Weinreb Amide Based Building Block for Convenient Access to Vinyl Ketones

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Abstract: A new strategy for the synthesis of vinyl ketones has been achieved. Hitherto unknown and easily accessible, β-phenylseleno-*N*-methoxy-*N*-methylpropanamide, obtained through two simple reactions, served as a building block for convenient access to vinyl ketones. The *N*-methoxy-*N*-methyl amide moiety ensured no overaddition of the Grignard reagent and, hence, the excellent formation of β-phenylseleno ketones; oxidative work-up with hydrogen peroxide provided ready access to the vinyl ketones with concomitant loss of phenylselanol.

Key words: Weinreb amide, selenoxide elimination, Grignard reaction, oxidation, vinyl ketone

Vinyl ketones **1** constitute an important functional unit providing a diverse range of reactivity for a multitude of synthetic endeavours in organic chemistry. The successful participation of this unit in a variety of reactions, such as Michael, aza-Michael, Diels–Alder, Heck, Stetter–Aldol, aza-Morita–Baylis–Hillman and cross-metathesis reaction has highlighted their utility as an excellent building block in the synthesis of important targets.[1] In the recent times, several elegant uses of this building block have been demonstrated. The first use of vinyl ketones in aza-Rauhut–Currier reaction initiated [4+2] annulations with *N*-sulfonyl-1-aza-1,3-dienes led to the synthesis of a highly functionalized tetrahydropyridine framework.[2a] Similarly, cross metathesis with vinyl ketones has paved the way for the synthesis of the natural product (+)-crocacin.[2b] Michael addition/cyclization of tryptamines with vinyl ketones has enabled enantioselective synthesis of pyrroloindolines,[2c] and the synthesis of enantiopure aziridinyl ketones have been achieved through aziridination of vinyl ketones.[2d]

Based on the excellent acylation capabilities of Weinreb amide (WA) functionality,[3] the addition of organomagnesium halide **4** on *N*-methoxy-*N*-methyl acrylamide (**5**) should provide the most convenient access to vinyl ketones **1**. However, attempts to access vinyl ketones either through addition of vinyl magnesium halide **2** to Weinreb amide **3** (approach A) or addition of organomagnesium reagent **4** to the WA of acrylic acid **5** (approach B) have been marred by the facile conjugate addition of the liberated *N*-methoxy-*N*-methylamine (**6**) during the workup (Figure 1).[4] The high reactivity of vinyl ketones **1** in general, coupled with the inevitable presence of the liberated amine **6** during work-up, precludes the survival of the target vinyl ketones **1**. Wuts and co-workers[5] first noted the conjugate addition of amine **6** onto an enone derived from the addition of vinylmagnesium bromide to the WA group in a leucine derivative.

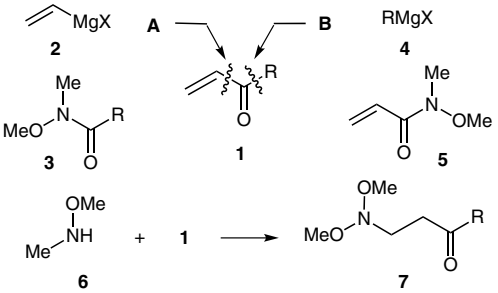
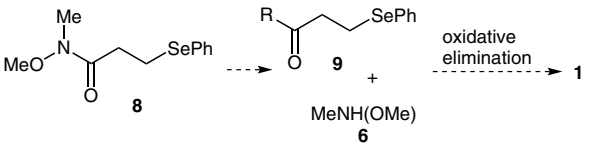


Figure 1 Possible approaches and limitations to the synthesis of vinyl ketones through Grignard addition to Weinreb amides

Wickberg and co-workers later made similar observations while attempting the addition of methylcyclopropenyllithium to WA.[6] In fact, this great disadvantage from the perspective of vinyl ketone synthesis was elegantly utilized by Gomtsyan and co-workers for the synthesis of β-aminoketones **7**, wherein the β-amino unit need not be restricted to *N*-methoxy-*N*-methylamine alone.[7] Creating the vinyl unit after removal of the amine **6** should provide an easy solution to circumvent this difficulty. This simple variation in the sequence of functionality generation should be amenable from hitherto unknown, β-phenylseleno-*N*-methoxy-*N*-methylpropanamide (**8**; Scheme 1). The envisaged building block **8** should allow addition of organomagnesium reagents onto WA and formation of β-phenylseleno ketones **9**. After removal of the side product **6**, oxidative conditions using hydrogen peroxide should facilitate creation of the vinyl unit through selenoxide-mediated elimination. Presented herein are the results of this simple solution, which has paved the way for an efficient synthetic scheme to access vinyl ketones **1** (Scheme 1).



