The other high-pressure runs were performed and analyzed as described above employing the concentrations and reaction times as shown in Table I.

Cantharidin (4) and *epi*-Cantharidin (5). A slurry of freshly prepared Raney nickel[18] in ethyl acetate (200 mL) was added to a solution of cycloaddition adducts **2** and **3** (14.4 g) in ethyl acetate (600 mL) under a nitrogen atmosphere. The mixture was stirred at reflux for 3 h and cooled slightly, and then the catalyst was removed by hot filtration. The collected catalyst residue was rinsed with warm acetone (500 mL), the acetone washings were combined with the early acetate portion, and the solvent was removed under reduced pressure to afford 12.94 g of a crude white solid. Selective recrystallization from ethyl acetate afforded 6.55 g (51%) of pure cantharidin (**4**): mp 210–211 °C; IR ($CHCl_3$) 1835, 1780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (s, 6), 1.76 (m, 4), 4.70 (m, 2). Anal. Calcd for $C_{10}H_{12}O_3$: C, 61.22; H, 6.16. Found: C, 61.40; H, 6.23.

Medium-pressure chromatography (silica, ether/hexane, 1:1) of the mother liquor afforded 0.647 g (8%) of pure *epi*-cantharidin (**5**): mp 193–194 °C; IR ($CHCl_3$) 1860, 1790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 6), 1.88 (m, 4), 4.66 (m, 2). Anal. Calcd for $C_{10}H_{12}O_3$: C, 61.22; H, 6.16. Found: C, 61.26; H, 6.35.

Registry No. **1**, 75532-25-1; **2**, 75558-06-4; **3**, 75532-26-2; **4**, 56-25-7; **5**, 80558-50-5; **7**, 96307-21-0; **8**, 20688-07-7; furan, 110-00-9.

(18) The W-6 Raney nickel was prepared according to Fieser: L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 729.

Relative Reactivities of Representative Aldehydes and Ketones toward Trimethylsilyl-Substituted Propargylic Boranes

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We recently reported that borane **1** reacts with representative aldehydes and ketones to form trimethylsilyl-substituted α-allenic alcohols with high regioselectivity and in excellent isolated yields (Scheme I).[1] Such allenes have recently been found to be useful for a variety of chemical reactions.[2] The bifunctional adduct **1** thus provides opportunities for achieving a wide array of transformations. This prompted us to investigate the relative reactivities of aldehydes and ketones toward **1**.

The relative reactivities of representative aldehydes and ketones toward **1** were studied by mixing 5 mmol of two carbonyl compounds in 10 mL of tetrahydrofuran and then introducing 5 mmol of **1** to the mixture. The amounts of the two products were determined by GLC and the relative reactivity was calculated according to the Ingold–Shaw equation.[3] The results summarized in Table I reveal an interesting chemoselectivity of **1**. Aldehydes are much more reactive than ketones; even pivalaldehyde is 40 times more reactive than cyclohexanone. Cyclohexanone is about 30 times more reactive than cyclopentanone; 2-pentanone, a methyl ketone, is about 9 times more reactive than 3-pentanone and cyclopentanone.

(1) Wang, K. K.; Nikam, S. S.; Ho, C. D. *J. Org. Chem.* **1983**, *48*, 5376–5377.
(2) (a) Danheiser, R. L.; Carini, D, J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935–947. (b) Danheiser, R. L.; Carini, D. J. *J. Org. Chem.* **1980**, *45*, 3925–3927.
(3) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2918–2926.

Scheme I

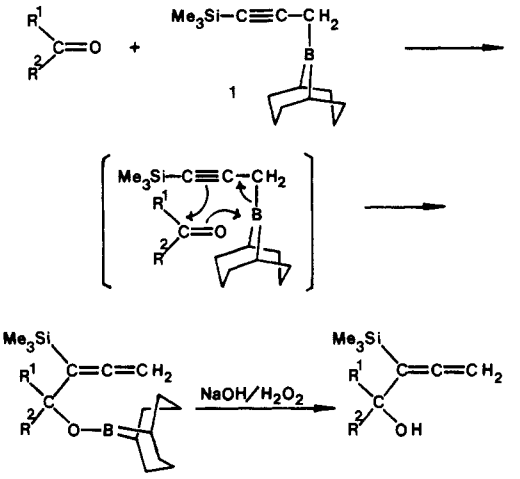


Table I. Relative Reactivities of Representative Aldehydes and Ketones toward Trimethylsilyl-Substituted Propargylic Borane 1 in THF at 25 °C

