, 132.1 (q, J = 32.94 Hz), 131.9, 131.6, 130.2, 128.4, 128.2, 127.4, 126.8, 126.33 (q, J = 3.72 Hz), 126.27 (q, J = 270.76 Hz); HRMS (ESI-QTOF) calcd for $C_{16}H_9F_3OSe$ 354.9849 ($[M + H]^+$), found 354.9851.

2-(4-Nitrophenyl)-4*H*-selenochromen-4-one (4l). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4l** as a pale-yellow solid (15.85 mg, 0.048 mmol, 48% yield), mp 172–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 7.6 Hz, 1H), 8.36 (d, J = 8.7 Hz, 2H), 7.81 (d, J = 8.7 Hz, 2H), 7.73 (d, J = 7.4 Hz, 1H), 7.65–7.54 (m, 2H), 7.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.4, 150.6, 148.9, 144.2, 136.2, 132.1, 131.5, 130.3, 128.4, 128.0, 127.4, 124.5, 123.6; HRMS (ESI-QTOF) calcd for $C_{15}H_9NO_3Se$ 331.9826 ($[M + H]^+$), found 331.9829.

4-(4-Oxo-4*H*-selenochromen-2-yl)benzonitrile (4m). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4m** as a pale-yellow solid (12.10 mg, 0.039 mmol, 39% yield), mp 194–195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 7.6 Hz, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.76–7.70 (m, 3H), 7.63–7.53 (m, 2H), 7.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.5, 151.2, 142.4, 136.3, 133.1, 132.0, 131.5, 130.3, 128.4, 128.3, 127.7, 127.0, 117.9, 114.3; HRMS (ESI-QTOF) calcd for $C_{16}H_9NOSe$ 311.9928 ($[M + H]^+$), found 311.9928.

2-(Pyridin-3-yl)-4*H*-selenochromen-4-one (4n). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 3 : 1 : 2) on silica gel gave **4n** as a pale-yellow solid (18.03 mg, 0.063 mmol, 63% yield), mp 153–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.75 (d, J = 2.96 Hz, 1H), 8.63 (d, J = 7.92 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 7.08 Hz, 1H), 7.62–7.52 (m, 2H), 7.45 (t, J = 5.56 Hz, 1H), 7.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.4, 151.6, 150.0, 147.7, 136.4, 134.3, 134.2, 131.9, 131.6, 130.3, 128.4, 128.2, 126.7, 123.9; HRMS (ESI-QTOF) calcd for $C_{14}H_9NOSe$ 287.9928 ($[M + H]^+$), found 287.9928.

2-(Thiophen-2-yl)-4*H*-selenochromen-4-one (4o). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4o** as a yellow solid (9.45 mg, 0.045 mmol, 45% yield), mp 142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 7.3 Hz, 1H), 7.55–7.43 (m, 4H), 7.35 (s, 1H), 7.13 (dd, J = 5.0, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 145.0, 140.8, 135.9, 131.9, 131.8, 130.1, 129.1, 128.5, 128.1, 127.9, 127.3, 123.6; HRMS (ESI-QTOF) calcd for $C_{13}H_8OSSe$ 292.9539 ($[M + H]^+$), found 292.9536.

2-(Thiophen-3-yl)-4*H*-selenochromen-4-one (4p). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4o** as a yellow solid (7.14 mg, 0.034 mmol, 34% yield), mp 146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 7.5 Hz, 1H), 7.70–7.62 (m, 2H), 7.54–7.47 (m, 2H), 7.47–7.43 (m, 1H), 7.41–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 147.0, 139.4, 136.2, 131.9, 131.7, 130.1, 128.2, 127.8, 127.6, 125.3, 124.9, 124.3; HRMS (ESI-QTOF) calcd for $C_{13}H_8OSSe$ 292.9539 ($[M + H]^+$), found 292.9537.

2-Phenyl-4*H*-selenochromen-4-one (5a). The title compound was prepared from **1a** (21 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 10 : 1 : 2) on silica gel gave **4i** as a pale-yellow solid (22.82 mg, 0.080 mmol, 80% yield), mp 127–128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 7.2 Hz, 1H), 7.64 (d, J = 3.2 Hz, 2H), 7.60–7.45 (m, 5H), 7.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 154.1, 138.2, 136.9, 131.8, 131.6, 130.7, 130.1, 129.3, 128.3, 127.9, 126.9, 125.7; HRMS (ESI-QTOF) calcd for $C_{15}H_{10}OSe$ 286.9975 ($[M + H]^+$), found 286.9973.

6,7-Dimethoxy-2-phenyl-4*H*-selenochromen-4-one (5b). The title compound was prepared from **1b** (26.9 mg, 0.1 mmol).

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Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **5b** as a pale-yellow solid (14.0 mg, 0.052 mmol, 52% yield), mp 176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.63 (dd, J = 6.6, 2.9 Hz, 2H), 7.51–7.47 (m, 3H), 7.37 (s, 1H), 7.08 (s, 1H), 4.01 (d, J = 5.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.8, 153.0, 152.6, 149.6, 138.2, 130.5, 129.3, 126.9, 125.8, 125.1, 110.3, 108.8, 56.3, 56.2; HRMS (ESI-QTOF) calcd for $C_{17}H_{14}O_3Se$ 347.0186 ($[M + H]^+$), found 347.0184.

7-Methyl-2-phenyl-4*H*-selenochromen-4-one (5c). The title compound was prepared from **1e** (22.3 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **5c** as a pale-yellow solid (16.7 mg, 0.075 mmol, 75% yield), mp 82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 8.2 Hz, 1H), 7.65–7.61 (m, 2H), 7.51–7.46 (m, 4H), 7.36–7.30 (m, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 153.6, 142.5, 138.2, 137.0, 130.6, 129.9, 129.5, 129.32, 129.28, 128.2, 126.9, 125.7, 21.5; HRMS (ESI-QTOF) calcd for $C_{16}H_{12}OSe$ 301.0132 ($[M + H]^+$), found 301.0136.

