Oxone Oxidation of Selenides: A Mild and Efficient Method for the Preparation of Selenones

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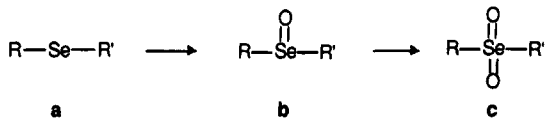
Received June 15, 1995

Selenide (**a**) to selenoxide (**b**) or selenone (**c**) oxidation is a useful operation in organic synthesis, and a variety of reagents have been developed for this purpose.



a **b** **c**

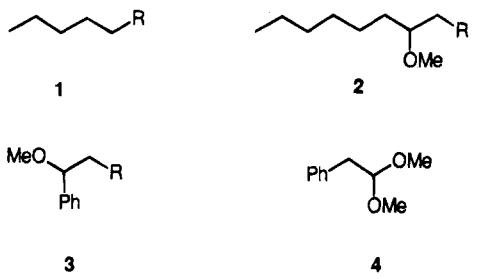
Most investigations have focused on the preparation and reactivity of selenoxides,[1] but selenones have received little attention. Selenones have been prepared by oxidation of selenides using an excess of peroxycarboxylic acids,[2] potassium permanganate,[2] or hydrogen peroxide in the presence of seleninic acid.[3] These methods have several disadvantages and can be applied only to selenides with limited structural features in the presence of selected solvents.

Herein, we report that potassium hydrogen persulfate, commercially available as Oxone, can be used effectively for the direct conversion of selenides to selenones under very mild conditions. When selenides are treated with 3 mol equiv of Oxone in a methanolic, aqueous, buffered solution (pH 8.0–8.5) at room temperature, selenones are produced in good yield. The amount of buffered solution added in these reactions is crucial for success to selenone formation because the oxidation process involves the generation of acids, and Oxone has shown a strong pH dependence as oxidant.[4]

This protocol was applied to the oxidation of three classes of substrates: alkylaryl selenides, β-methoxyalkyl selenides, and β-hydroxyalkyl selenides. The reactions can easily be monitored by TLC since selenones are more polar than selenides but less polar than selenoxide intermediates. Selenones exhibit a characteristic IR absorption at 870–970 and 912–1059 cm^{-1},[5] and in ^{13}C NMR spectra, a strong deshielding occurs at the carbon bearing the heteroatom during the oxidation of selenides to selenoxides and then to selenones, allowing easy identification of these functional groups.

There are a number of interesting features in published methodology. The most common method used for the preparation of selenones is Krief's oxidation of selenides[2] using a large excess of *m*-CPBA in dichloromethane that involves a tedious workup procedure and fails to recover selenones in the presence of nucleophiles. The selenone moiety behaves like a leaving group,[2] but the *m*-CPBA generated in the oxidation process, or the excess of *m*-CPBA, transforms the selenone into a much better leaving group,[6] allowing easy transformation of C–Se into a C–O[6] or C–N[7] bond even in the presence of weak nucleophiles. The process is accompained by skeletal rearrangement when applied to selenides that have a phenyl group vicinal to the phenylselenium moiety[8] and to some β-methoxyalkyl or β-hydroxyalkyl selenides.[6,8]

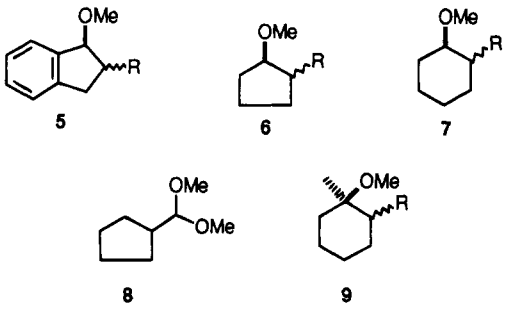
Oxidation of selenide **1a**[9] with Oxone afforded selenone **1b** (91%), whose structure was unambiguously confirmed by displacement of the selenyl moiety with sodium methoxide (**1c**).[10] Similarly, β-methoxyselenones **2b**



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

a: R = SePh; b: R = SeO_2Ph; c: R = OMe

(84%), **3b** (95%), and **5b** (99%) were obtained from the corresponding selenides. As expected, acid treatment (PTSA) of selenones **2b** and **5b** in methanol gave rise to the substitution products **2c**, **5c**, and **5d**; acetal **4** was recovered from **3b** under the same reaction conditions. Selenones were also obtained in excellent yield by the oxidation of selenides **6a**[6] and **7a**.[6] The selenone **7b** was transformed into acetal **8** by interaction with acids in methanol, thus confirming the tendency of the β-methoxyselenonyl moiety in a six-membered ring to generate ring contraction before methanol attack.[6] Unexpectedly, selenide **9a**[6] was more resistent to Oxone oxidation, and the reaction took place only at pH 11 to yield the β-methoxy alcohol **9e**.