aldehyde or ketone	relative reactivity[a]
hexanal	100
isobutyraldehyde	87
benzaldehyde	37
crotonaldehyde	31
pivalaldehyde	3.0
cyclohexanone	7.3×10^{-2}
2-methylcyclohexanone	5.2×10^{-2}
acetone	4.4×10^{-2}
2-pentanone	2.1×10^{-2}
acetophenone	1.8×10^{-2}
cyclopentanone	2.5×10^{-3}
3-pentanone	2.4×10^{-3}
2-methylcyclopentanone	1.0×10^{-3}
butyrophenone	5.9×10^{-4}

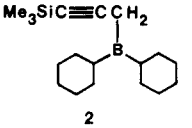
[a] Normalized; hexanal = 100.

Table II. Relative Reactivities of Representative Ketones toward Trimethylsilyl-Substituted Propargylic Borane 2 in THF at 25 °C

	relative reactivity[a]	
ketone	2	1
cyclohexanone	100	100
2-pentanone	28	29
acetophenone	17	25
cyclopentanone	9.4	3.5
3-pentanone	2.8	3.2

[a] Normalized; cyclohexanone = 100.

We also investigated the relative reactivities of ketones toward **2** (Table II). Similar results were observed when compared with **1**.

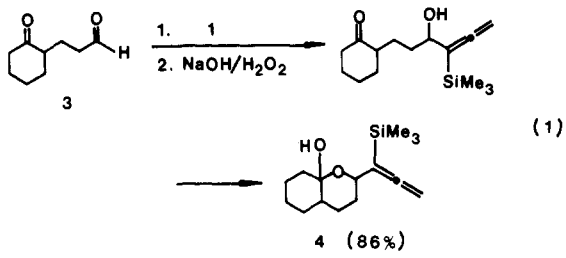


2

The data in Table I indicate that **1** will selectively react with an aldehyde group in the presence of a keto group. Indeed, this selectivity was observed with **3** (eq 1), and the hemiketal **4** was obtained. The hemiketal as the preferred tautomer had also been observed for 2-(3-hydroxypropyl)cyclohexanone.[4]

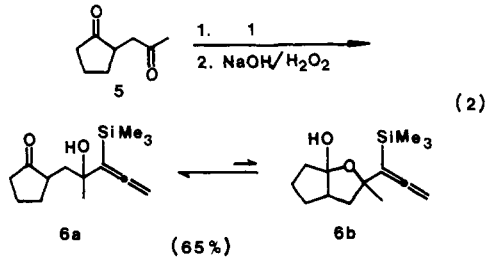
(4) Cazaux, M.; De Jeso, B. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1980**, *290*(2), 49–51.

0022-3263/85/1950-2578$01.50/0



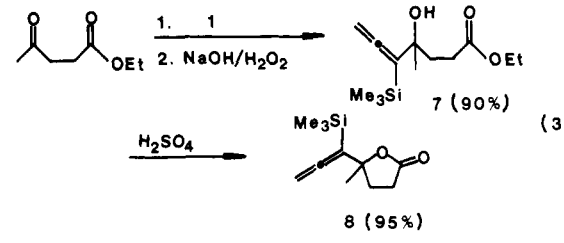
(1)

The higher reactivity of methyl ketone was also exploited for selective reaction, and **6** was obtained from **5** (eq 2). The IR and ^{13}C NMR spectra indicate the existence of an equilibration between **6a** and **6b** as observed previously for 2-(2-hydroxypropyl)cyclopentanone.[4]

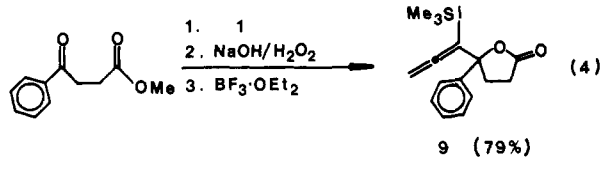


(2)

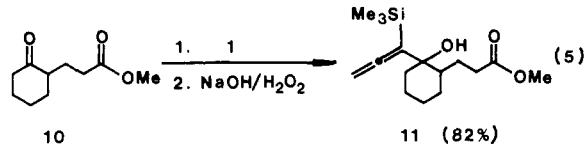
We also found that carboxylic esters exhibit no significant reactivity toward **1**. Consequently, ethyl levulinate was treated with **1** to afford **7** and then was further converted to γ-lactone **8** (eq 3). Similarly, γ-lactone **9** was obtained from methyl 3-benzoylpropionate (eq 4). The reaction with **10** provided the δ-hydroxy ester **11** (eq 5).



