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Synthesis of selenoxides by oxidation of selenides with superoxide radical anions and 2-nitrobenzenesulfonyl chloride

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Abstract—Alkyl phenyl selenoxides were produced in excellent yields by oxidation of the corresponding selenides with 2-nitrobenzenesulfonyl chloride and potassium superoxide in dry acetonitrile at −15 °C.

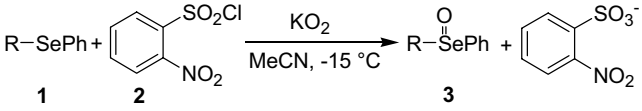
Organoselenium reagents are routinely employed in many synthetic transformations. Among the various types of organoselenium compounds, selenoxides are frequently employed as versatile intermediates.[1] The most commonly used reaction of these compounds is the spontaneous *syn*-elimination[2] which provides a facile route to olefins and to α,β-unsaturated carbonyl compounds. Allylic selenoxides, on the other hand, undergo a facile [2,3] sigmatropic rearrangement to afford allylic alcohols.[3,1] Selenoxides are also known as mild reagents for oxidation of various organic compounds[4] such as olefins, thiols, sulfides, phosphines, hydrazides, amines, alcohols and catechols. It has also been recently demonstrated[5] that selenoxides can be used as catalysts in the activation of hydrogen peroxide for the oxidation of bromide anions.

Only sporadic reports on the preparation and isolation of stable selenoxides from aryl-, benzyl- or methyl-substituted selenides are present in the literature.[6] Selenoxides can be isolated whenever the *syn*-elimination reaction is impossible because of the absence of hydrogen atoms in the β-carbon or because the oxygen atom of the selenoxide gives an hydrogen bond with a close acidic hydrogen atom. Also isolable are those β-alkoxy selenoxides in which the elimination can only proceed by abstraction of an hydrogen atom linked to a carbon holding an oxygen function.[7]

Selenoxides are generally prepared from the corresponding selenides using common oxidants such as hydrogen peroxide,[8] ozone,[9] *tert*-butyl hydroperoxide,[10] oxaziridines,[11] sodium metaperiodate,[12] *m*-PBA,[13] (dichloroiodo)benzene,[12] *N*-chlorosuccinimide,[14] *tert*-butyl hypochlorite[14] or nitrogen oxides.[15] Due to the several synthetic utilities of the selenoxides, their preparation is an area of current interest.

We now report that various alkyl phenyl selenides **1** can be oxidized to the corresponding selenoxides **3**, in excellent yields and under mild reaction conditions, by the 2-nitrobenzenesulfonyl peroxy intermediates generated in situ from the reaction of 2-nitrobenzenesulfonyl chloride **2** with potassium superoxide at −15 °C in dry acetonitrile (Scheme 1). This method was previously employed for the oxidation of sulfides to sulfoxides[16] and of sulfoxides to sulfones.[17] The reactions of superoxide radical anions with sulfinyl,[16] sulfonyl[17] and silyl[18] chlorides generate the corresponding peroxy radical intermediates which were found to be more efficient oxidizing agents than the superoxide itself.

The oxidation reactions were carried out according to the following general procedure. To a stirred solution



1 2 3

Scheme 1.

