JOC The Journal of Organic Chemistry

pubs.acs.org/joc

Note

Selenocyanation of Aryl and Styryl Methyl Ketones in the Presence of Selenium Dioxide and Malononitrile: An Approach for the Synthesis of α-Carbonyl Selenocyanates

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Cite This: J. Org. Chem. 2021, 86, 1980−1986

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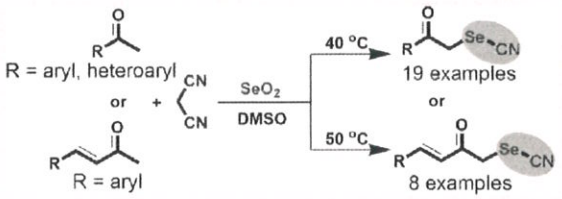
ABSTRACT: A convenient method has been developed for the synthesis of α-carbonyl selenocyanates from aryl methyl ketones/styryl methyl ketones using selenium dioxide as the selenating agent under simple reaction conditions. This reaction has notable advantages over the traditional methods in terms of accessibility and affordability of the starting materials. The method features the interaction of aryl methyl ketones/styryl methyl ketones with selenium dioxide and malononitrile to afford a series of α-carbonyl selenocyanates in moderate to good yields.



Organoselenium compounds have attracted a great deal of interest in recent years because of their unique biological properties and promising wide applications in organic synthesis.[1] Of the vast number of organoselenium compounds, the organo-selenocyanate derivatives have shown considerable potential as active intermediates[2] in organic synthesis and have been extensively studied for their anticancer properties[3] besides other important biological activities.[4] In particular, the α-carbonyl selenocyanates are considered to be synthetically important since the presence of the carbonyl and cyano functions serve as the basic scaffold for the construction of an array of selenium containing heterocycles[5] and other selenoorganic compounds.[6] Surprisingly only scanty reports are available in the literature for the synthesis of α-carbonyl selenocyanates.[5e,7−10] The few reported methods includes the synthesis of α-carbonyl selenocyanates from aromatic alkenes,[7] α-haloketones,[5e] or aryl ketones[8] using selenocyanate salts as the selenocyanate source (Scheme 1a). Kachanov and group reported a direct reaction of diketones with triselenium dicyanide to gives dicarbonyl selenocyanate products (Scheme 1b).[9] In 2019, Xiao et al. employed selenocyanobenziodoxolone as the selenocyanating agent for the synthesis of diverse α-carbonyl selenocyanate compounds from derivatives of esters, ketones, and *N*-acetyl-α-arylenamine (Scheme 1c).[10] Although these methods are quite efficient for the synthesis of α-carbonyl selenocyanates, they are accompanied by certain limitations. The harsh reaction conditions, low substrate scope, and low product yield limits their scope of applications. The multistep procedures coupled with high cost of the starting materials render these methods less easily accessible. Therefore, the development of alternative synthetic strategies for the synthesis of structurally diverse α-carbonyl selenocyanates under mild reaction conditions is therefore highly required.

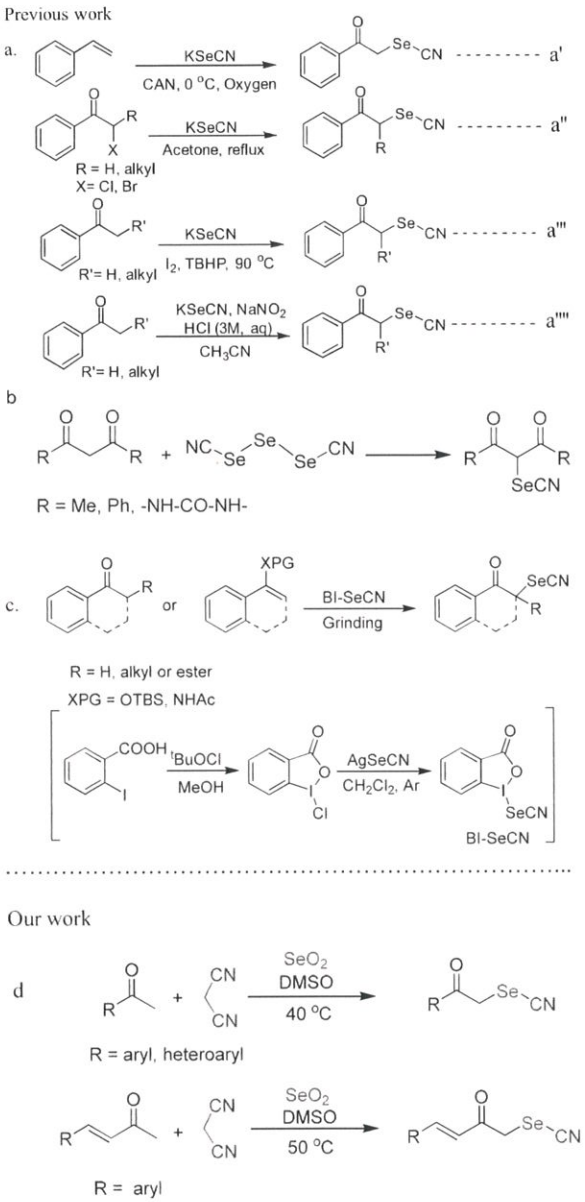
Recently, we have demonstrated the versatility of selenium dioxide as a selenating agent in the synthesis of α-oxoselenoamides from aryl methyl ketones and secondary amines.[11] As part of our ongoing research on the synthetic utility of selenium dioxide in organic synthesis,[11,12] we wish to report here a direct and efficient one step protocol for the selenocyanation of aryl methyl ketones/styryl methyl ketones by selenium dioxide and malononitrile to give the α-carbonyl selenocyanates (Scheme 1d).