6-Fluoro-2-phenyl-4*H*-selenochromen-4-one (5d). The title compound was prepared from **1f** (22.7 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **5d** as a pale-yellow solid (9.5 mg, 0.042 mmol, 42% yield), mp 155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 9.8, 2.9 Hz, 1H), 7.71 (dd, J = 8.7, 5.0 Hz, 1H), 7.66–7.62 (m, 2H), 7.53–7.49 (m, 3H), 7.38 (s, 1H), 7.34 (td, J = 8.5, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.9 (d, J = 2.3 Hz), 162.4 (d, J = 248.7 Hz), 154.6, 137.9, 133.6 (d, J = 6.6 Hz), 131.6 (d, J = 2.7 Hz), 130.9, 130.2 (d, J = 7.3 Hz), 129.4, 126.9, 124.9, 120.2 (d, J = 23.7 Hz), 115.8 (d, J = 22.8 Hz); HRMS (ESI-QTOF) calcd for $C_{15}H_9FOSe$ 326.9700 ($[M + Na]^+$), found 326.9736.

2-Phenyl-6-(trifluoromethyl)-4*H*-selenochromen-4-one (5e). The title compound was prepared from **1g** (27.7 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 5 : 1 : 2) on silica gel gave **5e** as a pale-yellow solid (15.2 mg, 0.055 mmol, 55% yield), mp 175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.66–7.62 (m, 2H), 7.54–7.50 (m, 3H), 7.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.7, 154.3, 140.7, 137.6, 131.9, 131.1, 130.3 (q, J = 33.5 Hz), 129.5, 129.3, 127.5 (q, J = 3.4 Hz), 127.4 (q, J = 4.1 Hz), 126.9, 125.6, 123.6 (q, J = 272.6 Hz); HRMS (ESI-QTOF) calcd for $C_{16}H_9F_3OSe$ 376.9668 ($[M + Na]^+$), found 376.9667.

2-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-4*H*-selenochromen-4-one (6a). The title compound was prepared from **1b** (26.9 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **5a** as a pale-yellow solid (24.32 mg, 0.060 mmol, 60% yield), mp 205–206 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.33 (s, 1H), 7.22 (d, J = 8.3 Hz, 1H), 7.15 (s, 1H), 7.06 (s, 1H), 6.95 (d, J = 8.4 Hz, 1H), 4.00 (d, J = 6.8 Hz, 6H), 3.95 (d, J = 6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.0, 152.9, 152.6, 151.2, 149.6, 149.5, 130.9, 130.4, 125.9, 124.0, 119.9, 111.4, 110.3, 109.5, 108.8, 56.3, 56.2, 56.1; HRMS (ESI-QTOF) calcd for $C_{19}H_{18}O_5Se$ 407.0397 ($[M + H]^+$), found 407.0391.

2-(3,4-Dimethoxyphenyl)-5,7-dimethoxy-4*H*-selenochromen-4-one (6b). The title compound was prepared from **1c** (26.9 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **6a** as a pale-yellow solid (15.40 mg, 0.038 mmol, 38% yield), mp 178–180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.16 (m, 2H), 7.13 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.72 (s, 1H), 6.51 (s, 1H), 3.96 (s, 6H), 3.94 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 163.7, 162.0, 151.1, 149.4, 147.8, 141.3, 130.1, 126.6, 120.0, 116.5, 111.3, 109.4, 102.9, 99.2, 56.3, 56.1, 56.1, 55.7; HRMS (ESI-QTOF) calcd for $C_{19}H_{18}O_5Se$ 407.0397 ($[M + H]^+$), found 407.0400.

2-(3,4-Dimethoxyphenyl)-5,6,7-trimethoxy-4*H*-selenochromen-4-one (6c). The title compound was prepared from **1d** (30 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **7a** as a yellow liquid (17.41 mg, 0.040 mmol, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 11.8 Hz, 2H), 7.13 (s, 1H), 6.94 (d, J = 11.8 Hz, 2H), 3.97 (d, J = 2.0 Hz, 6H), 3.96 (s, 3H), 3.94 (d, J = 1.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 156.6, 156.1, 151.1, 149.5, 148.9, 143.0, 134.0, 130.2, 125.8, 120.9, 119.9, 111.3, 109.4, 105.7, 62.0, 61.4, 59.2, 56.1, 56.1; HRMS (ESI-QTOF) calcd for $C_{20}H_{20}O_6Se$ 437.0503 ($[M + H]^+$), found 437.0502.

5,6,7-Trimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-selenochromen-4-one (6d). The title compound was prepared from **1d** (30 mg, 0.1 mmol). Flash chromatography (hexane/EtOAc/CH_2Cl_2 = 2 : 1 : 2) on silica gel gave **7b** as a pale-yellow solid (13.96 mg, 0.030 mmol, 30% yield), mp 195–197 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 1H), 6.93 (s, 1H), 6.83 (s, 2H), 3.97 (d, J = 3.3 Hz, 6H), 3.93 (s, 9H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 156.7, 156.2, 153.7, 149.1, 143.1, 140.0, 134.0, 133.2, 126.5, 120.9, 105.7, 104.2, 62.0, 61.4, 61.0, 56.3, 56.2; HRMS (ESI-QTOF) calcd for $C_{21}H_{22}O_7Se$ 467.0609 ($[M + H]^+$), found 467.0605.

Acknowledgements

We are grateful to Mirae Fine Chemical Co., Ltd and Vismer Co., Ltd for technical assistance.

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