Keywords: Selenides; Selenoxides; Oxidation; Potassium superoxide.
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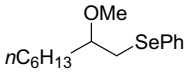
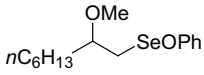
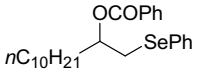
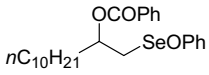
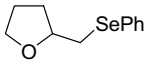
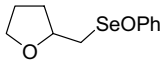
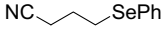
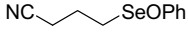
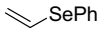
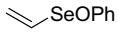
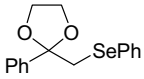
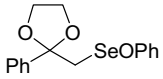
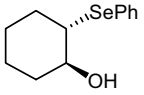
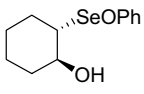
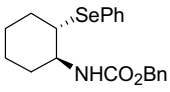
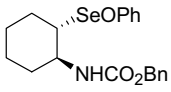
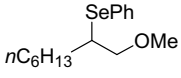
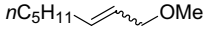
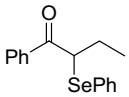
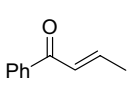
of 2-nitrobenzenesulfonyl chloride (0.154 g, 0.7 mmol) and benzyl phenyl selenide **1a** (0.124 g, 0.5 mmol) in dry acetonitrile (10 ml), under argon atmosphere and at −15 °C, potassium superoxide (0.106 g, 1.5 mmol) was added. After stirring for 1 h at −15 °C, the reaction mixture was allowed to slowly reach room temperature. Stirring was continued until TLC analysis showed that the starting selenide was completely converted into the corresponding selenoxide. The reaction mixture was diluted with anhydrous dichloromethane and then filtered through Celite. The filtrate was dried and concentrated to afford the highly pure selenoxide **3a** in excellent yield and with spectral data in good agreement with those reported in the literature.[15] The stable selenoxides which could be isolated are reported in Table 1 (entries a–j).

It can be observed that excellent yields were obtained in most cases. Good results were obtained in the cases in which the *syn*-elimination reaction cannot occur (entries a and g), in the case of β-oxy selenoxides (entries c–e and h)[19,7] and in the cases in which the oxygen atom of the selenoxide gave an hydrogen bond with a close acidic hydrogen atom (entries i and j). The primary alkyl phenyl selenoxides **3b** and **f** were also obtained[20] in moderate to good yields. This result was not surprising since it is known that the *syn*-elimination reaction of simple alkyl phenyl selenoxides is retarded in polar solvents.[21] Moreover, in these cases the elimination would afford a terminal alkene. The undesired oxidation of selenoxides to selenones did not occur with the present method. This was confirmed by the comparison of the spectral data of **3c** with those of an authentic sample of the corresponding selenone[23] which was prepared by oxidation with *m*-chloroperoxybenzoic acid in tetrahydrofuran in the presence of potassium hydrogenphosphate, as recently described.[22] Selenoxide **3c** showed the charac-

Table 1. Oxidation of selenides **1** with 2-nitrobenzenesulfonyl chloride and potassium superoxide in MeCN at −15 °C[a]

Entry	Selenides **1**	Time (h)	Reaction products		Yield[b] (%)
a	$PhCH_2$–SePh	2	$PhCH_2$–SeOPh	**3**	88
b	$nC_{10}H_{21}$–SePh	23	$nC_{10}H_{21}$–SeOPh	**3**	45[c,d]
c		36		**3**	76[c]
d		2		**3**	82[e]
e		5		**3**	98
f		5		**3**	90
g		7		**3**	85
h		22		**3**	89
i		6		**3**	98
j		6		**3**	94[c]
k		72		**4**	75[f]
l		18		**5**	67[g]

[a] Molar ratio KO_2:$ArSO_2Cl$:selenide = 3:1.4:1.
[b] Isolated yields. All compounds were characterized by IR and NMR spectroscopy.
[c] The pure selenoxide was obtained after column chromatography on a silica gel column (CH_2Cl_2/MeOH, 5%).
[d] A 28% of the eliminated product was isolated.
[e] Oxidation with 4-nitrobenzenesulfonyl chloride and superoxide anion under the same reaction conditions yielded the selenoxide in 90%.
[f] Mixture of the two geometrical isomers.
[g] A 15% of the starting selenide was recovered.

teristic IR absorption at 820 cm^{-1} and the selenone absorptions at 870–970 and 912–1059 cm^{-1} were not present. Moreover, in the ^{13}C NMR spectra the carbon bearing the heteroatom is gradually deshielded on passing from the selenides to the selenoxides and to the selenones. No absorptions due to the selenone were observed in the spectrum of **3c**.