Scheme 1 A new route to vinyl ketones

Multigram quantities of compound **8** were easily prepared in high yields by using commercially available β-bromo-

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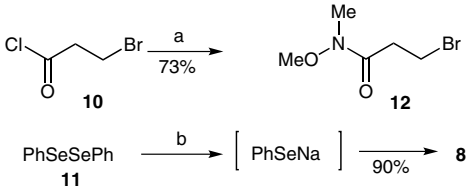
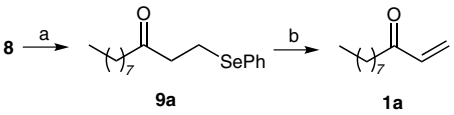
propanoyl chloride (**10**) and diphenyl diselenide (**11**) as starting material (Scheme 2).[8] The phenyl selenide anion generated by reduction of **11** with sodium borohydride[9] in ethanol reacts cleanly with β-bromo-*N*-methoxy-*N*-methylpropanamide (**12**),[10] affording the desired building block **8**, as a yellow oil[11] after simple purification by silica gel column chromatography.



Scheme 2 *Reagents and conditions*: (a) MeO(Me)NH·HCl (1.1 equiv), Et_3N (2.2 equiv), CH_2Cl_2, 0 °C, 3 h; (b) $NaBH_4$ (2.1 equiv), EtOH; 15 min stirring at 0 °C; then **12** (2 equiv), 4 h.

To investigate the proposed synthetic scheme for vinyl ketones **1**, WA-based building block **8** was then subjected to nucleophilic addition with Grignard reagents (Scheme 3). Octylmagnesium bromide, as a representative alkylmagnesium halide, was used for addition onto **8** at −10 °C. To our delight, a clean reaction ensued, furnishing the expected β-phenylseleno ketone **9a** (72%) after aqueous NH_4Cl work up and purification by silica gel column chromatography. Ketone **9a**, on oxidation with aqueous hydrogen peroxide through a reported procedure[12] at 0 °C and warming to room temperature, afforded vinyl ketone **1a** in excellent yield (90%), thereby validating the proposed new scheme for convenient access to vinyl ketones.



Scheme 3 *Reagents and conditions*: (a) $Me(CH_2)_7MgBr$ (3 equiv), THF, −10 °C, 2 h (72%); (b) 30% aq. H_2O_2 (8 equiv), THF, 0 °C to r.t., 30 min (66–90%).

The scheme was generalized with other organomagnesium bromides (Table 1). All products, β-phenylseleno ketones **9a–l**[13] and vinyl ketones **1a–l**,[14] displayed satisfactory spectral and analytical details.

In summary, a convenient synthetic route to alkyl/aryl/heteroaryl vinyl ketones has been developed through the use of β-phenylseleno-*N*-methoxy-*N*-methylpropanamide (**8**) as a new WA-based building block. The simplicity of its preparation on a multigram scale, enabling clean nucleophilic addition followed by facile oxidative generation of vinyl residue in high yield, is a significant advantage. Due to the importance of vinyl ketones in synthetic endeavours, the developed methodology for the synthesis of vinyl ketones should be valuable.

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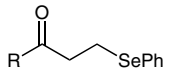
Table 1 Grignard Addition to **8** and the Vinyl Ketones Obtained upon Oxidative Elimination

Entry	RMgBr		Yield (%)[a]		Yield (%)[a]
	R	**9**		**1**	
1	$(CH_2)_7Me$	**9a**	72	**1a**	90
2	$(CH_2)_{10}Me$	**9b**	60	**1b**	83
3	Ph	**9c**	72	**1c**	70
4	4-MeC_6H_4	**9d**	68	**1d**	76
5	4-$MeOC_6H_4$	**9e**	75	**1e**	89
6	4-FC_6H_4	**9f**	67	**1f**	89
7	4-ClC_6H_4	**9g**	71	**1g**	86
8	2-thienyl	**9h**	65	**1h**	79
9	3,4-$Cl_2C_6H_4$	**9i**	68	**1i**	88
10	3,4,5-$(MeO)_3C_6H_2$	**9j**	62	**1j**	69
11	$(CH_2)_4OTHP$	**9k**	54	**1k**	75
12	4-$THPOC_6H_4$	**9l**	65	**1l**	76