(3)



(4)



(5)

In summation, this study provides information concerning the relative reactivities of aldehydes and ketones toward trimethylsilyl-substituted propargylic boranes. This allows one to predict whether a carbonyl group could be selectively reacted in the presence of other carbonyl groups. The resulting products of such reactions have many reactive sites for further synthetic elaborations. The transformations of these highly functionalized compounds to natural products are in progress.

Experimental Section

The general procedures described in ref 1 were followed. Mass spectra were obtained on a Finnigan 4021 instrument. Elemental analyses were performed by Galbraith Laboratories (Knoxville, TN).

Relative Reactivity. The relative reactivities were studied as described in the text. *n*-Hexadecane was used as internal standard for GLC analyses. The carbonyl pairs selected for studies included hexanal/cyclohexanone, benzaldehyde/cyclohexanone, hexanal/isobutyraldehyde, hexanal/benzaldehyde, benzaldehyde/crotonaldehyde, benzaldehyde/pivalaldehyde, cyclohexanone/acetone, acetone/acetophenone, acetone/3-pentanone, acetophenone/3-pentanone, 2-methylcyclohexanone/3-pentanone, 2-methylcyclohexanone/acetone, pivalaldehyde/cyclohexanone, acetone/cyclopentanone, acetone/2-pentanone, 2-methylcyclopentanone/3-pentanone, and 3-pentanone/butyrophenone.

Borane **2** was similarly prepared from methyl dicyclohexylborinate[5] as described previously.[1] The selected ketone pairs included 2-pentanone/cyclopentanone, 2-pentanone/cyclohexanone, 2-pentanone/acetophenone, and 3-pentanone/cyclopentanone.

1-Hydroxy-3-[1-(trimethylsilyl)-1,2-propadienyl]-2-oxabicyclo[4.4.0]decane (4). To a solution of **3**[6] (1.54 g, 10 mmol) of THF (10 mL) at −78 °C was added **1** (10 mmol). The mixture was stirred at −78 °C for 1.5 h and then allowed to warm to −15 °C. After the oxidative workup, the product was column chromatographed (silica gel/hexane) to afford 2.29 g (86% yield) of **4** as a white solid: mp 50–51 °C; IR (KBr) 3450 (s, OH), 1935 (s, C=C=C), 1250 (s), 1055 (s), 830 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.65 (br, 1 H), 4.45 (d, 2 H, J = 2 Hz), 2.2–1.2 (br, 14 H), 0.15 (s, 9 H); ^{13}C NMR (Me_2SO-d_6) δ 207.6, 98.7, 95.8, 70.3, 68.7, 43.5, 37.8, 32.5, 29.2, 25.8, 25.1, 22.9, −0.2; MS, m/e 266 (M^+), 249 (M^+ − OH), 155 (M^+ − $Me_3SiC{=}C{=}CH_2$), 137, 111 ($Me_3SiC{=}C{=}CH_2^+$), 98, 73. Anal. Calcd for $C_{15}H_{26}O_2Si$: C, 67.62; H, 9.84. Found: C, 67.40; H, 9.69.

