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Note

Metal-Free Three-Component Coupling Reaction of Ketones with Electron-rich Arenes and Selenium Dioxide for the Synthesis of α-Arylselanyl Ketones

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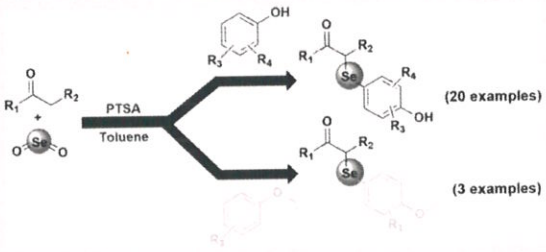
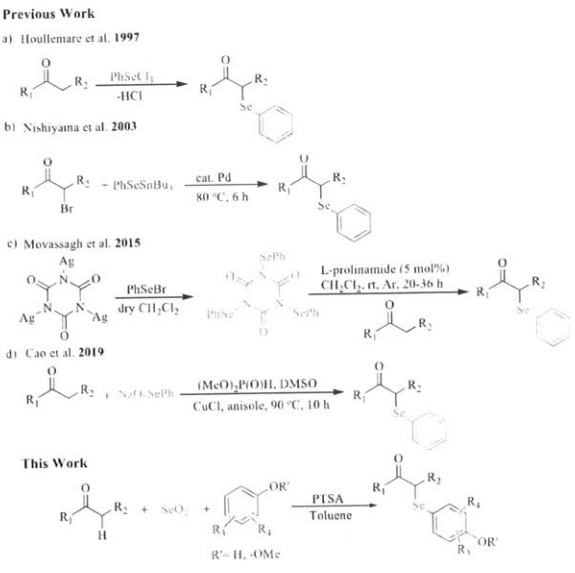
ABSTRACT: A metal-free three-component coupling reaction of aryl alkyl/alkyl ketones, SeO_2, and phenols/anisoles is described. This multicomponent reaction provides a straightforward and facile pathway for the synthesis of α-((4-hydroxy/methoxyphenyl)selanyl)-aryl alkyl/alkyl ketones in the presence of *p*-toluenesulfonic acid for the C−Se bond formation process. The method offers an attractive and simple procedure using commonly available shelf reagents to deliver organoselenides that, to our knowledge, are being reported here for the first time.



The last three decades have witnessed the emergence of organoselenium compounds as important reagents and intermediates in organic synthesis. Many of these compounds have been studied and reported because of their interesting reactivities,[1] potential biological activities, and pharmaceutical properties.[2] Among these compounds, α-phenylseleno ketones have been recognized as the versatile intermediates in organic synthesis, particularly for the introduction of unsaturated function via *syn*-elimination.[3] In addition, α-phenylseleno ketones can also be transformed into other useful synthetic intermediates, which are common structural elements found in naturally occurring substances[4a] and in a number of pharmaceutically relevant molecules[4b,c] such as α-hydroxy esters,[4d] allylic alcohols,[4e] allylic amines,[4f] α-amino acids,[4g] and terminal aziridines.[4h] Very recently, Pandey et al. have extended the synthetic utility of α-phenylseleno ketones as a precursor in the synthesis of intermolecular α-arylation of ketones by cross-coupling with electron-rich arenes.[5] Furthermore, Cotgreave[6a] and Engman[6b] have described the biological importance of α-phenylseleno ketones and reported that it mimics the properties of glutathione peroxidase, like ebselen. Various synthetic methods employing different selenium sources have been developed for the synthesis of α-phenyl selenylation of ketones.[3−11] In 1997, Houllemare and co-workers have reported a method for the preparation of α-phenylseleno ketones and aldehydes using phenylselenium trichloride as an electrophilic selenium reagent (Scheme 1a).[7e] Nishiyama et al. have shown that the synthesis of α-phenylseleno ketones can be achieved by the palladium metal complex-catalyzed method in the reaction of α-haloketones with phenyl tributylstannyl selenide as the phenylselenylating agents (Scheme 1b).[8c] In 2015, Movassagh

Scheme 1. Synthesis of α-Phenylseleno Ketones



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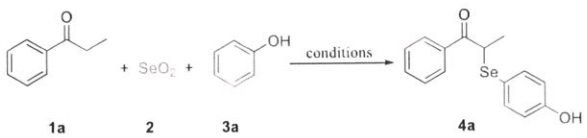
and Takallou reported a method using a versatile reagent *N,N,N*-triphenylselenylisocyanuric acid (TPSCA) in the L-prolinamide-promoted process for the α-phenylselenenylation of ketones (Scheme 1c).[10c] Recently, Cao and his group have shown the direct selenylation of ketones using sodium selenites-based reagents (Scheme 1d).[11] Although the literature review revealed that the reported methods are adequate; however, some of the selenylating reagents suffer various drawbacks as they require well-defined reaction conditions due to their instability toward air and moisture, are synthesized in multiple step reactions, form various reactive byproducts, are expensive, and release malodorous and highly toxic vapors. Thus, an alternative method for the synthesis of α-phenylseleno ketones using stable selenium reagents under mild reaction conditions would indeed be useful to organic chemists.

