Preparation of a Selenenic Acid and Isolation of Selenoseleninates

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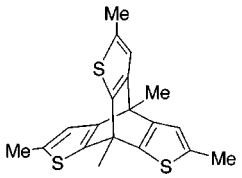
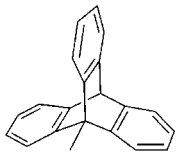
Received October 9, 1998

Selenenic acids and the related compounds have drawn considerable attention as highly reactive intermediates in oxidation of selenols, β-elimination of selenoxides and so on[1] and also in relation to the activity of the tetrameric selenoenzyme glutathione peroxidase;[2] thus, the chemistry of these compounds is a topic of current interest.[3] While some areneselenenic acids, stabilized by electron-withdrawing substituents at the ortho-position[4] or steric protection of reaction-bowl type substituents,[3] were isolated, alkaneselenenic acids have not been isolated nor have they been observed in solution.[5] On the other hand, Se-substituted selenoseleninates, which are condensation products of selenenic acids[5] or the initial oxidation product of diselenides,[6,7] have also eluded isolation, although a few were detected by low-temperature ^{77}Se NMR.[5] We have now investigated the synthesis of selenenic acids which are sterically protected by thiophenetriptycl (Thtrip-)[8,9] or 9-triptycyl (Trip-)[10] groups.



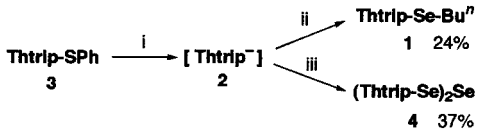
Thtrip-



Trip-

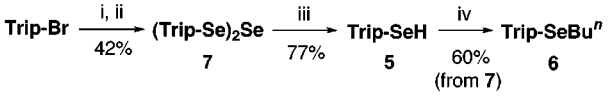
We examined the β-elimination of selenoxides and direct oxidation of selenols. Butyl thiophenetriptycyl selenide **1** was prepared by reaction of thiophenetriptycyllithium **2**, generated by reduction of the sulfide **3** with lithium 4,4′-di-*tert*-butylbiphenilide (LiDBB), with dibutyl diselenide (Scheme 1). Reaction of the lithium salt **2** with elemental selenium gave not the desired selenol but the triselenide **4**[11] as the main product. Reduction of **4** with $LiAlH_4$ followed by quenching with acid gave **4** again. On the other hand,

Scheme 1[a]



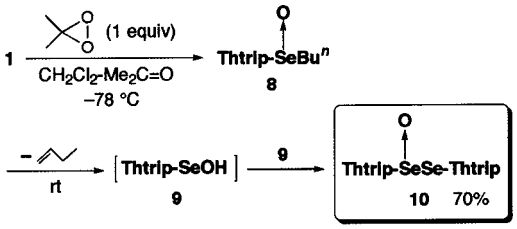
[a] Reagents: (i) LiDBB (10 mol equiv), THF, −78 °C, 1 h; (ii) (n-BuSe)$_2$ (5.3 equiv), −78 °C, 1.5 h and then rt, 50 min; (iii) Se (8 mol equiv), −78 °C, 1 h and then rt, 30 min.

Scheme 2[a]



[a] Reagents: (i) t-BuLi (2 equiv), PhH-Et$_2$O, −18 °C; (ii) Se (3 mol equiv), reflux, 20 h; (iii) $LiAlH_4$ (2.8 mol equiv), Et$_2$O, 0 °C, then rt, 50 min; (iv) NaH, THF, −18 °C, then n-BuBr (large excess), rt, 12 h.

Scheme 3



9-triptyceneselenol **5** and butyl 9-triptycyl selenide **6** were readily prepared from di-9-triptycyl triselenide **7** by the reactions shown in Scheme 2.

Butyl thiophenetriptycyl selenide **1** was oxidized with dimethyldioxirane (DMD)[12] at −78 °C. The initial oxidation product, selenoxide **8**, was rather stable in solution below 0 °C, and its existence could be detected by thin-layer chromatography and ^{1}H NMR. Decomposition of the selenoxide **8** occurred gradually in solution at room temperature and, instead of the desired selenenic acid (**9**), *Se*-thiophenetriptycyl thiophenetriptyceneselenoseleninate **10**[13,14] was isolated as yellow crystals in 70% yield (Scheme 3). The selenoseleninate **10** presumably is formed by self-condensation of the selenenic acid **9**.