2-[2-Hydroxy-2-methyl-3-(trimethylsilyl)-3,4-pentadienyl]cyclopentanone (6a) and 1-Hydroxy-3-methyl-3-[1-(trimethylsilyl)-1,2-propadienyl]-2-oxabicyclo[3.3.0]octane (6b). To a solution of **5**[7] (1.4 g, 10 mmol) in THF (10 mL) at −20 °C was introduced **1** (10 mmol). After 1.5 h, the reaction mixture was warmed to −10 °C. The usual workup followed by distillation afforded 1.63 g (65% yield) of **6a** and **6b** as a colorless liquid: bp 72 °C (5 × 10^{-3} torr); IR (neat) 3450 (s, OH), 1930 (s, C=C=C), 1725 (s, C=O), 1240 (s), 1050 (m), 835 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.3 (m, 2 H, C=C=CH_2), 2.4–1.4 (br, 10 H), 1.3 (s, 3 H), 0.2 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 224.5 (C=O), 223.1 (C=O), 207.4 (=C=), 206.8 (=C=), 206.1 (=C=), 117.2 (HOCO of **6b**), 106.1 ($Me_3SiC{=}$), 105.1 ($Me_3SiC{=}$), 105.0 ($Me_3SiC{=}$), 86.6 (CO of **6b**), 74.3 (COH of **6a**), 73.6 (COH of **6a**), 70.9 ($H_2C{=}$), 70.2 ($H_2C{=}$), 69.9 ($H_2C{=}$), 48.7, 47.3, 47.0, 46.6, 43.0, 42.8, 40.5, 37.8, 37.5, 32.1, 31.9, 31.7, 29.8, 29.5, 24.2, 21.2, 21.0, 0.3, 0.1; MS, m/e 235 (M^+ − OH), 141 (M^+ − $Me_3SiC{=}C{=}CH_2$), 123 (M^+ − $Me_3SiC{=}C{=}CH_2$ − H_2O). Anal. Calcd for $C_{14}H_{24}O_2Si$: C, 66.61; H, 9.58. Found: C, 66.23; H, 9.82. The ^1H NMR and ^{13}C NMR spectra indicated that the product contained **6b** and two diastereomeric *dl* pairs of **6a**.

Ethyl 4-Hydroxy-4-methyl-5-(trimethylsilyl)-5,6-heptadienoate (7). The reaction was carried out by adding 1.42 mL of ethyl levulinate (1.44 g, 10 mmol) obtained from Aldrich to **1** at 25 °C and the solution was stirred for 2 h. After the usual workup, distillation afforded 2.30 g (90% yield) of **7** as a colorless liquid: bp 70 °C (5 × 10^{-2} torr); IR (neat) 3520 (m, OH), 1920 (s, C=C=C), 1725 (s, C=O), 1240 (s), 825 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.5 (s, 2 H), 4.1 (q, 2 H), 2.35 (m, 3 H), 1.95 (m, 2 H), 1.3 (s, 3 H), 1.2 (t, 3 H), 0.1 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 207.0, 174.6, 104.8, 74.1, 71.2, 60.4, 37.9, 30.3, 29.8, 14.2, 0.3.

4-Hydroxy-4-methyl-5-(trimethylsilyl)-5,6-heptadienoic Acid Lactone (8). To **7** (1.28 g, 5 mmol) in 20 mL of anhydrous ether was added 3 drops of concentrated sulfuric acid. After being stirred for 30 min, the mixture was washed with water and then distilled to afford 1.00 g (95% yield) of **8** as a colorless liquid: bp 58 °C (2 × 10^{-2} torr); IR (neat) 1925 (s, C=C=C), 1775 (s, C=O),

(5) Brown, H. C.; Sinclair, J. A. *J. Organomet. Chem.* **1977**, *131*, 163–169.

(6) (a) Cope, A. C.; Nealy, D. L.; Scheiner, P.; Wood, G. *J. Am. Chem. Soc.* **1965**, *87*, 3130–3135. (b) Allan, R. D.; Cordiner, B. G.; Wells, R. J. *Tetrahedron Lett.* **1968**, 6055–6056.

(7) (a) Nienhouse, E. J.; Irwin, R. M.; Finni, G. R. *J. Am. Chem. Soc.* **1967**, *89*, 4557–4558. (b) Negishi, E.; Luo, F.-T. *J. Org. Chem.* **1983**, *48*, 2427–2430.

1250 (s), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.75 (s, 2 H), 2.7–2.2 (m, 2 H), 1.55 (s, 3 H), 0.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 206.9, 176.1, 102.2, 87.0, 71.8, 35.3, 29.0, 28.4, –0.4; MS, *m/e* 210 (M^+), 195 ($M^+ - CH_3$), 111 ($Me_3SiC{=}C{=}CH_2^+$), 99 ($M^+ - Me_3SiC{=}C{=}CH_2$), 73 (Me_3Si^+). Anal. Calcd for $C_{11}H_{18}O_2Si$: C, 62.81; H, 8.62. Found: C, 62.78; H, 8.50.