[a] Isolated yield.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(8) **Preparation of compound 8:** $NaBH_4$ (1.58 g, 41.5 mmol) was added portionwise to a stirred solution of diphenyldiselenide (5.97 g, 19.1 mmol) in absolute EtOH (100 mL) under nitrogen at 0 °C (addition of $NaBH_4$ was exothermic with rapid evolution of hydrogen gas). After complete addition of $NaBH_4$, within 15 min the reaction medium became colourless. When the evolution of hydrogen ceased, a solution of **12** (6.22 g, 31.9 mmol) in absolute EtOH (11 mL) was added dropwise at 0 °C. The reaction mixture was stirred over a period of 4 h and monitored by TLC. Upon completion of the reaction, brine (10 mL) was added and the solvent was evaporated under vacuum. The residue was dissolved in EtOAc (100 mL) and washed with H_2O (3 × 20 mL) and brine. The organic layer was separated, dried over Na_2SO_4, evaporated under vacuum and purified by silica gel column chromatography (EtOAc–hexane, 20%) to afford **8** 8.67g (90%) as a pale-yellow liquid.

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(11) **Compound 8:** Yield: 8.67 g (90%); R_f = 0.62 (hexane–EtOAc, 9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.86 (t, *J* = 7.6 Hz, 2 H, $COCH_2$), 3.18–3.15 (m, 5 H, $SeCH_2$, NCH_3), 3.61 (s, 3 H, OCH_3), 7.25–7.30 (m, 3 H, ArH), 7.52–7.55 (m, 2 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.7 ($COCH_2$), 32.2 (NCH_3), 33.0 ($SeCH_2$), 61.3 (OCH_3), 127.0 (ArCH), 129.1 (ArCH), 130.0 (ArC), 132.7 (ArCH), 172.9 (CO, amide). IR ($CHCl_3$): 2972, 2940, 2433, 2400, 2350, 1655, 1579, 1525, 1520, 1502 cm^{-1}. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{15}NNaO_2Se$: 296.0166; found: 296.0171.

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(13) **Preparation of Grignard Reagent and Synthesis of 9a–l; General Procedure:** Grignard reagent was prepared from 1-bromooctane (1.92 g, 9.93 mmol) and magnesium (0.24 g, 9.93 mmol, activated with iodine/methyl iodide) in anhydrous THF (10 mL) at 55 °C. After complete consumption of magnesium, the solution was allowed to cool to r.t. and the resulting solution was slowly added to **8** (0.90 g, 3.31 mmol) dissolved in THF (3 mL) at −10 °C and stirring was continued for 2 h. Sat. NH_4Cl was added cautiously at 0 °C, and reaction mixture was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography (EtOAc–hexane, 2%), which afforded **9a** (0.77 g, 72%) as a yellow liquid. R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.25–1.30 (m, 10 H), 1.52–1.57 (m, 2 H, CH_2), 2.36 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.81 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.07 (t, *J* = 7.5 Hz, 2 H, CH_2), 7.24–7.28 (m, 3 H, ArH), 7.48–7.50 (m, 2 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.7 (CH_2), 22.7 (CH_2), 23.8 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 31.9 (CH_2), 43.1 (CH_2), 43.2 (CH_2), 127.2 (ArCH), 129.2 (ArCH), 129.9 (ArC), 132.9 (ArCH), 209.7 (CH_2CO). IR ($CHCl_3$): 2929, 2856, 2400, 1712, 1579, 1524, 1477, 1438, 1375 cm^{-1}. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{26}NaOSe$: 349.1047; found: 349.1047.