To identify the optimum reaction conditions, 4-methylacetophenone (**1b**) was taken as the model substrate and allowed to react with malononitrile (**2**) and selenium dioxide by varying the solvent used, reaction temperature, and time. The results are summarized in Table 1. Thus, when 1 equiv of 4-methylacetophenone (**1b**), malononitrile (**2**) and selenium dioxide was carried out in DMSO at ambient temperature, TLC of the reaction mixture showed only the presence of unreacted substrates. The reaction was then heated to 40 °C for 2 h when a single product spot appeared on the TLC plate. Workup and purification of the reaction mixture yielded α-carbonyl selenocyanates (**3b**) in 40% yield (Table 1, entry 1). When the amount of selenium dioxide was increased to 2

Received: November 5, 2020
Published: December 30, 2020

https://dx.doi.org/10.1021/acs.joc.0c02630
J. Org. Chem. 2021, 86, 1980−1986

Scheme 1. Synthesis of α-Carbonyl Selenocyanate



equiv, there was an improvement in product formation to 50% yield (Table 1, entry 2). Ultimately, it was found that increasing the amounts of malononitrile **2** from 1 equiv to 1.5 equiv and that of selenium dioxide from 2 equiv to 3 equiv, the optimum yield of the product was obtained at 72% (Table 1, entry 3). Further increase in the amount of substrate **2** or selenium dioxide did not increase the yield of the product any further. Similarly, any decrease or increase in the reaction time or temperature did not show any improvement in the yield of the product (Table 1, entries 4–6). It was noted that when the reaction was carried out at room temperature for 5 h, only a trace amount of the product formation was observed (Table 1, entry 7). To further investigate the possibility of increasing the product yield, a series of solvents were examined where DMF

Table 1. Optimization of Reaction Conditions[a]

entry	substrate 2 (equiv)	SeO_2(equiv)	solvent	temp (°C)	time (h)	yield (%)
1	1	1	DMSO	40	2	40
2	1	2	DMSO	40	2	50
3	**1.5**	**3**	**DMSO**	**40**	**2**	**72**
4	1.5	3	DMSO	40	1.5	55
5	1.5	3	DMSO	40	3	68
6	1.5	3	DMSO	55	2	70
7	1.5	3	DMSO	RT	5	trace
8	1.5	3	DMF	40	2	50
9	1.5	3	toluene	50	5	
10	1.5	3	acetonitrile	50	5	
11	1.5	3	THF	50	5	

[a]Reaction was carried out with **1b** (1 mmol, 1 equiv) and 3 mL of solvent.

gave a moderate yield of 50% while toluene, acetonitrile, and THF give no product at all even at elevated temperatures (Table 1, entries 8–11).

With the optimum reaction conditions obtained (Table 1, entry 3), the generality of the reaction was investigated employing a wide range of aryl methyl ketone derivatives, and the results are summarized in Scheme 2. As a whole, the reaction shows a wide substrate scope with aromatic methyl ketones (**1**) and malononitrile (**2**). Aromatic ketones, unsubstituted (4-H) or substituted by electron-donating (e.g., 4-CH_3, 4-OCH_3, 3-OCH_3, 3-CH_3, 2-OCH_3, 2-CH_3) or electron-withdrawing substituents (e.g., 4-NO_2, 3-NO_2) were successfully converted to their desired products (**3a**, 70%; **3b**, 72%; **3c**, 75%; **3d**, 62%; **3h**, 65%; **3i**, 65%; **3k**, 73%; **3l**, 67%) in moderate to good yield. The solid product of **3a** formed a well defined crystal where its XRD data (included in the Supporting Information) further strengthen the structure of the final product. The reaction also proceeded smoothly with the halo substituted ketones (e.g., 4-Cl, 4-Br, 4-F, 3-Cl, 2-Cl, 2-Br) to afford the corresponding products (**3e**, 70%; **3f**, 67%; **3g**, 79%; **3j**, 71%; **3m**, 66%; **3n**, 55%) in good to excellent yield. Furthermore, the yield of the product was not affected by the steric hindrance on the ring system of the ketones where the disubstituted **1o** and **1p** and trisubstituted ketones **1q** give products (**3o**, 70%; **3p**, 69%; and **3q**; 72%) in excellent yield. We further extent our curiosity to the behavior of heteroaryl methyl ketones toward this reaction. With a large amount of content, we found the promising conversions of the heteroaryl methyl ketones (**1r** and **1s**) to the expected products **3r** and **3s** in 72% and 77% yield. The reaction was extended to six membered nitrogen heterocycles, such as 2-acetylpyridine and 4-acetylpyridine, and resulted in an inextricable mass, thus failing to afford the targeted products. Similarly, the current method was ineffective toward aliphatic methyl ketones leading to the formation of multiple products.