4-Hydroxy-5-(trimethylsilyl)-4-phenyl-5,6-heptadienoic Acid Lactone (9). Methyl 3-benzoylpropionate (1.92 g, 10 mmol) obtained from Alfa was used and the reaction was carried out as described for **8** except that the crude α-allenic alcohol in 20 mL of anhydrous ether was treated with 5 drops of $BF_3{\cdot}OEt_2$. Distillation furnished 2.15 g (79% yield) of **9** as a colorless liquid: bp 101 °C (5×10^{-3} torr); IR (neat) 1935 (m, C=C=C), 1780 (s, C=O), 1250 (m), 835 (s), 755 (m), 695 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45 (s, 5 H), 4.8 (s, 2 H), 3.1–2.1 (m, 4 H), –0.05 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 207.9, 175.9, 143.6, 128.1, 127.3, 124.3, 100.9, 89.4, 72.2, 36.7, 29.1, –0.7; MS, *m/e* 161 ($M^+ - Me_3SiC{=}C{=}CH_2$), 73 (Me_3Si^+).

Methyl 3-[2-hydroxy-2-[1-(trimethylsilyl)-1,2-propadienyl]cyclohexyl]propionate (11) was prepared from **10**[8] (1.84 g, 10 mmol) as described for **7**. Distillation afforded 2.43 g (82% yield) of **11** as a white solid: bp 92 °C (2×10^{-2} torr); mp 51–52 °C; IR (KBr) 3570 (m, OH), 1930 (s, C=C=C), 1735 (s, C=O), 1245 (s), 835 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.45 (s, 2 H), 3.65 (s, 3 H), 2.5–2.1 (br, 3 H), 2.1–1.2 (br, 11 H), 0.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 206.5, 174.4, 105.6, 76.4, 71.5, 51.5, 44.2, 41.0, 32.3, 26.9, 25.9, 25.7, 21.8, 0.5; MS, *m/e* 296 (M^+), 279 ($M^+ - OH$), 185 ($M^+ - Me_3SiC{=}C{=}CH_2$), 153, 125, 73 (Me_3Si^+). Anal. Calcd for $C_{16}H_{28}O_3Si$: C, 64.82; H, 9.52. Found: C, 64.59, H, 9.71.

Acknowledgment. We thank the National Science Foundation for support of this work.

Registry No. **1**, 96413-63-7; **2**, 96503-43-4; **3**, 2568-20-9; **4**, 96503-44-5; **5**, 60415-94-3; **6a** (isomer 1), 96503-50-3; **6a** (isomer 2), 96503-51-4; **6b**, 96503-45-6; **7**, 96503-46-7; **8**, 96503-47-8; **9**, 96503-48-9; **10**, 10407-33-7; **11**, 96503-49-0; ethyl levulinate, 539-88-8; methyl 3-benzoylpropionate, 25333-24-8; hexanal, 66-25-1; isobutyraldehyde, 78-84-2; benzaldehyde, 100-52-7; crotonaldehyde, 4170-30-3; pivalaldehyde, 630-19-3; cyclohexanone, 108-94-1; 2-methylcyclohexanone, 583-60-8; acetone, 67-64-1; 2-pentanone, 107-87-9; acetophenone, 98-86-2; cyclopentanone, 120-92-3; 3-pentanone, 96-22-0; 2-methylcyclopentanone, 1120-72-5; butyrophenone, 495-40-9.

(8) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207–222.

Preparation and Single-Crystal X-ray Characterization of 4-Selenanone

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The concept of isosteric exchange has long been used by medicinal chemists as a tool for modifying the activity of biologically important molecules.[1] One very important isosteric pair is that of sulfur and selenium. A wide variety of sulfur-containing compounds have been synthesized in which the sulfur atom has been replaced by a selenium atom.[1]