1-(Phenylselanyl)tetradecan-3-one (9b): Yield: 0.40 g (60%); yellow liquid; R_f = 0.64 (hexane–EtOAc, 9.5:0.5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.24 (s, 16 H), 1.52–1.57 (m, 2 H, CH_2), 2.36 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.81 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.07 (t, *J* = 7.2 Hz, 2 H, CH_2), 7.24–7.28 (m, 3 H, ArH), 7.47–7.50 (m, 2 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.7 (CH_2), 22.8 (CH_2), 23.8 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.0 (CH_2), 43.1 (CH_2), 43.2 (CH_2), 127.2 (ArCH), 129.2 (ArCH), 129.9 (ArC), 132.9 (ArCH), 209.7 (CH_2CO). IR ($CHCl_3$): 2928, 2875, 2401, 1711, 1581, 1524, 1473 cm^{-1}.

1-Phenyl-3-(phenylselanyl)propan-1-one (9c): Yield: 1.92 g (72%); colourless solid; mp 61–63 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.17 (t, *J* = 7.5 Hz, 2 H, $COCH_2$), 3.32 (t, *J* = 7.5 Hz, 2 H, $SeCH_2$), 7.17–7.22 (m, 3 H, ArH), 7.35–7.38 (m, 2 H, ArH), 7.44–7.50 (m, 3 H, ArH), 7.82–7.83 (m, 2 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.2 ($COCH_2$), 39.5 ($SeCH_2$), 127.2 (ArCH), 128.1 (ArCH), 128.7 (ArCH), 129.3 (ArCH), 129.9 (ArC), 132.9 (ArCH), 133.4 (ArCH), 136.6 (ArC), 198.7 (CH_2CO). IR ($CHCl_3$): 2401, 1684, 1599, 1579, 1524, 1477, 1448, 1438, 1344 cm^{-1}. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}NaOSe$: 313.0108; found: 313.0104. Anal. Calcd for $C_{15}H_{14}OSe$: C, 62.29; H, 4.88. Found: 62.52; H, 4.97.

3-(Phenylselanyl)-1-(*p*-tolyl)propan-1-one (9d): Yield: 0.52 g (64%); colourless solid; mp 73–75 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 3.24 (t, *J* = 7.2 Hz, 2 H, $COCH_2$), 3.36 (t, *J* = 7.2 Hz, 2 H, $SeCH_2$), 7.22–7.28 (m, 5 H, ArH), 7.51–7.53 (m, 2 H, ArH), 7.80 (d, *J* = 8.0 Hz, 2 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 ($COCH_2$), 21.7 (CH_3), 39.4 ($SeCH_2$), 127.1 (ArCH), 128.2 (ArCH), 129.2 (ArCH),

129.4 (ArCH), 130.0 (ArC), 132.9 (ArCH), 134.1 (ArC), 144.2 (ArC), 198.4 (CH_2CO). IR ($CHCl_3$): 2401, 1679, 1607, 1579, 1522, 1477, 1423, 1339, 1218 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}NaOSe$: 327.0264; found: 327.0255.

1-(4-Methoxyphenyl)-3-(phenylselanyl)propan-1-one (9e): Yield: 0.97 g (75%); colourless solid; mp 83–85 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^1H NMR (500 MHz, $CDCl_3$): δ = 3.17 (t, *J* = 7.0 Hz, 2 H, $COCH_2$), 3.27 (t, *J* = 7.0 Hz, 2 H, $SeCH_2$), 3.79 (s, 3 H, OCH_3), 6.82–6.85 (m, 2 H, ArH), 7.17–7.22 (m, 3 H, ArH), 7.44–7.46 (m, 2 H, ArH), 7.80–7.83 (m, 2 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5 ($COCH_2$), 39.1 ($SeCH_2$), 55.6 (OCH_3), 113.9 (ArCH), 127.1 (ArCH), 129.2 (ArCH), 129.7 (ArC), 130.1 (ArC), 130.4 (ArCH), 132.9 (ArCH), 163.7 (ArC), 197.2 (CH_2CO). IR ($CHCl_3$): 2401, 1674, 1601, 1577, 1510, 1477, 1420 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}NaO_2Se$: 343.0213; found: 343.0202. Anal. Calcd for $C_{16}H_{16}O_2Se$: C, 60.19; H, 5.05. Found: 60.76; H, 4.93.