Recently, we have demonstrated the successful use of SeO_2 as an efficient inorganic reagent, which, in the presence of a Lewis acid, facilitated the reaction between aromatic ketones and aromatic hydrocarbons to affect C−C coupling at the α-carbon atom,[12a] while the same reaction catalyzed by an organic acid *p*-toluenesulfonic acid monohydrate (PTSA) yielded unsymmetrical benzils.[12b] Again, aryl methyl ketones reacted efficiently with secondary amines in DMSO in the presence of SeO_2 to affect α-selenoamidation of aryl methyl ketones,[12c] while in the presence of PTSA, alkyl/aryl ketones reacted with aliphatic alcohols mediated by SeO_2 to generate a library of α-ketoacetals.[12d] It is evident from these reactions involving SeO_2 that the nature of the acid and/or the solvent used to play a major role in determining the path of the reaction. We were keen to know, therefore, the direction the reaction would take when alkyl/aryl ketones are allowed to react with phenols in the presence of PTSA. Thus, inspired by our earlier success in the use of SeO_2-mediated reactions in organic syntheses and in continuation of our work in this area of research, we wish to report here a new method for the synthesis of α-((hydroxy/methoxyphenyl)selanyl)-aryl/alkyl ketones by reacting aryl/alkyl ketones with phenols/anisoles in the presence of SeO_2 catalyzed by PTSA. To the best of our knowledge, this is the first instance where selenium dioxide is directly used as the selenium source in a one-pot reaction between ketones and phenols/anisoles, resulting in the incorporation of selenium at the α-carbon of the ketones.

We began our investigation by employing propiophenone (**1a**) and phenol (**3a**) as the model substrates to determine the optimal reaction conditions (Table 1). In an initial attempt, a mixture of propiophenone (**1a**, 1 equiv), phenol (**3a**, 1.2 equiv), and selenium dioxide (**2**, 1 equiv) was stirred with PTSA (0.25 equiv) in toluene (1 mL) at room temperature for 18 h, where we obtained only 20% yield of the desired product **4a** (Table 1, entry 1). When the same reaction was carried out for a longer reaction time (36 h), the yield of the product increases to 50% (Table 1, entry 2). When the reaction temperature was raised to 60 °C, the yield of **4a** remained at 50%, but the reaction time was greatly reduced (Table 1, entry 3). With further optimization by varying amounts of the acid (Table 1, entries 4 and 5), it was found that 0.5 equiv of PTSA gave the optimum yield of the product **4a** (85%, Table 1, entry 4). When the amount of PTSA was increased (Table 1, entry 5), multiple spot formation was observed, and only 40% yield of product **4a** was obtained. Among the acids (Table 1, entries 4, 6 and 7) and solvents (Table 1, entries 4, 8−10) studied, PTSA is the most efficient catalyst, and toluene is the best medium that provides the best result in terms of yields (Table 1, entry 4). Finally, no desired product was formed in the absence of PTSA (Table 1, entry 11), demonstrating its indispensable role in the reaction scheme.

Table 1. Optimization of Reaction Conditions[a]



1a **2** **3a** **4a**

entry	acid (equiv)	solvent	temperature (°C)	time (h)	yield (%)
1	PTSA (0.25)	toluene	rt	18	20
2	PTSA (0.25)	toluene	rt	36	50
3	PTSA (0.25)	toluene	60	6	50
4	PTSA (0.5)	toluene	60	3	85
5	PTSA (0.7)	toluene	60	3	40
6	$BF_3{\cdot}Et_2O$ (0.5)	toluene	60	3	50
7	TFA (0.5)	toluene	60	3	55
8	PTSA (0.5)	DCM	60	3	30
9	PTSA (0.5)	CH_3CN	60	18	20
10	PTSA (0.5)	DMSO	60	18	0
11		toluene	60	24	NR

[a]Reaction conditions: ketone (**1a**) (1 mmol, 1.0 equiv), SeO_2 (**2**) (1 mmol, 1.0 equiv), phenol (**3a**) (1.2 mmol, 1.2 equiv), solvent (1 mL), 60 °C.

With the optimal reaction conditions in hand, the scope of the reaction was investigated. Differently substituted aryl ethyl ketones, such as propiophenone (**1a**), 4-methylpropiophenone (**1b**), 4-chloropropiophenone (**1c**), 4-bromopropiophenone (**1d**) and 2-chloropropiophenone (**1e**), were first selected to react with phenol (**3a**) (Scheme 2). Aryl ethyl ketones bearing electron-donating or electron-withdrawing groups in the ring were successfully converted to give the corresponding products in excellent yields (**4a**, 85%; **4b**, 80%; **4c**, 86%; **4d**, 79%; **4e**, 88%). The scope of the reaction was further applied to aromatic ketones with an extended aliphatic counterpart with equal success. Thus, butyrophenone (**1f**) and valerophenone (**1g**) gave 2-((4-hydroxyphenyl)selanyl)-1-phenylbutan-1-one (**4f**) and 2-((4-hydroxyphenyl)selanyl)-1-phenylpentan-1-one (**4g**), respectively, in good yields.

Next, we investigated the substrate scope of electron-donating phenols derivatives reacting with different substituted aryl ethyl ketones including 2-methylphenol (**3b**) with 2-chloropropiophenone (**1e**) and 2-methoxyphenol (**3c**) with propiophenone (**1a**), where the desired products **4h** and **4i** were obtained in 87% and 82% yields. Under similar conditions, phenols with an electron-withdrawing group such as 2-chlorophenol (**3d**) when reacted with 4-methylpropiophenone (**1b**) also afforded the desired product **4j** in good yield (78%). Disubstituted phenols such as 2,5-dimethyl phenol (**3e**) and 2,6-dimethyl phenol (**3f**), which contribute to the steric hindrance effect, gave the corresponding products **4k** and **4l** in satisfactory yields (75% and 86%). Unfortunately, when 2-napthol was treated with **1a**, the expected product was not obtained. Also, reactions of substituted phenols at the *para*-position such as 4-nitrophenol and 4-aminophenol were carried out; however, the desired products were not obtained as the *para*-position, which is the reactive site, was blocked. This protocol was also extended toward anisole and aniline derivatives. To our delight, anisole (**5a**) and 2-methyl anisole