5 **6** **7** **8** **9**

a: R = α SePh; b: R = α SeO_2Ph
c: R = α OMe; d: R = β OMe; e: R = β OH

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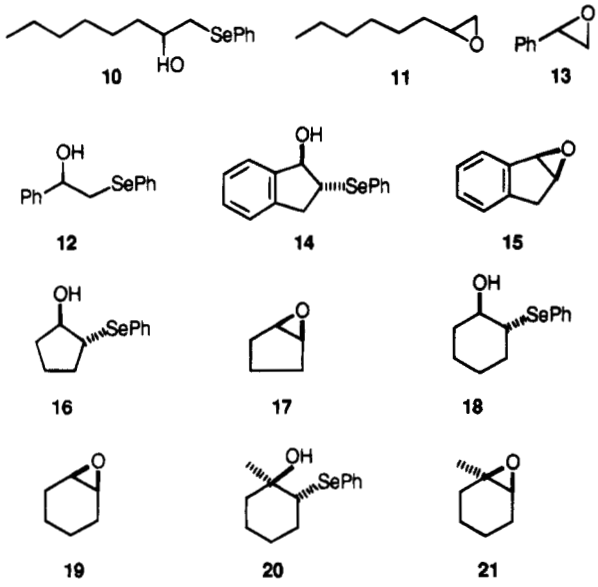
In the oxidation of β-hydroxy selenides **10**,[11] **12**,[12] **14**,[13] **16**,[13] **18**,[14] and **20**[15] the corresponding epoxides (**11**, **13**, **15**, **17**, **19**, and **21**) were obtained as the only reaction products. This apparently occurs *via* the participation of the neighboring hydroxy group in the displacement of the selenone intermediate.



Compared to all the existing procedures for selenone formation, this method appears to be more general, the reaction conditions are milder, the yields are usually better, and the isolation of the desired products is achieved without additional purification. The transposition products observed in the *m*-CPBA oxidation of β-hydroxy selenides[8] and β-methoxy selenides[6] were never detected.

Experimental Section

General. The same general procedures were followed as described previously.[16] Oxone was purchased from Fluka. Reaction products such as **4**, **11**, **13**, **17**, and **19** are commercially available.

CAUTION. Selenium-containing compounds are toxic and should be handled with care. Most of the selenium-containing compounds described here are sufficiently high boiling that volatility does not pose a severe toxicity or odor problem. PhSeCl, however, is volatile enough to have pronounced odor.

Oxidation of Selenides with Oxone: General Procedure. Oxone (10 mL of 0.3 M aqueous solution) was added to a stirred solution of alkyl phenyl selenide (1 mmol) in MeOH (30 mL) and buffered water (15 mL, 0.5 M Na_2HPO_4/NaOH 1 M, pH 11). The mixture was well-stirred for 1 h at room temperature and then diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers, dried (Na_2SO_4) and evaporated under vacuum, yielded pure compound.

1-(Phenylselenonyl)pentane (1b): white solid (91%); mp 64–65 °C; IR 945 (s), 890 (s), cm^{-1}; ^1H NMR δ 0.87 (t, 3 H, J = 7.0 Hz), 1.20–2.0 (m, 6 H), 3.48 (t, 2 H, J = 7.0 Hz), 7.5–8.0 (m, 5 H); ^{13}C NMR δ 140.9, 134.0, 130.0, 126.8, 59.7, 30.3, 21.9, 21.7 13.4. Anal. Calcd for $C_{11}H_{15}O_2Se$: C, 51.17; H, 5.86. Found: C, 51.25; H, 5.79.

2-Methoxy-1-(phenylselenonyl)octane (2b): white solid (84%); mp 103–105 °C; IR 948 (s), 890 (s) cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, J = 7.0 Hz), 1.2–1.8 (m, 10 H), 3.26 (s, 3 H), 3.55–3.78 (m, 2 H), 3.98 (m, 1 H), 7.55–8.05 (m, 5 H); ^{13}C NMR δ 143.2, 133.5, 129.4, 126.5, 74.5, 64.6, 56.2, 31.9, 31.2, 28.7, 23.9, 22.0, 13.6. Anal. Calcd for $C_{15}H_{21}O_3Se$: C, 54.88; H, 6.45. Found: C, 54.93; H, 6.40.