Encouraged by these results, we next turned our attention toward styryl methyl ketones which when the reaction was carried out at 50 °C afforded **5a** in 62% yields (Scheme 3). In a similar fashion the *p*-substituted, *o*-substituted styryl methyl ketone readily gave the selenocyanate products in satisfactory

https://dx.doi.org/10.1021/acs.joc.0c02630
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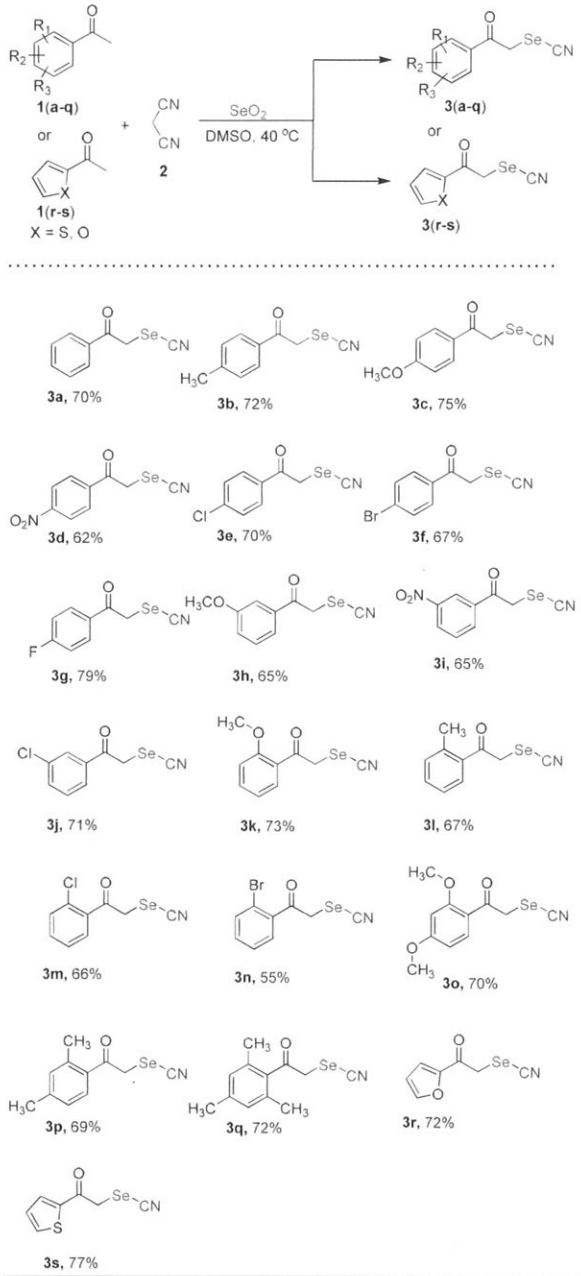
Scheme 2. Substrate Scope of Aryl Methyl Ketones[a]

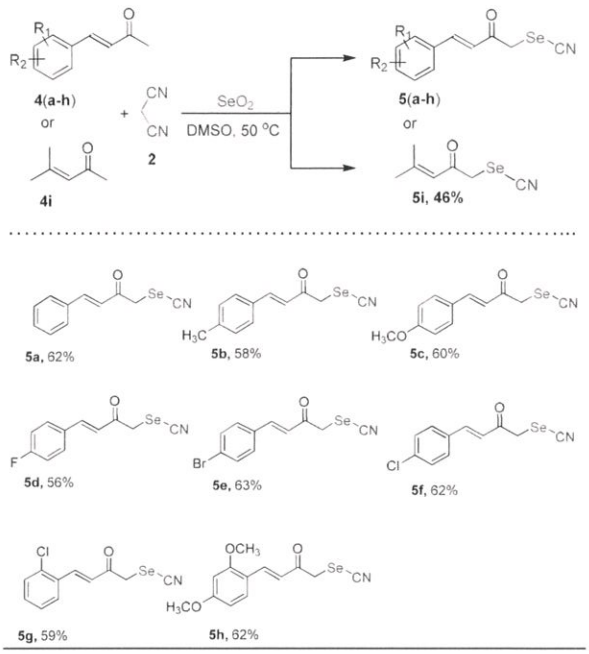


[a]Reaction was carried out with **1a–1s** (1 mmol, 1 equiv), **2** (1.5 mmol, 1.5 equiv, 99 mg), and selenium dioxide (3 mmol, 3 equiv, 333 mg) in DMSO at 40 °C for 2 h.

yields (**5b**; 58%, **5c**; 60%, **5d**; 56%, **5e**; 63%, **5f**; 62%, **5g**; 59%). Similarly, the disubstituted styryl methyl ketone **4h** gave the desired product **5h** in 62% yield. It may be noted that when the reaction was extended toward heteroaryl styryl methyl ketones, no product formation was observed. However, aliphatic α,β-unsaturated methyl ketone, isobutenyl methyl ketones (**4i**) gave the desired product **5i** in 46% yield.