We next investigated the preparation of 9-triptyceneselenenic acid **11**. Thus, the selenide **6** was treated with DMD at −78 °C, and then the reaction mixture was warmed to room temperature. The intermediary selenoxide **12** was fairly stable at room temperature[15] but gradually decomposed in solution at room temperature to give the desired

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(8) For convenience, We call 2,4,5′,6-tetramethyl-4,8-dihydro-4,8[3′,2′]-thiophenobenzo[1,2-*b*:5,4-*b*′]dithiophen-8-yl "thiophenetriptycyl" and abbreviate it to "Thtrip" in this communication: Ishii, A.; Maeda, K.; Kodachi, M.; Aoyagi, N.; Kato, K.; Maruta, T.; Hoshino, M.; Nakayama, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1277.

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(10) Nakamura, N. *J. Am. Chem. Soc.* **1983**, *105*, 7172.

(11) The structures of **4**, **13**, and **15** were determined by single-crystal X-ray analysis.

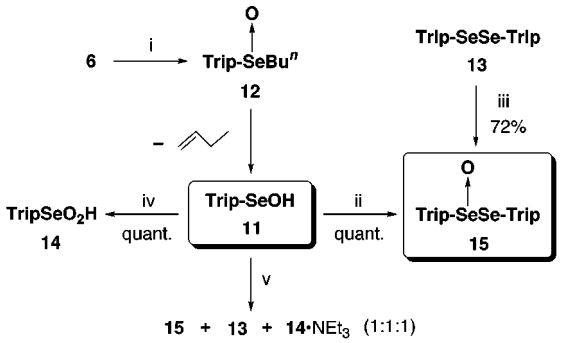
(12) Adam, W.; Hadjiarapoglou, L.; Smerz, A. *Chem. Ber.* **1991**, *124*, 227.

(13) **10**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.19 (s, 3H), 2.22 (s, 3H), 2.35 (s, 9H), 2.37 (s, 9H), 6.70 (d, J = 0.9 Hz, 3H), 6.72 (d, J = 0.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.90 (CH$_3$), 14.92 (CH$_3$), 15.3 (CH$_3$), 15.4 (CH$_3$), 50.1 (C), 50.3 (C), 119.3 (CH), 120.1 (CH), 134.8 (C), 136.5 (C), 145.7 (C), 152.1 (C), 157.7 (C), 159.3 (C) (two peaks of the *C*-Se were not observed under usual conditions); IR (KBr) 840 cm^{-1} (Se═O).

(14) Crystal data for **10**: $C_{36}H_{30}OS_6Se_2$, monoclinic, $P2_1/n$, a = 13.429(2), b = 14.465(2), c = 9.288(2) Å, β = 93.59(1)°, V = 1800.8(4) Å^3, D_c = 1.528 g cm^{-3}, Z = 2, μ(Cu−Kα) = 60.693 mm^{-1}. 3918 reflections measured, 3011 unique reflections. The structure was solved by direct methods and refined by a full-matrix least-squares method using 2254 reflections [$I \geq 2\sigma(I)$] for 220 parameters. R (R_w) = 0.0659 (0.0560) and GOF = 2.291; max/min residual electron density = 1.06/−0.67 e Å^{-3}. The refinement was done on a half of the molecule so the positions of selenium and oxygen could not be determined definitely. In these circumstances, C−Se(1), Se(1)−Se(2), and Se(1)−O(1) distances are 1.974(7), 2.439(2), and 1.89(3) Å, respectively, and ∠C−Se(1)−Se(2) is 96.6(3)° (necessarily ∠C−Se(1)−Se(2)−C = 180°). In Figure 1, one of the oxygen atoms, which should appear on Se(2) with 0.5 of occupancy, is omitted to avoid confusion.