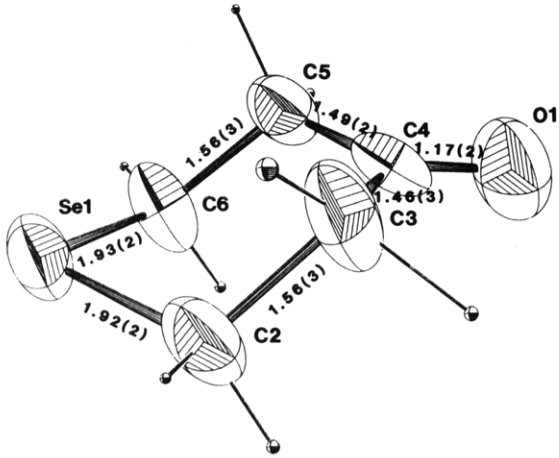
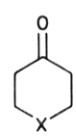


Figure 1. Projection view of 4-selenanone (**4**). The bond distances may be compared to those in **3**:[7a] C(2)–C(3), 1.527 (3) Å; C–S, 1.804 (3) Å.

Tetrahydro-4*H*-thiapyran-4-one (**3**) is a key intermediate



1. X = NCH_3
2. X = $^+N(CH_3)_2, I^-$
3. X = S
4. X = Se

in the synthetic scheme of a great many cyclic systems which contain sulfur. An extensive survey of the literature revealed that the *selenium* analogue **4** was heretofore unknown.[2] We now report the first synthesis of 4-selenanone (**4**) which has been accomplished via a reaction sequence that bears a remote similarity to that for **3**.[3] Ketone **4** fills a gap in the family of 1-heteracyclohexanones involving O, S, and now Se.[2d]

The synthetic scheme involved treatment of *N*-methylpiperidone (**1**) with methyl iodide to generate the corresponding oxopiperidinium iodide **2**. A mixture of powdered elemental selenium and $NaBH_4$ was used to generate NaHSe[4] and the resulting mixture was treated with **2**. This type of displacement of a secondary amine has some precedent in the formation of the sulfur analogue **3** as cited previously.[3] Although the yield is modest (56–63%), the reaction is easy to perform.

For comparison purposes, the $\lambda_{C=O}$ for sulfide **3** was 1710 cm^{-1} (KBr). Interestingly, the ^{13}C chemical shifts for C(2,6), C(3.5), and C(4) in $\mathbf{1}^{2d}$ ($DCCl_3$) were 55.3, 41.0, and 207.1 ppm, in $\mathbf{2}^{2d}$ (Me_2SO-d_6) were 60.6, 35.0, and 201.7 ppm, in $\mathbf{3}^{2d}$ ($DCCl_3$) were 30.3, 44.0, and 208.0 ppm, and

(1) (a) Klayman, D. L. In "Organic Selenium Compounds: Their Chemistry and Biology"; Klayman, D. L., Gunther, W. H. H., Eds.; Wiley: New York, 1973; pp 727–761. (b) Ganther, H. E. In "Selenium"; Zingaro, R. A., Cooper, W. C., Eds.; Van Nostrand Reinhold Co.: New York, 1974; pp 580–588. (c) Burger, A. In "Medicinal Chemistry", 3rd ed.; Burger, A., Ed.; Wiley-Interscience: New York, 1970; Part 1, pp 64–80. (d) Chu, S.; Mautner, H. G. *J. Med. Chem.* **1968**, *11*, 446–447.

(2) (a) Reid, D. H., Senior Reporter "Organic Compounds of Sulphur, Selenium, and Tellurium"; The Chemical Society: London, 1970; Specialist Periodical Report. (b) Parker, W.; Senior Reporter "Aliphatic, Alicyclic, and Saturated Heterocyclic Chemistry", The Chemical Society: London, 1973; Vol. 1–5; Specialist Periodical Report. (c) Lambert, J. B.; Featherman, S. I. *Chem. Rev.* **1975**, *75*, 611. (d) Hirsch, J. A.; Havinga, E. *J. Org. Chem.* **1976**, *41*, 455–462.

(3) (a) Johnson, P. Y.; Berchtold, G. A. *J. Org. Chem.* **1970**, *35*, 584–592. (b) Garst, M. E.; McBride, B. J.; Johnson, A. T. *J. Org. Chem.* **1983**, *48*, 8–16. *CAUTION* should be exercised in the handling of all selenium reagents in the described experiments since it is necessary to presume such materials could be toxic. Ketone **4** does sublime and therefore exposure of this compound to the atmosphere should be avoided.

(4) Klayman, D. L.; Griffin, T. S. *J. Am. Chem. Soc.* **1973**, *95*, 197–199.

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