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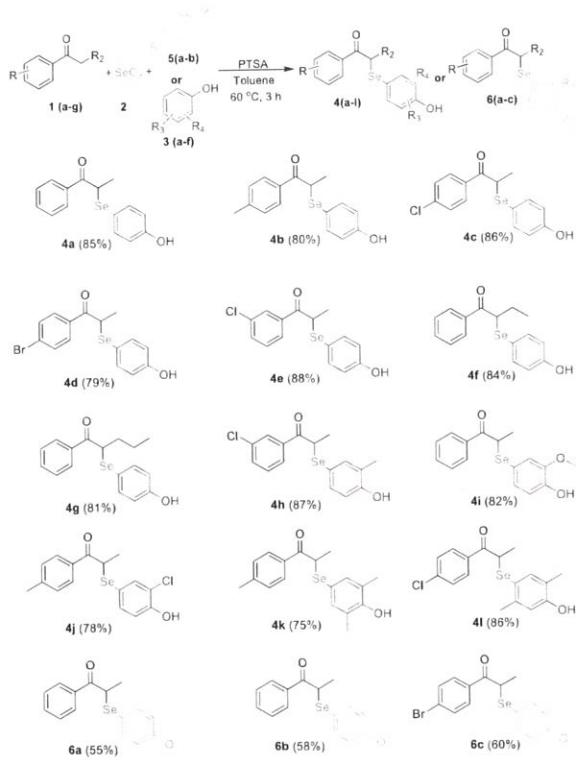
Scheme 2. Substrate Scope of Aryl Alkyl Ketones[a]

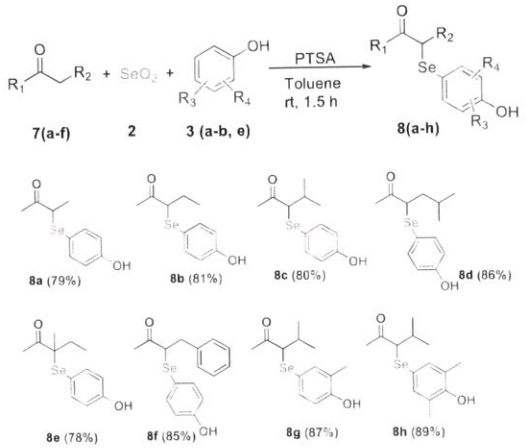


[a]Reaction conditions: ketones (**1**) (1 mmol, 1.0 equiv), SeO_2 (**2**) (1 mmol, 1.0 equiv), phenols (**3**)/anisoles (**5**) (1.2 mmol, 1.2 equiv), PTSA (0.5 mmol, 0.5 equiv), solvent (1 mL), 60 °C.

(**5b**) also coupled with propiophenone (**1a**) and 4-bromopropiophenone (**1d**) to give the α-selenylated product **6a**, **6b**, and **6c** in moderate yields (55–60%). However, the formation of the desired product was not observed when aryl ethyl ketone was treated with aniline. Other aromatic systems like chlorobenzene and benzaldehyde do not react at all with aryl ethyl ketones, while the reaction with acetophenone displayed multiple spot formation. This explains that the method is reactive toward those substrates that have phenol-like reactivity.

The generality of this protocol was further expanded to aliphatic ketones. The synthesis of α-((4-hydroxyphenyl)-selanyl)alkyl ketones, however, proceeded at room temperature (Scheme 3). Reactions of phenol with aliphatic ketones such as ethyl methyl ketone (**7a**) and methyl propyl ketone (**7b**) afforded the corresponding products **8a** and **8b** in 79% and 81% yields, respectively. Likewise, reactions of branched aliphatic ketones such as isobutyl methyl ketone (**7c**) and isopentyl methyl ketone (**7d**) furnished the desired products **8c** in 80% and **8d** in 86% yields. When 3-methyl-2-butanone (**7e**) and benzyl acetone (**7f**) were allowed to react with phenol, the desired products **8e** and **8f** were obtained in 78% and 85% yields, respectively. It was observed that reactions of isobutyl methyl ketone (**7c**) with electron-donating substituted phenols such as 2-methyl phenol (**3b**) and 2,6-dimethyl phenol (**3e**) resulted in high yields of the corresponding products **8g** (87%) and **8h** (89%). Further, the confirmation of the

Scheme 3. Substrate Scope of Alkyl Methyl Ketones[a]

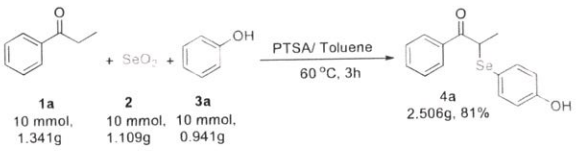


[a]Reaction conditions: ketones (**1**) (1 mmol, 1.0 equiv), SeO_2 (**2**) (1 mmol, 1.0 equiv), phenols (**3**)/anisoles (**5**) (1.2 mmol, 1.2 equiv), PTSA (0.5 mmol, 0.5 equiv), solvent (1 mL), rt.

structure of the products was defined by the XRD data of compound **8c** (included in the Supporting Information).

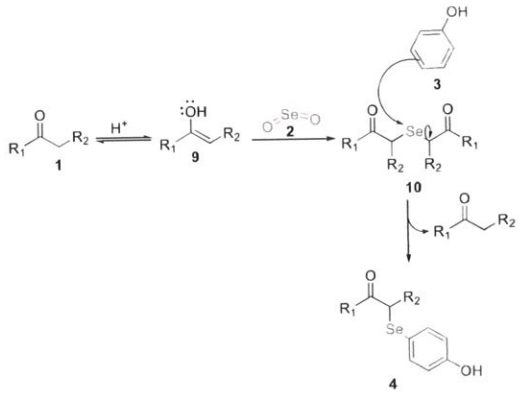
To demonstrate the potential applicability of the method in organic synthesis, a gram scale reaction of **1a** with **2** and **3a** was carried out under standard conditions, yielding the product **4a** in 81% yield (Scheme 4).