10.1021/jo982039g CCC: $18.00
Published on Web 01/23/1999

Scheme 4[a]



[a] Reagents: (i) DMD (1 equiv), CH_2Cl_2-Me_2CO, −78 °C, and then rt, 17 h; (ii) CH_2Cl_2, reflux; (iii) MCPBA (0.76 equiv), CH_2Cl_2, 0 °C, then rt; (iv) DMD (1 equiv), CH_2Cl_2−Me_2CO, 0 °C; (v) Et_3N, CH_2Cl_2, 0 °C to rt.

selenenic acid **11** in 79% yield (Scheme 4). On the other hand, direct oxidation of the selenol **5** with DMD in dichloromethane at −78 °C gave the corresponding diselenide **13**[11] in 52% yield.

Selenenic acid **11** was obtained as a pale yellow crystalline compound after recrystallization and is the first isolable alkaneselenenic acid. In the ^{1}H NMR, the SeOH proton appeared at δ 2.63 as a broad signal, which disappeared on shaking with D_2O, and in the ^{77}Se NMR the selenium resonates at δ 1108. Other spectroscopic data and single-crystal X-ray analysis also support the structure.[16,17] An ORTEP drawing of **11** is depicted in Figure 1. The difference in the stability of selenenic acids **9** and **11** is mostly due to the steric factor of the two substituents.

Oxidation of the selenenic acid **11** with DMD or MCPBA gave the seleninic acid **14** quantitatively. Self-condensation of the selenenic acid **11** took place on heating over 40 °C to give the selenoseleninate **15**[11,18] quantitatively, which was also obtained by oxidation of diselenide **13** with MCPBA. The above condensation was not accelerated by *m*-chlorobenzoic acid, while Et_3N converted **11** to selenoseleninate **15**, diselenide **13**, and the salt of seleninic acid **14** (the molar ratio was ca. 1:1:1). This result suggests that the selenoseleninate **15** once formed is hydrolyzed at an appropriate rate under basic conditions to yield seleninic acid **14** and selenol **5**, and the latter reacts with the remaining selenenic acid **11** giving diselenide **13** and water.

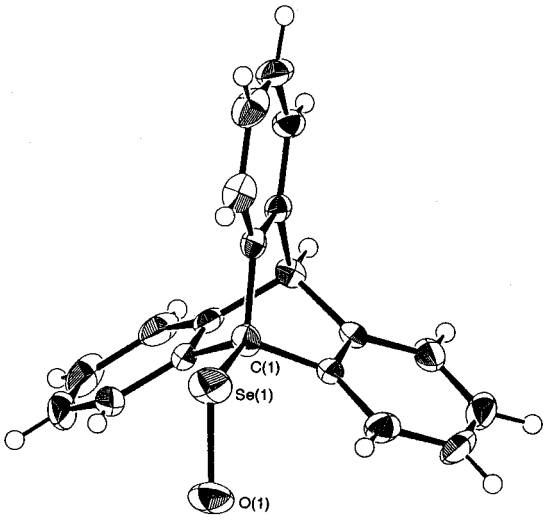


Figure 1. ORTEP drawing (50% ellipsoids) of Trip-SeOH (**11**).[17]

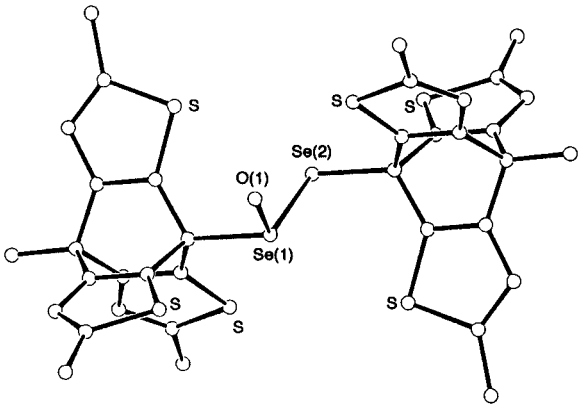


Figure 2. Molecular structure of Thtrip-Se(O)Se−Thtrip (**10**) (H atoms are omitted).[14]