2-Methoxy-2-phenyl-1-(phenylselenonyl)ethane (3b): white solid (95%); mp 156–158 °C; IR 948 (s), 890 (s) cm^{-1}; ^1H NMR δ 3.18 (s, 3 H), 3.58 (dd, 1H, J = 2.5 and 12.5 Hz), 3.85 (dd, 1 H, J = 11.0 and 13.0 Hz), 7.2–8.0 (m, 5 H); ^{13}C NMR δ 143.6, 136.8, 133.8, 129.7, 128.9, 126.9, 126.4, 126.2, 77.0, 66.6, 56.4. Anal. Calcd for $C_{15}H_{16}O_3Se$: C, 58.74; H, 4.99. Found: C, 55.81; H, 4.92.

***trans*-1-Methoxy-2-(phenylselenonyl)indan (5b):** white solid (99%); mp 181–183 °C; IR 948 (s), 890 (s) cm^{-1}; ^1H NMR δ 3.39 (s, 3 H), 3.43 (d, 2 H, J = 7.0 Hz), 4.23 (ddd, 1 H, J = 7.0, 7.0 and 4.0 Hz), 7.0–7.8 (m, 9 H); ^{13}C NMR δ 139.6, 138.8, 138.7, 133.8, 129.6, 129.3, 127.3, 127.0, 124.9, 124.3, 83.4, 74.2, 57.0, 31.1. Anal. Calcd for $C_{16}H_{16}O_3Se$: C, 57.32; H, 4.81. Found: C, 57.37; H, 4.75.

***trans*-2-Methoxy-1-(phenylselenonyl)cyclopentane (6b):** white solid (94%); mp 73–74 °C; IR 942 (s), 890 (s) cm^{-1}; ^1H NMR δ 1.7–2.3 (m, 6 H), 3.22 (s, 3 H), 3.87 (ddd, 1 H, J = 3.5, 7.0, and 12.0 Hz), 4.34 (m, 1 H), 7.5–8.0 (m, 5 H); ^{13}C NMR δ 139.0, 133.6, 129.6, 126.8, 81.1, 75.0, 56.4, 31.7, 25.1, 22.9. Anal. Calcd for $C_{12}H_{16}O_3Se$: C, 50.18; H, 5.61. Found: C, 50.25; H, 5.54.

***trans*-2-Methoxy-1-(phenylselenonyl)cyclohexane (7b):** white solid (95%); mp 95–97 °C; IR 940 (s), 885 (s) cm^{-1}; ^1H NMR δ 1.0–2.6 (m, 8 H), 3.28 (s, 3 H), 3.5–3.7 (m, 2 H), 7.4–8.0 (m, 5 H); ^{13}C NMR δ 143.4, 132.4, 128.5, 126.0, 76.6, 76.5, 54.5, 29.7, 24.4, 24.0, 23.3. Anal. Calcd for $C_{13}H_{18}O_3Se$: C, 51.83; H, 6.02. Found: C, 51.77; H, 6.07.

***cis*-2-Methyl-2-methoxycyclohexanol (9e):** colorless oil (69%); ^1H NMR δ 1.32 (s, 3 H), 3.17 (dd, 1 H, J = 12.5 and 8.0 Hz), 3.54 (s, 3 H); ^{13}C NMR δ 86.1, 72.6, 56.8, 37.5, 26.3, 23.3, 22.5, 21.1. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.67; H, 11.15.

1,2-Epoxyoctane (11): colorless oil (93%). Identified by comparison with a commercial sample.

Treatment of Selenones with Acids: General Procedure. PTSA (1.2 mmol) was added to a solution of selenone (1 mmol) in methanol (20 mL), and the resulting solution was stirred at 60 °C for 1 h. A saturated solution of $NaHCO_3$ (20 mL) was added, and the mixture was extracted with *n*-pentane (2 × 20 mL). The combined organic layers, dried (Na_2SO_4) and evaporated, yielded pure methoxy derivative.

1-Methoxypentane (1c):[17] colorless oil (98%).

1,2-Dimethoxyoctane (2c):[18] colorless oil (91%).

2-Phenylethanal dimethyl acetal (4): colorless oil (91%). Identified by comparison with a commercial sample.

Indene oxide (15): colorcolorless oil (92%); ^1H NMR;[19] ^{13}C NMR.[20]

Styrene oxide (13): colorless oil (85%). Identified by comparison with a commercial sample.

Cyclopentene oxide (17): colorless oil (87%). Identified by comparison with a commercial sample.

Cyclohexene oxide (19): colorless oil (97%). Identified by comparison with a commercial sample.

1-Methylcyclohexene-1-oxide (21):[21] colorless oil (95%).

1,2-Dimethoxyindan (5c, 5d):[6] colorless oil, **5c** (44%) and **5d** (51%).

1,2-Dimethoxycyclopentane (6c, 6d):[6] colorless oil, **6c** (17%) and **6d** (44%).

Cyclopentane carbaldehyde dimethyl acetal (8):[6] colorless oil (90%).

Acknowledgment. The support of this research by the CNR (Rome) and MURST is gratefully acknowledged.

JO951086V

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