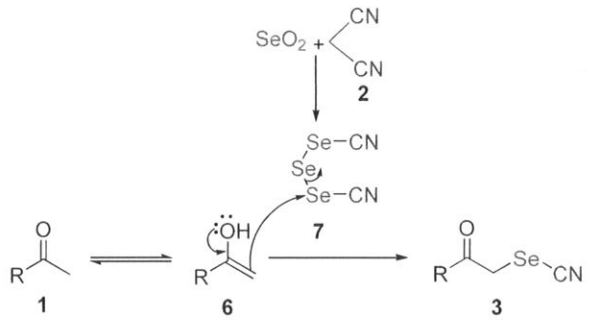
The plausible mechanism is depicted in Scheme 4. Evidently, the first step in the reaction is the enolization of

Scheme 3. Substrate Scope of Styryl/Isobutenyl Methyl Ketones[a]



[a]Reaction was carried out with **4a–4i** (1 mmol, 1 equiv), **2** (1.5 mmol, 1.5 equiv, 99 mg), and selenium dioxide (3 mmol, 3 equiv, 333 mg) in DMSO at 50 °C for 2 h.

Scheme 4. Plausible Mechanism



ketone followed by the subsequent nucleophilic attack of enolate ketone **6** on the electrophilic selenium atom of triselenodicyanide (TSD) (**7**), a selenocyanating intermediate formed from the reaction of selenium dioxide and malononitrile (**2**),[9,13] which led to the formation of 1-aryl-2-selenocyanatoethan-1-one **3**.

In summary, we have developed a simple and general method for the selenocyanation of aromatic ketones using readily available selenium dioxide and malononitrile. Further, this reaction has the advantage wherein the substrates are all added together in one-pot bypassing the prepreparation of the intermediate (TSD), thus providing divergent access to a series of 1-aryl-2-selenocyanatoethan-1-one and novel 4-aryl-1-selenocyanatobut-3-en-2-one compounds which are important synthons and have potential application in selenoorganic synthesis. In addition, the use of easily available starting materials, unique versatility, shorter reaction time, and high

https://dx.doi.org/10.1021/acs.joc.0c02630
J. Org. Chem. 2021, 86, 1980–1986

substrate scope adds to the operational simplicity of this method.

EXPERIMENTAL SECTION

General Information. Unless otherwise specified, all chemicals are commercially available without further purification or prepared by a known procedure. All reactions were carried out in a temperature control magnetic stirrer using an oil bath. Reactions were monitored by TLC using precoated aluminum sheets (silica gel 60 F254 0.2 mm thickness) and visualized by UV fluorescence light at 254 nm using an appropriate mixture of ethyl acetate and hexane. Column chromatography was carried out on silica gel (100−200 mesh) eluting with an appropriate mixture of ethyl acetate and hexane. IR spectra were recorded on a PerkinElmer Spectrum 400 FTIR instrument, and the frequencies are expressed in cm^{-1}. ^1H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker Avance II-400 spectrometer in $CDCl_3$ and/or DMSO-d_6 where TMS is the internal standard and the chemical shift are expressed in ppm. Mass spectral data were obtained with a Waters UPLC−TQD mass spectrometer (ESI-MS). High-resolution mass spectra (ESI-HRMS) were recorded on an Agilent 6545, quadrupole time-of-flight (Q-TOF). ^{77}Se NMR spectra were recorded on a ECZR series 600 MHz NMR spectrometer (Jeol, Japan), where the chemical shifts are expressed in ppm. The melting points of all synthesized compound are recorded by the open capillary tube method and are uncorrected. All commercial chemicals were purchased from Sigma-Aldrich, TCI Chemicals, and Alfa Aesar and used directly as received.

General Procedure for the Synthesis of 1-Aryl-2-selenocyanatoethan-1-one (3). A mixture of aryl methyl ketones **1** (1 mmol, 1 equiv), malononitrile **2** (1.5 mmol, 1.5 equiv, 99 mg), and selenium dioxide (3 mmol, 3 equiv, 333 mg) were allowed to stir in 3 mL of DMSO at a temperature of 40 °C for 2 h in an oil bath. On completion of the reaction, the mixture was extracted and diluted with ethyl acetate (10 mL) and then washed with brine (15 mL). The organic layer was separated and dried over anhydrous sodium sulfate where it was concentrated to a minimum amount by a rotatory evaporator. The compounds were then either purify by column chromatography on silica gel (100−200 mesh) using a mixture of ethyl acetate and hexane as the eluents or separated by vacuum filtration followed by washing with an appropriate mixture of ethyl acetate and hexane to get the product.

General Procedure for the Synthesis of 4-Aryl-1-selenocyanatobut-3-en-2-one (5). A mixture of styryl methyl ketones 4 (1 mmol, 1 equiv), malononitrile **2** (1.5 mmol, 1.5 equiv, 99 mg), and selenium dioxide (3 mmol, 3 equiv, 333 mg) were allowed to stir in 3 mL of DMSO at a temperature of 50 °C for 2 h in an oil bath. On completion of the reaction, the mixture was extracted and diluted with ethyl acetate (10 mL) and then washed with brine (15 mL). The organic layer was separated and dried over anhydrous sodium sulfate where it was concentrated to a minimum amount by a rotatory evaporator. The compounds were then either purified by column chromatography on silica gel (100−200 mesh) using a mixture of ethyl acetate and hexane as the eluents or separated by vacuum filtration followed by washing with an appropriate mixture of ethyl acetate and hexane to get the product.