Selenoseleninates **10** and **15** are the first examples of isolable selenoseleninates, and their selenoseleninate structure [RSe(O)SeR] was confirmed by single-crystal X-ray analyses. Figure 2 shows the molecular structure of **10**.[14] In the crystals, both compounds take an *s-trans* conformation about the Se−Se single bond with the center of symmetry at the middle of the bond. The formation of selenoseleninates in the present case is quite in contrast with that of selenenic anhydrides (ArSeOSeAr) from areneselenenic acids.[4,7b,19]

Acknowledgment. This work was supported by Grants-in Aid for Scientific Research Nos. 09640624 and 09440213 from the Ministry of Education, Science, Sports and Culture of Japan.

Supporting Information Available: Experimental procedures and characterization data (^{1}H, ^{13}C, and ^{77}Se NMR, IR, and MS) for **1**, **3**−**8**, and **10**−**15**; structure determination summaries and tables of X-ray structure data for **4**, **10**, **11**, **13**, and **15**.

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(15) Similar stability of some alkyl 9-triptycyl selenoxides was also observed by Prof. N. Nakamura (Hosei University, Japan): private communication.

(16) **11**: ^{1}H NMR δ 2.63 (br s, 1H), 5.42 (s, 1H), 7.02−7.06 (m, 6H), 7.35−7.40 (m, 3H), 7.41−7.45 (m, 3H); ^{13}C NMR δ 54.1 (CH), 64.1 (C), 122.9 (CH), 123.7 (CH), 125.3 (CH), 125.8 (CH), 144.1 (C), 145.7 (C); MS *m/z* 350 (M^+); IR (KBr) 3444 cm^{-1} (O−H).

(17) Crystal data for **11**: $C_{20}H_{14}OSe$, monoclinic, $P2_1/a$, a = 13.8220(7), b = 8.0070(8), c = 14.851(1) Å, β = 116.830(4)°, V = 1466.7(2) Å^3, Z = 4, ρ_{calcd} = 1.582 g cm^{-3}, μ(Mo−Kα) = 25.297 mm^{-1}. Oscillation and nonscreen Weissenberg photographs were recorded on the imaging plates of a MacScience DIP3000 diffractometer at 153 K. 3516 independent reflections. The structure was solved by direct methods and refined by a full-matrix least-squares method using 2785 reflections [$I \geq 2\sigma(I)$] for 260 parameters. R (R_w) = 0.0472 (0.0483) and GOF = 2.191; max/min residual electron density = 0.99/−1.267 e Å^{-3}. The position of the oxygen atom is disordered. The oxygen atom appeared at the position shown in Figure 1 [O(1)] and also at position O(2), omitted in Figure 1 to avoid confusion, that was obtained by 120° counterclockwise rotation of the O(1) about the axis containing the C(1)−Se(1) bond. The occupancy of O(1) and O(2) is 0.62 and 0.38, respectively. In these circumstances, the observed bond lengths of C(1)−Se(1), Se(1)−O(1), and Se(1)−O(2) are 1.956(2), 1.866(3), and 1.908-(5) Å, respectively, clearly indicating the single-bond character of these bonds, and the bond angles of C(1)−Se(1)−O(1) and C(1)−Se(1)−O(2) are 98.1(1) and 100.8(2)°, respectively.

(18) **15**: ^{1}H NMR δ 5.48 (s, 1H), 5.49 (s, 1H), 6.98−7.21 (m, 13H), 7.35−7.52 (m, 7H), 7.88−8.23 (m, 4H); ^{13}C NMR δ 54.3 (2CH), 67.8 (C), 78.0 (C), 123−124 (br, CH), 123.5 (CH), 124.1 (CH), 124.6 (CH), 125.1 (CH), 125.2 (CH), 126.2 (CH), 126.3 (CH), 141.1−142.6 (br, C), 144.9 (C), 145.2 (C), 145.3−146.1 (br, C); ^{77}Se NMR δ 656, 1122; IR (KBr) 844 cm^{-1} (Se=O); UV−Vis (CH_3CN) λ_{max} (log ϵ) 279.5 nm (3.76), 272.0 (3.76).

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