1-(4-Fluorophenyl)-3-(phenylselanyl)propan-1-one (9f): Yield: 67% (0.68 g); colourless crystalline solid; mp 93–95 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^1H NMR (500 MHz, $CDCl_3$): δ = 3.23 (t, *J* = 7.0 Hz, 2 H, $COCH_2$), 3.36 (t, *J* = 7.0 Hz, 2 H, $SeCH_2$), 7.08–7.13 (m, 2 H, ArH), 7.25–7.29 (m, 3 H, ArH), 7.50–7.53 (m, 2 H, ArH), 7.90–7.94 (m, 2 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.1 ($COCH_2$), 39.4 ($SeCH_2$), 115.8 (d, *J* = 21.7 Hz, ArCH), 127.3 (ArCH), 129.3 (ArCH), 129.8 (ArC), 130.8 (d, *J* = 9.37 Hz, ArCH), 131.6 (ArC), 133.0 (ArCH), 165.9 (d, *J* = 253.7 Hz, ArCF), 197.1 (CH_2CO). IR ($CHCl_3$): 2400, 2344, 1683, 1600, 1509, 1477, 1420, 1340, 1216 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{13}FNaOSe$: 331.0013; found: 331.0008.

1-(4-Chlorophenyl)-3-(phenylselanyl)propan-1-one (9g): Yield: 0.76 g (71%); colourless crystalline solid; mp 95–97 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.23 (t, *J* = 6.8 Hz, 2 H, $COCH_2$), 3.36 (t, *J* = 6.8 Hz, 2 H, $SeCH_2$), 7.26–7.28 (m, 3 H, ArH), 7.39–7.43 (m, 2 H, ArH), 7.50–7.53 (m, 2 H, ArH), 7.81–7.85 (m, 2 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 ($COCH_2$), 39.5 ($SeCH_2$), 127.3 (ArCH), 129.1 (ArCH), 129.3 (ArCH), 129.5 (ArCH), 129.8 (ArC), 133.0 (ArCH), 134.9 (ArC), 139.8 (ArC), 197.5 (CH_2CO). IR ($CHCl_3$): 2400, 1683, 1590, 1524, 1478, 1436, 1402, 1340, 1217 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{13}ClNaOSe$: 346.9718; found: 346.9728.

3-(Phenylselanyl)-1-(2-thienyl)propan-1-one (9h): Yield: 0.63 g (65%); pink solid; mp 57–59 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.24 (t, *J* = 6.8 Hz, 2 H, $COCH_2$), 3.31 (t, *J* = 6.8 Hz, 2 H, $SeCH_2$), 7.10 (t, *J* = 4.4 Hz, 1 H, ArH), 7.26–7.28 (m, 3 H, ArH), 7.52–7.54 (m, 2 H, ArH), 7.63 (d, *J* = 4.8 Hz, 2 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 ($COCH_2$), 40.1 ($SeCH_2$), 127.3 (ArCH), 128.2 (ArCH), 129.3 (ArCH), 129.7 (ArC), 132.1 (ArCH), 133.1 (ArCH), 134.0 (ArCH), 143.9 (ArC), 191.5 (CH_2CO). IR ($CHCl_3$): 2401, 1661, 1579, 1518, 1477, 1416, 1359, 1336, 1213 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{13}H_{12}NaOSSe$: 318.9672; found: 318.9686. Anal. Calcd for $C_{13}H_{12}OSSe$: C, 52.88; H, 4.10. Found: 53.09; H, 4.01.

1-(3,4-Dichlorophenyl)-3-(phenylselanyl)propan-1-one (9i): Yield: 0.80 g (68%); light-yellow crystalline solid; mp 61–63 °C; R_f = 0.65 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.18 (t, *J* = 6.8 Hz, 2 H, $COCH_2$), 3.30 (t, *J* = 6.8 Hz, 2 H, $SeCH_2$), 7.24 (s, 3 H, ArH), 7.48 (d, *J* = 6.4 Hz, 3 H, ArH), 7.67 (d, *J* = 4.4 Hz, 1 H, ArH), 7.92 (s, 1 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9 ($COCH_2$), 39.5 ($SeCH_2$), 127.1 (ArCH), 127.4 (ArCH), 129.3 (ArCH), 129.6 (ArC), 130.1 (ArCH), 130.9 (ArCH), 133.1 (ArCH), 133.5 (ArC), 136.1 (ArC), 138.0 (ArC), 196.5 (CH_2CO). IR ($CHCl_3$): 2400, 1693, 1582, 1556, 1523, 1478, 1439, 1390, 1336 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{12}Cl_2NaOSe$: 380.9328; found: 380.9316.