*1-Phenyl-2-selenocyanatoethan-1-one (**3a**).*[5e,7−9,14] The product was prepared *via* the general procedure from acetophenone (1 mmol, 120 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (157 mg, 70%); mp 80−82 °C; IR (KBr): 3448, 2943, 2152, 1665, 1592, 1184, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 7.2 Hz, J = 7.6 Hz, 1H), 7.46 (t, J = 8 Hz, J = 7.6 Hz, 2H), 4.88 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.2, 134.9, 133.7, 129.1, 128.7, 101.9, 38.4 ppm. MS (ES^+) calcd for C_9H_7NOSe, 224.97, found m/z, 226.04 $[M + H]^+$.

*2-Selenocyanato-1-(p-tolyl)ethan-1-one (**3b**).*[7,8] The product was prepared *via* the general procedure from 4-methylacetophenone (1 mmol, 134 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (8:2); yellow solid (172 mg, 72%); mp 123−124 °C IR (KBr): 3447, 2931, 2208, 1653, 1504, 806 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 2H), 7.30−7.24 (m, 2H), 4.87 (s, 2H), 2.38 (s, 3H)) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.7, 146.2, 131.2, 129.8, 128.8, 102.1, 38.6, 21.8 ppm. MS (ES^+) calcd for $C_{10}H_9NOSe$, 238.94, found m/z, 240.20 $[M + H]^+$

*1-(4-Methoxyphenyl)-2-selenocyanatoethan-1-one (**3c**).*[5e] The product was prepared *via* the general procedure from 4-methoxyacetophenone (1 mmol, 150 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (7:3); yellow solid (191 mg, 75%); mp 102−104 °C; IR (KBr): 3448, 2933, 2149, 1642, 1601, 1568, 1171, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 4.85 (s, 2H), 3.83 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 191.5, 164.8, 131.2, 126.7, 114.3, 102.3, 55.7, 38.6 ppm. MS (ES^+) calcd for $C_{10}H_9NO_2Se$, 254.98, found m/z, 256.15 $[M + H]^+$

*1-(4-Nitrophenyl)-2-selenocyanatoethan-1-one (**3d**).* The product was prepared *via* the general procedure from 4-nitroacetophenone (1 mmol, 165 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; white solid (167 mg, 62%); mp 110−112 °C; IR (KBr): 3445, 2933, 2150, 1666, 1601, 1532, 1178, 888 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 9.2 Hz, 2H), 4.85 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 191.8, 151.1, 138.0, 129.8, 124.3, 100.9, 37.3 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_9H_7N_2O_3Se$, 270.9622; found 270.9615.

*1-(4-Chlorophenyl)-2-selenocyanatoethan-1-one (**3e**).*[5e,7,9] The product was prepared *via* the general procedure from 4-chloroacetophenone (1 mmol, 154 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; yellow solid (181 mg, 70%); mp 159−160 °C; IR (KBr): 3447, 2932, 2152, 1658, 1589, 1180, 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 4.83 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.0, 141.6, 132.0, 130.0, 129.5, 101.6, 38.0 ppm. MS (ES^+) calcd for $C_9H_6ClNOSe$, 258.93, found m/z, 260.01 $[M + H]^+$

*1-(4-Bromophenyl)-2-selenocyanatoethan-1-one (**3f**).*[5e,8,7] The product was prepared *via* the general procedure from 4-bromoacetophenone (1 mmol, 199 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (7:3); white solid (202 mg, 67%); mp 178−180 °C; IR (KBr): 3448, 2932, 2208, 1657, 1583, 1178, 811 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 4.82 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$: DMSO-d_6): δ 192.6, 132.6, 132.2, 130.3, 129.7, 102.1, 36.9 ppm. MS (ES^+) calcd for $C_9H_6BrNOSe$, 302.88, found m/z, 304.36 $[M + H]^+$

*1-(4-Fluorophenyl)-2-selenocyanatoethan-1-one (**3g**).*[8,9] The product was prepared *via* the general procedure from 4-fluoroacetophenone (1 mmol, 138 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; pink solid (192 mg, 79%); mp 113−114 °C; IR (KBr): 3448, 2934, 2153, 1658, 1595, 1297, 1104, 877 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, J = 5.2 Hz, 2H), 7.14 (t, J = 8.4 Hz, J = 8.8 Hz, 2H), 4.84 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 191.6, 166.7 (d, $^1J_{C-F}$ = 256.8 Hz), 131.5 (d, $^3J_{C-F}$ = 9.7 Hz), 130.2 (d, $^4J_{C-F}$ = 3.0 Hz), 116.5 (d, $^2J_{C-F}$ = 22.0 Hz), 101.7, 38.1 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −101.1 ppm. MS (ES^+) calcd for C_9H_6FNOSe, 242.95, found m/z, 244.03 $[M + H]^+$.

*1-(3-Methoxyphenyl)-2-selenocyanatoethan-1-one (**3h**).*[8] The product was prepared *via* the general procedure from 3-methoxyacetophenone (1 mmol, 150 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; orange solid (165 mg, 65%); mp 110−112 °C; IR (KBr): 3446, 2937, 2155, 1663, 1595, 1192, 861 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 7.6 Hz, 1H), 7.38−7.34 (m, 2H), 7.15−7.13 (m, 1H), 4.85 (s, 2H), 3.80 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.0, 160.0, 134.9, 130.1, 121.4, 121.4, 112.5, 101.9, 55.5, 38.5 ppm. MS (ES^+) calcd for $C_{10}H_9NO_2Se$, 254.97, found m/z, 256.30 $[M + H]^+$.

https://dx.doi.org/10.1021/acs.joc.0c02630
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*1-(3-Nitrophenyl)-2-selenocyanatoethan-1-one (**3i**).* The product was prepared *via* the general procedure from 3-nitroacetophenone (1 mmol, 165 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (7:3); orange solid (175 mg, 65%); mp 93–94 °C; IR (KBr): 3357, 2934, 2150, 1686, 1572, 1034, 885 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.48–8.46 (m, 1H), 8.24 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 4.86 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$: DMSO-d_6): δ 191.7, 148.3, 135.2, 134.5, 130.4, 128.4, 123.6, 101.8, 35.9 ppm; ^{77}Se NMR (600 MHz, DMSO): δ 210.871 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_9H_7N_2O_3Se$, 270.9622; found 270.9632.