Scheme 4. Gram-Scale Reaction



The plausible mechanism involved in the reaction of ketone **1** with phenol **3** in the presence of SeO_2 and PTSA is depicted in Scheme 5. The initial reaction of the enolate anion **9** with SeO_2 resulted in the formation of α,α-diketoselenide **10** (isolated and characterized). Evidently, nucleophilic attack by phenol **3** on the selenium intermediate yielded product **4** with

Scheme 5. Plausible Mechanism



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the elimination of one mole of the ketone, which presumably takes part again in the diselenide formation. The formation of the proposed intermediate **10** was further strengthened by the reaction of **1a** with SeO_2 and PTSA in toluene where the intermediate 2,2′-selenobis(1-phenylpropan-1-one) (**10**) was isolated in 80% yield.

In conclusion, we have developed a new method for the selenylation of ketones by the direct coupling of alkyl/aryl ketones with phenols derivatives via a selenium bridge using cheap and easily available SeO_2 in a one-step procedure, in the presence of PTSA. All reactions carried out provide easy access to hitherto unreported α-phenylseleno ketones in moderate to excellent yields.

■ EXPERIMENTAL SECTION

General Information. All reagents and solvents were purchased from commercial suppliers and used without further purification. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel $60F_{254}$ (0.2 mm thicknesses), in which the spots were visualized with UV light (λ = 254 nm). For purification, column chromatography was carried out on silica gel 100−200 mesh. Melting points were recorded by the open capillary tube method and are uncorrected. IR spectra were recorded on a PerkinElmer Spectrum 400 FTIR instrument, and the frequencies are expressed in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II-400 spectrometer in $CDCl_3$ and DMSO-d_6 using tetramethylsilane (TMS) as an internal standard; chemical shifts (δ) values are expressed in parts per million (ppm) and coupling constants (J) in hertz (Hz). HRMS was recorded on an Agilent 6520 Q-TO spectrometer, and ESI-MS was recorded on a Waters UPLC-TQD mass spectrometer. ^{77}Se NMR spectra were recorded on a Mercury Plus 300 Hz NMR spectrometer in ppm using Me_2Se as an internal standard.

Gram-Scale Synthesis of 4a. In a round-bottom flask, a mixture of aryl alkyl ketones (**1**) (10 mmol, 1.341 g, 1.0 equiv), SeO_2 (**2**) (10 mmol, 1.109 g, 1.0 equiv), phenols (**3**) (12 mmol, 0.941 g, 1.2 equiv), PTSA (5 mmol, 0.951 g, 0.5 equiv), and toluene (10 mL) was added. The reaction mixture was allowed to stir for 3 h at 60 °C in an oil bath. After the completion of the reaction, which was monitored by thin-layer chromatography (TLC), the mixture was cooled to room temperature and diluted with ethyl acetate (200 mL). The combined filtrate was transferred to a separating funnel, neutralized with aqueous $NaHCO_3$ (2 × 100 mL), and washed with aqueous NaCl (2 × 100 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and reduced under a vacuum. The crude product was purified by silica column chromatography (5:95 ethyl acetate/hexane) to obtain the corresponding product **4a** in 81% yield.

General Procedure A for the Synthesis of 2-((4-Hydroxy/methoxy-phenyl)selanyl)-aryl Alkyl Ketones (4a−l/6a−c). A mixture of aryl alkyl ketones (**1**) (1.0 mmol), SeO_2 (**2**) (1.0 mmol, 111 mg), phenols (**3**)/anisoles (**5**) (1.2 mmol), PTSA (0.5 mmol, 95 mg), and toluene (1 mL) was added in a round-bottom flask. The reaction mixture was allowed to stir in an oil bath at 60 °C for 3 h. After the completion of the reaction, which was monitored by thin-layer chromatography (TLC), the mixture was cooled to room temperature and diluted with ethyl acetate (2 × 10 mL). The combined filtrate was transferred to a separating funnel, neutralized with aqueous $NaHCO_3$ (2 × 10 mL), and washed with aqueous NaCl (2 × 10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and reduced under a vacuum. The crude products were purified by silica column chromatography using ethyl acetate−hexane as an eluent to obtain the corresponding products (**4a−l/6a−c**).

General Procedure B for the Synthesis of 3-((4-Hydroxyphenyl)selanyl)-alkyl ketones 8a−h. A mixture of alkyl ketones (**7**) (1.0 mmol), SeO_2 (**2**) (1.0 mmol, 111 mg), phenols (**3**) (1.2 mmol), PTSA (0.5 mmol, 95 mg), and toluene (1 mL) was added in a round-bottom flask. The reaction mixture was stirred at room temperature for 1.5 h. The completion of the reaction was monitored by thin-layer chromatography (TLC). The mixture was diluted with ethyl acetate (2 × 10 mL). The combined filtrate was transferred to a separating funnel, neutralized with aqueous $NaHCO_3$ (2 × 10 mL), and washed with aqueous NaCl (2 × 10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and reduced under a vacuum. The crude products were purified by silica column chromatography using ethyl acetate−hexane as an eluent to obtain the corresponding products **8a−h**.

*2-((4-Hydroxyphenyl)selanyl)-1-phenylpropan-1-one (**4a**).* This compound was prepared following procedure A, using a mixture of propiophenone (134 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (260 mg, 85%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3491, 1674, 1487, 1427, 1223, 708 cm^{-1}; mp 88−90 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.93 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 6.67 (d, J = 8.4 Hz, 2H), 4.93 (q, J = 6.8 Hz, 1H), 1.40 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.9, 157.8, 139.2, 135.6, 133.1, 128.7, 128.5, 116.5, 115.1, 38.9, 16.5 ppm; ^{77}Se NMR (57.25 MHz, $CDCl_3$) δ 359.35 ppm; HRMS (ESI) m/z calcd for $C_{15}H_{14}O_2Se$ $[M + H]^+$ 307.0237, found 307.0208.