Also reported in Table 1 are the results of two oxidation reactions (entries k and l) from which the selenoxides could not be isolated because of their rapid elimination reactions. In the first case the selenoxide obtained from the secondary selenide **1k** gave a spontaneous *syn*-elimination reaction to afford excellent yield of the internal alkene **4** as a 4:1 mixture of the two *E*/*Z* isomers. As expected the selenoxide derived from of the α-phenylseleno ketone **1l** gave the elimination reaction to afford the conjugated enone **5**.[24]

In conclusion, the present results demonstrate that the 2-nitrobenzenesulfonyl chloride–potassium superoxide system is a good reagent for the oxidation of selenides to selenoxides. The proposed method represents a simple protocol which is compatible with a variety of functional groups and should be of general application in synthesis.

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References and notes

1. (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon: Oxford, 1986; (b) Liotta, D. *Organoselenium Chemistry*; Wiley: New York, 1987; (c) *Organoselenium Chemistry—A Practical Approach*; Back, T. G., Ed.; Oxford: New York, 2000; (d) Organoselenium Chemistry: Modern Developments in Organic Synthesis. In *Topics in Current Chemistry*; Wirth, T., Ed.; Springer: Berlin, 2000.
2. Sharpless, K. B.; Lauer, L. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137–6139; Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5813–5815.
3. Campbell Bourland, T.; Carter, R. G.; Yokochi, A. F. T. *Org. Biomol. Chem.* **2004**, *2*, 1315–1329, and references cited therein.
4. Mlochowski, J.; Braszcz, M.; Giurg, M.; Palus, J.; Wojtowicz, H. *Eur. J. Org. Chem.* **2003**, 4329–4339, and references cited therein.
5. Detty, M. R.; Goodman, M. A. *Organometallics* **2004**, *23*, 3016–3020.
6. Uemura, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1992; Vol. 7, pp 769–774.
7. Tiecco, M.; Testaferri, L.; Tingoli, M.; Marini, F. *J. Org. Chem.* **1993**, *58*, 1349–1354, and references cited therein.
8. Sharpless, K. B.; Lauer, L. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697–2699.
9. Jones, D. N.; Mundy, D.; Whitehouse, R. D. *J. Chem. Soc., Chem. Commun.* **1970**, 86–87.
10. Sharpless, K. B.; Hiroi, T. *J. Org. Chem.* **1978**, *43*, 1689–1697.
11. Davis, F. A.; Stringer, O. D.; Billmers, J. M. *Tetrahedron Lett.* **1983**, 1213–1216.
12. Cinquini, M.; Colonna, S.; Giovini, R. *Chem. Ind. (London)* **1969**, 1737–1740.
13. Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 3250–3252.
14. Detty, M. R. *J. Org. Chem.* **1980**, *45*, 274–279.
15. Kochi, J. K.; Bosch, E. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2731–2737.
16. Kim, Y. H.; Yoon, D. C. *Tetrahedron Lett.* **1988**, *29*, 6453–6456.
17. Kim, Y. H.; Lee, H. K. *Chem. Lett.* **1987**, 1499–1502.
18. Chen, Y. J.; Huang, Y. P. *Tetrahedron Lett.* **2000**, *41*, 5233–5236.