*1-(3-Chlorophenyl)-2-selenocyanatoethan-1-one (**3j**).*[8] The product was prepared *via* the general procedure from 3-chloroacetophenone (1 mmol, 154 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; pink solid (184 mg, 71%); mp 66–67 °C; IR (KBr): 3425, 2933, 2147, 1664, 1571, 1424, 1184, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (t, J = 2.0 Hz, 1H), 7.78–7.75 (m, 1H), 7.59–7.57 (m, 1H), 7.42 (t, J = 8 Hz, 1H) 4.82 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.0, 135.5, 135.1, 134.7, 130.5, 128.6, 126.8, 101.4, 37.8 ppm. MS (ES^+) calcd for $C_9H_6ClNOSe$, 258.93, found m/z, 260.05 $[M + H]^+$.

*1-(2-Methoxyphenyl)-2-selenocyanatoethan-1-one (**3k**).* The product was prepared *via* the general procedure from 2-methoxyacetophenone (1 mmol, 150 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; pink solid (186 mg, 73%); mp 64–65 °C; IR (KBr): 3447, 3006, 2948, 2155, 1634, 1595, 1161, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 7.6 Hz, 1H), 7.55–7.51 (m, 1H), 7.02–6.95 (m, 2H), 4.81 (s, 2H), 3.92 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.9, 159.8, 136.2, 131.4, 123.2, 121.2, 111.8, 102.9, 55.8, 43.2 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{10}H_{10}NO_2Se$, 255.9877; found 255.9872.

*2-Selenocyanato-1-(o-tolyl)ethan-1-one (**3l**).*[8] The product was prepared *via* the general procedure from 2-methylacetophenone (1 mmol, 134 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; pink solid (160 mg, 67%); mp 98–100 °C; IR (KBr): 3447, 2970, 2148, 1661, 1564, 1174, 985, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 7.2 Hz, 1 Hz), 7.46–7.41(m, 1H), 7.29–7.24 (m, 2H), 4.89 (s, 2H), 2.49 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.3, 140.6, 133.7, 132.8, 132.8, 130.5, 126.2, 102.1, 40.9, 22.1 ppm. MS (ES^+) calcd for $C_{10}H_9NOSe$, 238.98, found m/z, 240.07 $[M + H]^+$.

*1-(2-Chlorophenyl)-2-selenocyanatoethan-1-one (**3m**).*[7] The product was prepared *via* the general procedure from 2-chloroacetophenone (1 mmol, 154 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; white solid (170 mg, 66%); mp 84–86 °C; IR (KBr): 3443, 2999, 2943, 2152, 1664, 1591, 1183, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, J = 1.2 Hz, 1H), 7.63–7.59 (m, 1H), 7.46 (t, J = 8.0 Hz, J = 7.6 Hz, 2H), 4.88 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.2, 134.8, 133.7, 129.1, 128.7, 101.9, 38.5 ppm. MS (ES^+) calcd for $C_9H_6ClNOSe$, 258.93 found m/z, 259.20 $[M]^+$

*1-(2-Bromophenyl)-2-selenocyanatoethan-1-one (**3n**).* The product was prepared *via* the general procedure from 2-bromoacetophenone (1 mmol, 199 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (166 mg, 55%); mp 78–79 °C; IR (KBr): 3445, 2943, 2152, 1664, 1575, 1183, 996, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, J = 1.6 Hz, 1H), 7.63–7.59 (m, 1H), 7.46 (t, J = 7.6 Hz, J = 8.0 Hz, 2H), 4.88 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.2, 134.8, 133.7, 129.1, 128.7, 101.9, 38.5 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_9H_7BrNOSe$, 303.8876; found 303.8849.

*1-(2,4-Dimethoxyphenyl)-2-selenocyanatoethan-1-one (**3o**).* The product was prepared *via* the general procedure from 2,4-dimethoxycetophenone (1 mmol, 180 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; white solid (199 mg, 70%); mp 94–95 °C; IR (KBr): 3448, 2944, 2842, 2149, 1670, 1590, 1120, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (t, J = 8.8 Hz, J = 8.4 Hz, 1H), 6.52 (d, J = 8.4 Hz, 2H), 4.53 (s, 2H), 3.77 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 196.0, 157.8, 132.8, 115.6, 104.0, 101.8, 56.0, 41.0 ppm; ^{77}Se NMR (600 MHz, DMSO) δ: 292.219 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}NO_3Se$, 285.9982; found 286.0026.