*2-((4-Hydroxyphenyl)selanyl)-1-(p-tolyl)propan-1-one (**4b**).* This compound was prepared following procedure A, using a mixture of 4-methylpropiophenone (148 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (257 mg, 80%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3329, 1648, 1601, 1578, 1218, 831 cm^{-1}; mp 120−122 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 2H), 7.28−7.23 (m, 4H), 6.85 (s, 1H), 6.68 (d, J = 8.8 Hz, 2H), 4.60 (q, J = 6.8 Hz, 1H), 2.43 (s, 3H), 1.59 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.9, 158.0, 144.2, 139.3, 133.2, 129.5, 128.8, 116.6, 115.4, 39.0, 21.8, 16.8 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Se$ $[M + H]^+$: 321.0394, found 321.0379.

*1-(4-Chlorophenyl)-2-((4-hydroxyphenyl)selanyl)propan-1-one (**4c**).* This compound was prepared following procedure A, using a mixture of 4-chloropropiophenone (168 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a brown crystalline solid (293 mg, 86%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3386, 1653, 1585, 1425, 1276, 1214, 827 cm^{-1}; mp 145−147 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.82 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.8 Hz, 2H), 6.62 (d, J = 8.4 Hz, 2H), 4.49 (q, J = 6.8 Hz, 1H), 1.52 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.7, 157.8, 139.6, 139.2, 133.9, 129.9, 129.0, 116.5, 114.9, 38.9, 16.4 ppm; ^{77}Se NMR (57.25 MHz, CDCl3) δ 456.60 ppm; HRMS (ESI) m/z calcd for $C_{15}H_{13}ClO_2Se$ $[M + H]^+$ 340.9848, found 340.9842.

*1-(4-Bromophenyl)-2-((4-hydroxyphenyl)selanyl)propan-1-one (**4d**).* This compound was prepared following procedure A, using a mixture of 4-bromopropiophenone (213 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (303 mg, 79%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3290, 1653, 1580, 1488, 1425, 1276, 1216, 834 cm^{-1}; mp 110−112 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.74 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 6.62 (d, J = 8.4 Hz, 2H), 4.48 (q, J = 6.8 Hz, 1H), 1.52 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.8, 157.8, 139.2, 134.4, 131.9, 130.0, 128.2, 116.5, 115.0, 38.9, 16.4 ppm; HRMS (ESI) m/z calcd for $C_{15}H_{13}BrO_2Se$ $[M + H]^+$ 384.9342, found 384.9324.

*1-(3-Chlorophenyl)-2-((4-hydroxyphenyl)selanyl)propan-1-one (**4e**).* This compound was prepared following procedure A, using a mixture of 3-chloropropiophenone (168 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (300 mg, 88%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3334, 1652, 1580, 1428, 1230, 826, 701 cm^{-1}; mp 114−116 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.76 (s, 1H), 7.67

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(d, J = 8.0 Hz, 1H), 7.43 (d, J = 8 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 6.8 Hz, 2H), 6.68 (d, J = 6.8 Hz, 2H), 4.44 (q, J = 6.8 Hz, 1H), 1.50 (d, J = 5.6 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.7, 158.7, 138.8, 137.6, 134.6, 132.5, 129.7, 128.4, 126.4, 116.5, 114.9, 39.7, 16.6 ppm; HRMS (ESI) m/z calcd for $C_{15}H_{13}ClO_2Se$ $[M + H]^+$ 340.9848, found 340.9840.

*2-((4-Hydroxyphenyl)selanyl)-1-phenylbutan-1-one (**4f**).* This compound was prepared following procedure A, using a mixture of butyrophenone (148 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (270 mg, 84%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3272, 1649, 1578, 1489, 1429, 1269, 1220, 1095, 701 cm^{-1}; mp 107−109 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.82 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 8.0 Hz, 2H), 7.12 (s, 1H), 7.09 (d, J = 8.4 Hz, 2H), 6.54 (d, J = 8.4 Hz, 2H), 4.21 (t, J = 7.2 Hz, 1H), 1.86−1.79 (m, 1H), 1.74−1.68 (m, 1H), 0.93 (t, J = 7.2 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.4, 158.0, 139.1, 136.0, 133.2, 128.7, 128.4, 116.5, 114.8, 47.1, 23.3, 12.7 ppm; HRMS (ESI) m/z calcd for $C_{17}H_{18}O_2Se$ $[M + H]$ 321.0394, found 321.0383.

*2-((4-Hydroxyphenyl)selanyl)-1-phenylpentan-1-one (**4g**).* This compound was prepared following procedure A, using a mixture of valerophenone (162 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (271 mg, 81%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3422, 1651, 1581, 1428, 1230, 702 cm^{-1}; mp 108−110 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 6.62 (d, J = 8.0 Hz, 2H), 6.56 (s, 1H), 4.38 (t, J = 7.2 Hz, 1H), 1.91−1.82 (m, 1H), 1.79−1.70 (m, 1H), 1.52−1.44 (m, 1H), 1.42−1.31 (m, 1H),0.88 (t, J = 7.6 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.5, 157.9, 139.1, 136.1, 133.1, 128.7, 128. 4, 116.5, 44.9, 32.2, 21.2, 13.9 ppm; HRMS (ESI) m/z calcd for $C_{17}H_{18}O_2Se$ $[M + H]^+$ 335.0550, found 335.0511.