3-(Phenylselanyl)-1-(3,4,5-trimethoxyphenyl)propan-1-one (9j): Yield: 0.43 g (62%); yellow viscous liquid; R_f = 0.35 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.24 (t, *J* = 6.8 Hz, 2 H, $COCH_2$), 3.36 (t, *J* = 6.8 Hz, 2 H, $SeCH_2$), 3.88 (s, 6 H, 2 × OCH_3), 3.90 (s, 3 H, OCH_3), 7.15 (s, 2 H, ArH), 7.25–7.29 (m, 3 H, ArH), 7.51–7.54 (m, 2 H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 ($COCH_2$), 39.1 ($SeCH_2$), 56.3 (OCH_3), 61.0 (OCH_3), 105.5 (ArCH), 127.2 (ArCH), 129.2 (ArCH), 129.9 (ArC), 131.8 (ArC), 132.8 (ArCH), 142.8 (ArC), 153.1 (ArC), 197.5 (CH_2CO). IR ($CHCl_3$): 2941, 2840, 2401, 1676, 1585, 1505, 1462, 1415, 1345 cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{20}NaO_4Se$: 403.0424; found: 403.0420.

(14) **Preparation of vinyl ketones 1a–l; General procedure:** To a solution of **9a** (0.20 g, 0.62 mmol) in THF (3 mL), 30% H_2O_2 (0.15 mL, 4.92 mmol) was added at 0 °C. Within 10 min, the reaction mixture became deep-yellow (the progress of the reaction was monitored by TLC) and after 30 min, aq $Na_2S_2O_3$ (0.1 M, 3 mL) was added and the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (15 mL) and washed with H_2O (3 × 4 mL) and the organic layer was separated, dried over Na_2SO_4, and concentrated. The product was purified by silica gel column chromatography (EtOAc–hexane, 1%) to afford **1a** (93 mg, 90%) as a yellow liquid. R_f = 0.68 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.26–1.29 (m, 10 H), 1.59–1.64 (m, 2 H, CH_2), 2.56 (t, *J* = 7.2 Hz, 2 H, CH_2), 5.79 (d, *J* = 10.8 Hz, 1 H, $=CH_bH_c$), 6.20 (d, *J* = 17.6 Hz, 1 H, $=CH_bH_c$), 6.34 (dd, *J* = 10.8, 17.6 Hz, 1 H, $COCH_a$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 22.7 (CH_2), 24.1 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 31.9 (CH_2), 39.8 (CH_2), 127.9 (CH), 136.7 (=CH_2), 201.2 (CO). IR ($CHCl_3$): 2931, 2865, 2408, 1686, 1617, 1524, 1456, 1410, 1218 cm^{-1}.

Tetradec-1-en-3-one (1b): Yield: 135 mg (83%); yellow liquid; R_f = 0.58 (hexane–EtOAc, 9.5:0.5). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.25–1.29 (m, 16 H), 1.59–1.64 (m, 2 H, CH_2), 2.57 (t, *J* = 7.6 Hz, 2 H, CH_2), 5.81 (dd, *J* = 1.2, 10.4 Hz, 1 H, $=CH_bH_c$), 6.21 (dd, *J* = 1.2, 17.6, Hz, 1 H, $=CH_bH_c$), 6.35 (dd, *J* = 10.8, 17.6 Hz, 1 H, $COCH_a$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 22.8 (CH_2), 24.1 (CH_2), 29.4 (CH_2), 29.47 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.0 (CH_2), 39.8 (CH_2), 128.0 (=CH), 136.7 (=CH_2), 201.3 (CH_2CO). IR ($CHCl_3$): 2928, 2855, 2401, 1679, 1614, 1524, 1464, 1405 cm^{-1}.

^1H and ^{13}C NMR spectra of synthesized vinyl ketones **1a–l** have been included in the Supporting Information. The spectral data for vinyl ketones **1c**,[2b] **1d**[15a] and **1e**[15b] were consistent with those reported in the literature.

(15) (a) Cai, M.; Zheng, G.; Ding, G. *Green Chem.* **2009**, *11*, 1687. (b) Aranha, R. M.; Bowser, A. M.; Madalengoitia, J. S. *Org. Lett.* **2009**, *11*, 575.