*1-(2,4-Dimethylphenyl)-2-selenocyanatoethan-1-one (**3p**).*[8] The product was prepared *via* the general procedure from 2,4-dimethylcetophenone (1 mmol, 148 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (182 mg, 72%); mp 90–91 °C; IR (KBr): 3437, 3020, 2984, 2152, 1660, 1610, 1563, 1190, 809 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 7.6 Hz, 1 Hz), 7.07 (d, J = 9.6 Hz, 2H), 4.90 (s, 2H), 2.47 (s, 3H), 2.32 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 194.5, 144.9, 141.0, 133.6, 131.0, 130.0, 126.9, 102.4, 41.2, 22.3, 21.6 ppm. MS (ES^+) calcd for $C_{11}H_{11}NOSe$, 253.00, found m/z, 254.14 $[M + H]^+$.

*1-Mesityl-2-selenocyanatoethan-1-one (**3q**).* The product was prepared *via* the general procedure from 2,4,6-trimethylacetophenone (1 mmol, 162 mg). The crude was purified by column chromatography using hexane/ethyl acetate (7:3) as the eluent; brown solid (292 mg, 72%); mp 62–63 °C: IR (KBr): 3357, 2980, 2934, 2150, 1686, 1608, 1445, 1143, 885 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.82 (s, 2H), 4.43 (s, 2H), 2.23 (s, 3H), 2.17 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 202.6, 140.2, 135.1, 133.4, 128.9, 101.1, 41.0, 21.1, 19.4 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{14}NOSe$, 268.0241; found 268.0230.

*1-(Furan-2-yl)-2-selenocyanatoethan-1-one (**3r**).*[8] The product was prepared *via* the general procedure from 2-acetylfuran (1 mmol, 110 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (155 mg, 72%); mp 99–100 °C; IR (KBr): 3448, 3121, 2939, 2154, 1644, 1561, 1463, 1079, 793 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.36 (d, J = 3.6 Hz, 1H), 6.65–6.64 (m, 1H), 4.60 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.3, 150.2, 147.9, 119.5, 113.2, 101.1, 35.2 ppm. MS (ES^+) calcd for $C_7H_5NO_2Se$, 214.94 found m/z, 215.93 $[M + H]^+$

*2-Selenocyanato-1-(thiophen-2-yl)ethan-1-one (**3s**).*[8] The product was prepared *via* the general procedure from 2-acetylthiophene (1 mmol, 126 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (8:2); yellow solid (177 mg, 77%); mp 100–101 °C; IR (KBr): 3250, 2930, 2207, 1632, 1510, 1409, 1172, 943, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 4.0 Hz, 2H), 7.21 (t, J = 4.4 Hz, 1H), 4.76 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.4, 140.1, 136.3, 134.3, 128.8, 101.5, 36.8 ppm. MS (ES^+) calcd for C_7H_5NOSSe 230.92, found m/z, 249.15 $[M + NH_4]^+$

*4-Phenyl-1-selenocyanatobut-3-en-2-one (**5a**).* The product was prepared *via* the general procedure from benzylideneacetone (1 mmol, 146 mg). The product was collected by vacuum filtration over Whatman-41 filter paper and washed with hexane/ethyl acetate (8:2); brown solid (155 mg, 62%); mp 106–107 °C; IR (KBr): 3454, 3051, 2942, 2208, 1672, 1574, 1150, 1002, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 16.4 Hz, 1H), 7.60–7.57 (m, 2H), 7.47–7.42 (m, 3H), 6.82 (d, J = 16.0 Hz, 1H), 4.57 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$: DMSO-d_6): δ 192.7, 146.7, 133.4, 131.5, 129.1, 128.7, 122.8, 101.9, 38.0 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}NOSe$, 251.9928; found 251.9919.

*1-Selenocyanato-4-(p-tolyl)but-3-en-2-one (**5b**).* The product was prepared *via* the general procedure from 4-methylbenzylideneacetone (1 mmol, 160 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (153 mg, 58%); mp 108–110 °C; IR (KBr): 3241, 3000, 2913, 2153, 1635, 1601, 1149, 1002, 804 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 16.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H), 6.77 (d, J = 16.4 Hz, 1H), 4.57 (s, 2H), 2.40 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.6, 147.0, 142.5, 130.6, 129.9, 128.8, 121.7, 101.9, 38.4, 21.6 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}NOSe$, 266.0084; found 266.0083.

https://dx.doi.org/10.1021/acs.joc.0c02630
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*4-(4-Methoxyphenyl)-1-selenocyanatobut-3-en-2-one (**5c**).* The product was prepared *via* the general procedure from 4-methoxybenzylideneacetone (1 mmol, 176 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (168 mg, 60%); mp 104−106 °C; IR (KBr): 3448, 3023, 2941, 2152, 1632, 1597, 1510, 1260, 1151, 807 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 16.0 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 16.4 Hz, 1H), 4.56 (s, 2H), 3.86 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.4, 162.5, 146.7, 130.7, 126.0, 120.3, 114.7, 102.0, 55.5, 38.5 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}NO_2Se$, 282.0033; found 282.0028.