*1-(3-Chlorophenyl)-2-((4-hydroxy-3-methylphenyl)selanyl)-propan-1-one (**4h**).* This compound was prepared following procedure A, using a mixture of propiophenone (168 mg, 1 mmol), 2-methylphenol (130 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow crystalline solid (309 mg, 87%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3403, 1667, 1568, 1483, 1334, 1223, 703 cm^{-1}; mp 88−90 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.74 (s, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.08 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.56 (d, J = 8.0 Hz, 1H), 5.26 (s,1H), 4.45 (q, J = 6.8 Hz, 1H), 2.11 (s, 3H), 1.54 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.2, 154.7, 139.1, 136.6, 135.4, 133.7, 131.7, 128.8, 127.6, 125.5, 124.2, 114.8, 114.6, 38.4, 15.5, 14.6 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{15}ClO_2Se$ $[M + H]^+$ 355.0004, found 354.9993.

*2-((4-Hydroxy-3-methoxyphenyl)selanyl)-1-phenylpropan-1-one (**4i**).* This compound was prepared following procedure A, using a mixture of propiophenone (134 mg, 1 mmol), 2-methoxyphenol (149 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow crystalline solid (275 mg, 82%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3359, 1665, 1581, 1499, 1442, 1309, 1211, 709 cm^{-1}; mp 75−77 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 8.0 Hz, 2H), 6.94 (d, J = 7.2 Hz, 1H), 6.76−6.74 (m, 2H), 5.65 (s, 1H), 4.57 (q, J = 7.2 Hz, 1H), 3.73 (s, 3H), 1.54 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.4, 145.9, 145.3, 135.0, 131.8, 130.0, 127.5, 127.4, 118.6, 115.0, 114.0, 54.9, 38.7, 15.9 ppm; ^{77}Se NMR (57.25 MHz, CDCl3) δ 464.76 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{16}O_3Se$ $[M + H]^+$ 337.0343, found 337.0331.

*2-((3-Chloro-4-hydroxyphenyl)selanyl)-1-(p-tolyl)propan-1-one (**4j**).* This compound was prepared following procedure A, using a mixture of 4-methylpropiophenone (148 mg, 1 mmol), 2-chlorophenol (155 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (277 mg, 78%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3324, 1644, 1569, 1397, 1293, 712 cm^{-1}; mp 96−98 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.30 (s, 1H), 7.19−7.16 (m, 3H), 6.83 (d, J = 8.4 Hz, 1H), 5.75 (s, 1H), 4.56 (q, J = 6.8 Hz, 1H), 2.35 (s, 3H), 1.53 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 152.7, 143.9, 137.7, 137.6, 133.1, 129.3, 128.5, 120.1, 117.1, 116.9, 39.6, 21.7, 16.9 ppm; ^{77}Se NMR (57.25 MHz, CDCl3) δ 458.67 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{15}ClO_2Se$ $[M + H]^+$ 355.0004, found 355.0009.

*2-((4-Hydroxy-3,5-dimethylphenyl)selanyl)-1-(p-tolyl)propan-1-one (**4k**).* This compound was prepared following procedure A, using a mixture of 4-methylpropiophenone (148 mg, 1 mmol), 2, 6-dimethylphenol (146 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (263 mg, 75%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3419, 1750, 1476, 1336, 1201, 746 cm^{-1}; mp 134−136 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.96 (s, 2H), 4.92 (s, 1H), 4.51 (q, J = 6.8 Hz, 1H), 2.35 (s, 3H), 2.09 (s, 6H), 1.53 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.3, 152.8, 142.6, 136.7, 132.4, 128.2, 127.6, 123.0, 114.8, 38.5, 20.7, 15.9, 14.7 ppm; HRMS (ESI) m/z calcd for $C_{18}H_{20}O_2Se$ $[M + H]^+$ 349.0707, found 349.0702.

*1-(4-Chlorophenyl)-2-((4-hydroxy-2,5-dimethylphenyl)selanyl)-propan-1-one (**4l**).* This compound was prepared following procedure A, using a mixture of 4-chloropropiophenone (168 mg, 1 mmol), 2,5-dimethylphenol (146 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow crystalline solid (318 mg, 86%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3416, 1656, 1588, 1372, 1232, 748 cm^{-1}; mp 108−110 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.68 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.03 (s, 1H), 6.55 (s, 1H), 5.13 (s, 1H), 4.44 (q, J = 6.8 Hz, 1H), 2.16 (s, 3H), 2.05 (s, 3H), 1.54 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.7, 154.5, 141.3, 140.4, 138.2, 133.2, 128.8, 127.6, 121.2, 116.6, 115.6, 38.4, 21.9, 15.5, 14.0 ppm; HRMS (ESI) m/z calcd for $C_{17}H_{17}ClO_2Se$ $[M + H]^+$ 369.0161, found 369.0182.

*2-((4-Methoxyphenyl)selanyl)-1-phenylpropan-1-one (**6a**).* This compound was prepared following procedure A, using a mixture of propiophenone (134 mg, 1 mmol), anisole (130 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow crystalline solid (177 mg, 55%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 1663, 1585, 1487, 1268,1241, 709 cm^{-1}; mp 77−79 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.2 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.8 Hz, 2H), 4.54 (q, J = 6.8 Hz, 1H), 3.73 (s, 3H), 1.51 (d, J = 7.2 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 160.6, 138.8, 135.9, 132.7, 128.5, 128.4, 116.8, 114.7, 55.2, 39.5, 16.9 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Se$ $[M + H]^+$ 321.0394, found 321.0380.