19. [(2-Methoxyoctyl)seleninyl]benzene **3c**. Mixture of two diastereoisomers (2:1). Oil. Major diastereoisomer: ^1H NMR (200 MHz, $CDCl_3$): δ 7.89–7.68 (m, 2H), 7.60–7.42 (m, 3H), 3.94–3.76 (m, 1H), 3.46 (s, 3H), 3.11–2.87 (m, 2H), 1.80–1.42 (m, 2H), 1.40–1.11 (m, 8H), 0.91–0.80 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 140.9, 131.0, 129.5 (2C), 125.7 (2C), 75.0, 60.2, 57.1, 32.7, 31.5, 29.2, 24.2, 22.4, 13.9. Minor diastereoisomer: ^1H NMR (200 MHz, $CDCl_3$): δ 7.80–7.68 (m, 2H), 7.60–7.42 (m, 3H), 3.40–3.15 (m, 1H), 3.21 (s, 3H), 3.11–2.87 (m, 2H), 1.82–1.43 (m, 2H), 1.40–1.11 (m, 8H), 0.91–0.80 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 140.1, 131.3, 129.5 (2C), 126.3 (2C), 76.2, 58.8, 55.9, 32.7, 31.5, 29, 24.4, 22.4, 13.9. FT-IR (diffuse reflectance): 2930, 1441, 1090, 819, 742, 691 cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_2Se$: C, 57.14; H, 7.67. Found: C, 57.08; H, 7.84.
1-[(Phenylseleninyl)methyl]undecyl benzoate **3d**. Mixture of two diastereoisomers (1.2:1). Oil. Major diastereoisomer: ^1H NMR (200 MHz, $CDCl_3$): δ 8.02–7.91 (m, 2H), 7.81–7.71 (m, 1H), 7.27–7.60 (m, 1H), 7.55–7.30 (m, 6H), 5.14–4.98 (m, 1H), 3.41 (dd, 1H, J = 12.9 and 8.4 Hz), 3.25 (dd, 1H, J = 12.9 and 3.1 Hz), 1.70–1.55 (m, 2H), 1.40–1.05 (m, 16H), 0.8 (t, 3H, J = 6.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.0, 140.3, 133.3, 131.3, 121.6 (3C), 129.3, 128.4 (3C), 126.1 (2C), 70.1, 58.9, 34.5, 31.7, 29.3 (2C), 29.1 (2C), 28.9, 24.9, 22.9, 14.0. Minor diastereoisomer: ^1H NMR (200 MHz, $CDCl_3$): δ 8.03–7.91 (m, 2H), 7.81–7.71 (m, 1H), 7.71–7.62 (m, 1H), 7.55–7.30 (m, 6H), 5.56–5.41 (m, 1H), 3.48 (dd, 1H, J = 12.7 and 9.5 Hz), 3.11 (dd, 1H, J = 12.7 and 2.9 Hz), 1.91–1.55 (m, 2H), 1.40–1.05 (m, 16H), 0.8 (t, 3H, J = 6.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 165.7, 140.8, 133.2, 131.2, 129.6 (3C), 129.3, 128.4 (3C), 125.8 (2C), 70.2, 59.3, 34.8, 31.7, 29.3 (2C), 29.1 (2C), 28.9, 24.9, 22.5, 14.0. FT-IR (diffuse reflectance): 2925, 1717, 1268, 1111, 828, 742 cm^{-1}. Anal. Calcd for $C_{25}H_{34}O_3Se$: C, 65.06; H, 7.43. Found: C, 64.93; H, 7.57.
20. (Decylseleninyl)benzene **3b**. Oil. ^1H NMR (200 MHz, $CDCl_3$): δ 7.70–7.61 (m, 2H), 7.50–7.38 (m, 3H), 2.92–2.66 (m, 2H), 1.85–1.45 (m, 2H), 1.41–1.13 (m, 14H), 0.81 (t, 3H, J = 6.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 140.1, 131.1, 129.5 (2C), 125.8 (2C), 52.7, 31.7, 29.3, 29.2 (2C), 29.1, 28.9, 22.5, 22.4, 14.0. FT-IR (diffuse reflectance): 2924, 2853, 817, 741, 691 cm^{-1}. Anal. Calcd for $C_{16}H_{26}OSe$: C, 61.33; H, 8.36. Found: C, 61.12; H, 8.66.
4-(Phenylseleninyl)butanenitrile **3f**. Oil: ^1H NMR (200 MHz, $CDCl_3$): δ 7.72–7.60 (m, 2H), 7.60–7.48 (m, 3H), 3.13–2.92 (m, 1H), 2.85–2.68 (m, 1H), 2.55–2.40 (m, 2H), 2.25–2.05 (m, 1H), 2.02–1.78 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 141.5, 139.5, 129.8 (2C), 125.6 (2C), 118.4, 48.2, 18.1, 17.0. FT-IR (diffuse reflectance): 3053, 2927, 2265, 1441, 871, 818, 743 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NOSe$: C, 50.01; H, 4.62; N, 5.83. Found: C, 50.14; H, 4.85; N, 5.77.

21. Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697–1705.
22. Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. *Chem. Eur. J.* **2004**, *10*, 1752–1764.
23. Ceccherelli, P.; Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *J. Org. Chem.* **1995**, *60*, 8412–8413.
24. Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc* **1975**, *97*, 5434–5447.