*4-(4-Fluorophenyl)-1-selenocyanatobut-3-en-2-one (**5d**).* The product was prepared *via* the general procedure from 4-fluorobenzylideneacetone (1 mmol, 164 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (150 mg, 56%); mp 100−102 °C; IR (KBr): 3447, 2996, 2943, 2154, 1645, 1595, 1509, 1235, 1152, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 16.0 Hz, 1H), 7.61−7.57 (m, 2H), 7.13 (t, J = 8.4 Hz, 2H), 6.75 (d, J = 16.0 Hz, 1H), 4.53 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.3, 164.6 (d, $^1J_{C-F}$ = 252.5 Hz), 145.5, 130.8 (d, $^3J_{C-F}$ = 8.7 Hz), 129.7(d, $^4J_{C-F}$ = 3.3 Hz), 122.4, 122.3, 116.5 (d, $^2J_{C-F}$ = 21.9 Hz), 101.7, 38.2 ppm; ^{19}F NMR (400 MHz, $CDCl_3$): δ −106.4 ppm; ^{77}Se NMR (600 MHz, DMSO): δ 196.782 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_9FNOSe$, 269.9833; found 269.9844.

*4-(4-Bromophenyl)-1-selenocyanatobut-3-en-2-one (**5e**).* The product was prepared *via* the general procedure from 4-bromobenzylideneacetone (1 mmol, 225 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; brown solid (207 mg, 63%); mp 98−100 °C; IR (KBr): 3446, 2992, 2937, 2154, 1644, 1584, 1154, 1071, 847 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.63−7.57 (m, 3H), 7.45 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 16.4 Hz, 1H), 4.53 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.3, 145.4, 132.5, 132.2, 130.0, 126.2, 123.0, 101.6, 38.1 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_9BrNOSe$, 329.9033; found 329.9012.

*4-(4-Chlorophenyl)-1-selenocyanatobut-3-en-2-one (**5f**).* The product was prepared *via* the general procedure from 4-chlorobenzylideneacetone (1 mmol, 180 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; white solid (176 mg, 62%); mp 100−102 °C; IR (KBr): 3448, 3056, 2947, 2157, 1643, 1589, 1154, 1088, 806 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 16.4 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 16.0 Hz, 1H), 4.53 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.3, 145.3, 137.7, 131.8, 129.8, 129.5, 123.0, 101.6, 38.2 ppm; ^{77}Se NMR (600 MHz, DMSO): δ 197.862 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_9ClNOSe$, 285.9538; found 285.9560.

*4-(2-Chlorophenyl)-1-selenocyanatobut-3-en-2-one (**5g**).* The product was prepared *via* the general procedure from 2-chlorobenzylideneacetone (1 mmol, 180 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; yellow solid (168 mg, 59%); mp 86−88 °C; IR (KBr): 3448, 3025, 2935, 2151, 1641, 1588, 1154, 981 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 16.4 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.42−7.32 (m, 2H), 6.80 (d, J = 16.4 Hz, 1H), 4.61 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.5, 142.5, 135.7, 132.3, 131.5, 130.4, 127.8, 127.3, 125.1, 101.6, 38.1 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_9ClNOSe$, 285.9538; found 285.9538.

*4-(2,4-Dimethoxyphenyl)-1-selenocyanatobut-3-en-2-one (**5h**).* The product was prepared *via* the general procedure from 2, 4-dimethoxybenzylideneacetone (1 mmol, 206 mg). The crude was purified by column chromatography using hexane/ethyl acetate (8:2) as the eluent; yellow solid (164 mg, 62%); mp 106−108 °C; IR (KBr): 3448, 3062, 2941, 2144, 1635, 1603, 1223, 1143, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 16.4 Hz, 1H), 7.06−6.99 (m, 2H), 6.89 (d, J = 9.2 Hz, 1H), 6.83 (d, J = 16.4 Hz, 1H), 4.65 (s, 2H), 3.88 (s, 3H), 3.80 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.2, 153.5, 153.3, 142.1, 123.4, 122.6, 119.0, 112.9, 112.4, 102.1, 56.0, 55.8, 38.6 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{14}NO_3Se$, 312.0139; found 312.0143.

*4-Methyl-1-selenocyanatopent-3-en-2-one (**5i**).* The product was prepared *via* the general procedure from 4-methylpent-3-en-2-one (1 mmol, 98 mg). The crude was purified by column chromatography using hexane/ethyl acetate (9.5:0.5) as the eluent; yellow oil (92 mg, 46%); IR (KBr): 2982, 2933, 2154, 1674, 1608, 1436, 1385, 1102, 1038, 872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.17−6.16 (m, 1H), 4.28 (s, 2H), 2.19 (d, J = 1.2 Hz, 3H), 1.98 (d, J = 1.2, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.0, 162.0, 120.0, 101.7, 41.3, 28.0, 21.4 ppm. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_7H_{10}NOSe$, 203.9928; found 203.9932.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02630.

Single-crystal XRD data of **3a** and copies of ^1H and ^{13}C NMR of all synthesized compounds (PDF)

Accession Codes

CCDC 2041476 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.

■ ACKNOWLEDGMENTS

The authors acknowledge SAIF-NEHU, SAIF-CDRI Lucknow, SAIF-IIT Bombay, and SAIF-IIT Madras for spectral analysis. The author thanks the financial support of University Grants Commission (UGC), India, under the Maulana Azad National Fellowship for Minority (MANF) Scheme. B.M. acknowledges financial assistance from SERB, DST (Grant SB/EMEQ-006/3013).

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https://dx.doi.org/10.1021/acs.joc.0c02630
J. Org. Chem. 2021, 86, 1980−1986