*2-((4-Methoxy-3-methylphenyl)selanyl)-1-phenylpropan-1-one (**6b**).* This compound was prepared following procedure A, using a mixture of propiophenone (134 mg, 1 mmol), 2-methylanisole (146 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (195 mg, 58%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 1662, 1587, 1489, 1247, 1133, 705 cm^{-1}; mp 80−82 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.90 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 8.0 Hz, 2H), 7.23−7.18 (m, 2H), 6.70 (d, J = 8.4 Hz, 1H), 4.60 (q, J = 6.8 Hz, 1H), 3.82 (s, 3H), 2.15 (s, 3H), 1.60 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.3, 158.8, 139.4, 136.2, 136.0, 132.7, 128.4, 127.5, 116.3, 110.4, 55.3, 39.6, 39.3, 16.9, 16.1 ppm; HRMS (ESI) m/z calcd for $C_{17}H_{18}O_2Se$ $[M + H]$ 335.0550, found 335.0533.

*1-(4-Bromophenyl)-2-((4-methoxy-3-methylphenyl)selanyl)-propan-1-one (**6c**).* This compound was prepared following procedure A, using a mixture of 4-bromopropiophenone (213 mg, 1 mmol), 2-methylanisole (146 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow solid (248 mg, 60%),

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which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 1662, 1588, 1447, 1334, 1230, 709 cm^{-1}; mp 100−102 °C; ^1H NMR (400 MHz, $CDCl_3$, with 1% v/v TMS) δ 7.65 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.8 Hz, 2H), 7.12−7.08 (m, 2H), 6.62 (d, J = 8.4 Hz, 1H), 4.45 (q, J = 6.4 Hz, 1H), 3.76 (s, 3H), 2.08 (s, 3H), 1.52 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.2, 158.9, 139.4, 136.1, 134.9, 131.6, 129.9, 127.7, 127.6, 116.2, 110.4, 55.3, 39.6, 16.7, 16.0 ppm; HRMS (ESI) m/z calcd for $C_{17}H_{17}BrO_2Se$ $[M + H]^+$ 412.9655, found 412.9631.

3-((4-Hydroxyphenyl)selanyl)butan-2-one ***(8a)***. This compound was prepared following procedure B, using a mixture of butanone (72 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (193 mg, 79%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3283, 1680, 1579, 1489, 1431, 1272, 1224, 835 cm^{-1}; mp 88−90 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 7.6 Hz, 2H), 6.91 (s, 1H), 6.59 (d, J = 8.0 Hz, 2H), 3.67 (q, J = 6.8 Hz, 1H), 2.35 (s, 3H), 1.36 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.7, 157.9, 138.7, 116.6, 114.7, 45.8, 27.1, 15.7 ppm; ^{77}Se NMR (57.25 MHz, CDCl3) δ 425.92 ppm; HRMS (ESI) m/z calcd for $C_{10}H_{12}O_2Se$ $[M + H]^+$ 245.0081, found 245.0073.

3-((4-Hydroxyphenyl)selanyl)pentan-2-one ***(8b)***. This compound was prepared following procedure B, using a mixture of pentanone (86 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow crystalline solid (209 mg, 81%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3201, 1672, 1580, 1490, 1360, 1294, 1230, 835 cm^{-1}; mp 87−89 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.2 Hz, 2H), 6.71 (s, 1H), 6.59 (d, J = 6.8 Hz, 2H), 3.42 (t, J = 7.6 Hz, 1H), 2.32 (s, 3H), 1.76−1.68 (m, 1H), 1.64−1.56 (m, 1H), 0.94 (t, J = 7.2 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.2, 157.8, 138.5, 116.6, 114.8, 54.2, 27.4, 22.8, 12.6 ppm; HRMS (ESI) m/z calcd for $C_{11}H_{14}O_2Se$ $[M + H]^+$ 259.0237, found 259.0230.

3-((4-Hydroxyphenyl)selanyl)-4-methylpentan-2-one ***(8c)***. This compound was prepared following procedure B, using a mixture of 4-methyl-2-pentanone (100 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow crystalline solid (218 mg, 80%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3451, 1645, 1491, 1438, 1228, 1193, 831 cm^{-1}; mp 74−76 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.0 Hz, 2H), 6.97 (s, 1H), 6.57 (d, J = 8.4 Hz, 2H), 3.24 (d, J = 10.0 Hz, 1H), 2.29 (s, 3H), 1.96−1.86 (m, 1H), 1.17 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.4 Hz, 3H), ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 205.7, 157.7, 138.1, 116.6, 115.4, 62.1, 27.7, 27.4, 21.5, 20.9 ppm; MS (ES+) calcd for $C_{12}H_{16}O_2Se$ 272.0, found m/z 273.0 $[M + H]^+$.

3-((4-Hydroxyphenyl)selanyl)-5-methylhexan-2-one ***(8d)***. This compound was prepared following procedure B, using a mixture of 5-methyl-2-hexanone (mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow crystalline solid (246 mg, 86%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3165, 1672, 1576, 1488, 1362, 1270, 827 cm^{-1}; mp 80−82 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.4 Hz, 2H), 7.18 (s, 1H), 6.57 (d, J = 8.8 Hz, 2H), 3.61 (t, J = 7.6 Hz, 1H), 2.33 (s, 3H), 1.70−1.64 (m, 1H), 1.58−1.48 (m, 2H), 0.87−0.82 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.4, 157.8, 138.5, 116.6, 115.3, 50.8, 38.2, 27.1, 26.7, 22.4, 22.4 ppm; HRMS (ESI) m/z calcd for $C_{13}H_{19}O_2Se$ $[M + H]^+$ 287.0550, found 286.0559.

3-((4-Hydroxyphenyl)selanyl)-3-methylpentan-2-one ***(8e)***. This compound was prepared following procedure B, using a mixture of 3-methyl-2-pentanone (100 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow crystalline solid (213 mg, 78%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3433, 1661, 1277, 1248, 839 cm^{-1}; mp 78−70 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.17(d, J = 7.2 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 2.39 (s, 3H), 1.91−1.82 (m, 1H), 1.77−1.68 (m, 1H), 1.37 (s, 3H), 0.89 (t, J = 7.6 Hz, 3H), ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.09, 158.0, 139.1, 116.5, 116.4, 58.8, 29.4, 24.9, 20.1, 9.9 ppm; HRMS (ESI) m/z calcd for $C_{12}H_{16}O_2Se$ $[M + H]^+$ 273.0394, found 273.0388.

3-((4-Hydroxyphenyl)selanyl)-4-phenylbutan-2-one ***(8f)***. This compound was prepared following procedure B, using a mixture of 4-phenyl-2-butanone (148 mg, 1 mmol), phenol (113 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a yellow solid (288 mg, 85%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3135, 1670, 1596, 1489, 1435, 1270, 833 cm^{-1}; mp 102−104 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.4 Hz, 2H), 7.21−7.10 (m, 5H), 6.74 (s, 1H), 6.64 (d, J = 8.0 Hz, 2H), 3.82 (t, J = 7.2 Hz, 1H), 3.10−3.05 (m, 1H), 2.97−2.91 (m, 1H), 2.27 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.5, 157.1, 137.9, 137.8, 127.9, 127.6, 125.7, 115.7, 113.8, 51.3, 35.0, 27.1 ppm; ^{77}Se NMR (57.25 MHz, CDCl3) δ 410.77 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Se$ $[M + H]^+$ 321.0394, found 321.0374.

3-((4-Hydroxy-3-methylphenyl)selanyl)-4-methylpentan-2-one ***(8g)***. This compound was prepared following procedure B, using a mixture of 4-methyl-2-pentanone (100 mg, 1 mmol), 2-methylphenol (130 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (250 mg, 87%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3422, 1672, 1587, 1272, 1079, 816 cm^{-1}; mp 87−89 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.49 (d, J = 8.0 Hz, 1H), 6.02 (s, 1H), 3.23 (d, J = 10.8 Hz, 1H), 2.26 (s, 3H), 2.10 (s, 3H), 1.97−1.89 (m, 1H), 1.17 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 203.7, 156.8, 138.5, 135.1, 125.6, 115.9, 115.5, 61.6, 28.5, 28.2, 21.7, 21.0, 16.2 ppm; HRMS (ESI) m/z calcd for $C_{13}H_{18}O_2Se$ $[M + H]^+$ 287.0550, found 287.0561.

3-((4-Hydroxy-3,5-dimethylphenyl)selanyl)-4-methylpentan-2-one ***(8h)***. This compound was prepared following procedure B, using a mixture of 4-methyl-2-pentanone (100 mg, 1 mmol), 2,6-dimethylphenol (146 mg, 1.2 mmol), and SeO_2 (111 mg, 1 mmol). The product was obtained as a pale yellow solid (269 mg, 89%), which was purified by column chromatography SiO_2 (5:95 ethyl acetate/hexane): IR (KBr film) 3398, 1684, 1580, 1474, 1360, 1196, 731 cm^{-1}; mp 116−118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 2H), 4.87 (s, 1H), 3.22 (d, J = 10.4 Hz, 1H), 2.20 (s, 3H), 2.11 (s, 6H), 1.97−1.90 (m, 1H), 1.15 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.5, 153.5, 136.4, 124.2, 116.7, 62.5, 28.3, 27.7, 21.6, 21.1, 15.8 ppm; ^{77}Se NMR (57.25 MHz, $CDCl_3$) δ 357.10 ppm; HRMS (ESI) m/z calcd for $C_{14}H_{20}O_2Se$ $[M + H]^+$ 301.0707, found 301.0694.

Synthesis of 2,2′-Selenobis(1-phenylpropan-1-one) ***(10)***. This compound was obtained by treating propiophenone (**1a**, 134 mg, 1.0 mmol, 1 equiv) with SeO_2 (**2**, 111 mg, 1.0 mmol, 1 equiv) in the presence of PTSA (95 mg, 0.5 mmol, 0.5 equiv) in toluene (1 mL) by heating in an oil bath at 60 °C for 2 h. After the completion of the reaction, which was monitored by thin-layer chromatography (TLC), the mixture was cooled to room temperature and diluted with ethyl acetate (2 × 10 mL). The combined filtrate was transferred to a separating funnel, neutralized with aqueous $NaHCO_3$ (2 × 10 mL), and washed with aqueous NaCl (2 × 10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and reduced under a vacuum. The product was obtained as a yellow solid (277 mg, 80%), which was purified by column chromatography SiO_2 (2:98 ethyl acetate/hexane): IR (KBr film) 3422, 1676, 1446, 1427, 1332, 1233, 797 cm^{-1}; mp 80−82 °C; H NMR (400 MHz, Chloroform-d) δ 8.00 (dd, J = 0.8 Hz, 1.6 Hz, 4H), 7.59 (tt, J = 1.2 Hz, 2.0 Hz, 1.2 Hz, 2H), 7.50 (dt, J = 1.2 Hz, 1.2 Hz, 1.6 Hz, 4H), 4.74 (q, J = 6.8 Hz, 2H), 1.60 (d, J = 6.8 Hz, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 135.6, 133.5, 128.9, 128.8, 128.7, 39.2, 18.2; MS (ES+) calcd for $C_{18}H_{18}O_2Se$ 345.31, found 368.85 $[M + Na]^+$.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02028.

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds and crystallographic descriptions for compound **8c** (PDF)

FAIR data, including the primary NMR FID files, for compounds, **4a−4l**, **6a−6c**, and **8a−8h** (ZIP)

Accession Codes

CCDC 1973308 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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