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First synthesis and characterization of isolable thioselenenic acid, triptycene-9-thioselenenic acid†

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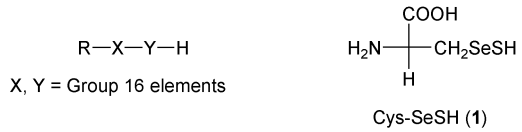
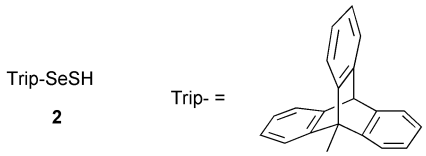
Triptycene-9-thioselenenic acid was synthesized by hydrolysis of acetyl triptycene-9-thioselenenate, the structure of which was determined by spectroscopic data and X-ray diffraction analysis.

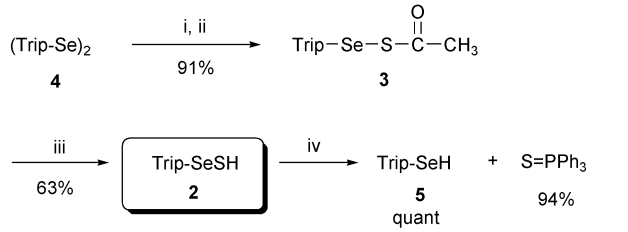
Hydrodichalcogenides R–X–Y–H, where X and Y are the same or different Group 16 elements, have drawn considerable interest from various points of view. While hydroperoxides (R–O–O–H) are compounds with a long history, the chemistry of sulfenic acids (R–S–O–H)[1] and selenenic acids (R–Se–O–H)[2,3] are of current interest. On the other hand, hydrodisulfides (R–S–S–H)[4,5] and selenosulfenic acids (R–S–Se–H)[6] have been claimed to be intermediates in enzymatic reactions of cystein and selenocystein with their lyases. A hydrodisulfide was found to be a key intermediate in thiol-mediated DNA-damage by leinamycin and its model compounds.[7] Thioselenenic acids, R–Se–S–H, are a member of this group and have not been isolated yet. To our knowledge, there are only two reports on the observation of Cys–SeSH [**1**, Cys = $(HO_2C)(H_2N)CHCH_2$] by UV–vis spectroscopy[8a] and RSeSLi (R = Bu, Ph) in THF by ^{77}Se NMR spectroscopy.[8b] We report herein the isolation and structure determination of triptycene-9-thioselenenic acid (**2**).





Acetyl triptycene-9-thioselenenate (**3**) was prepared using a method analogous to that for the synthesis of acetyl alkyl disulfides (R–S–S–Ac).[9] Thus, di-9-triptycyl diselenide (**4**)[3c] was treated with MCPBA and then with thioacetic acid to give **3**[10] in 91% yield; it is not essential to isolate the intermediary formed selenoseleninate (Trip–Se(O)Se–Trip[3c,11]). The acetyl thioselenenate **3** was hydrolyzed with 60% perchloric acid in refluxing ethanol–dichloromethane to furnish the desired thioselenenic acid **2** in 63% yield. The sulfur atom of **2** was removed readily by treatment with triphenylphosphine to give the selenol **5**[3c] and triphenylphosphine sulfide almost quantitatively (Scheme 1).

The structure of thioselenenic acid **2** was determined by spectroscopic data and X-ray diffraction analysis.[12] An ORTEP drawing is depicted in Fig. 1 with relevant bond lengths and angles data. The Se1–S1 bond length was 2.1796(9) Å, indicating the single bond character, and the C1–Se1–S1 bond angle was 103.85(7)°. The SH proton appeared at δ 2.64 in the ^{1}H NMR spectrum, and an absorption due to the S–H stretching vibration was observed at 2520 cm^{-1} in the IR spectrum.



Scheme 1 *Reagents and conditions*: i, MCPBA, CH_2Cl_2, 0 °C; ii, $CH_3C(O)SH$, 0 °C, and then rt; iii, $HClO_4$, EtOH, CH_2Cl_2, refl., 6 h; iv, PPh_3, PhH, rt, 2 h.

Thioselenenic acid **2** was stable under acidic conditions, as is evident from the preparation conditions, whereas it decomposed to selenol **5** and a small amount of diselenenyl sulfide **6**[15] by treatment with triethylamine followed by neutralization[4e] [Scheme 2, (a)]; when a solution of **2** was evaporated to dryness in the presence of triethylamine, diselenenyl sulfide **6** and diselenide **4** were formed [Scheme 2, (b)]. Treatment of **2** with triphenyltin chloride in the presence of triethylamine yielded stannyl thioselenenate **7**[16] and stannyl selenide **8**[16] [Scheme 2, (c)].

Polidoro and coworkers reported that treatment of $(Cys–Se)_2$ with Na_2S in an aqueous NaOH solution $1(1\times10^{-3}$ M) generated Cys–Se–SH that exhibited an absorption maximum at 375 nm in the UV–vis spectrum.[8] Fig. 2 shows UV–Vis spectra of thioselenenic acid **2** and diselenenyl sulfide **6** in dichloro-

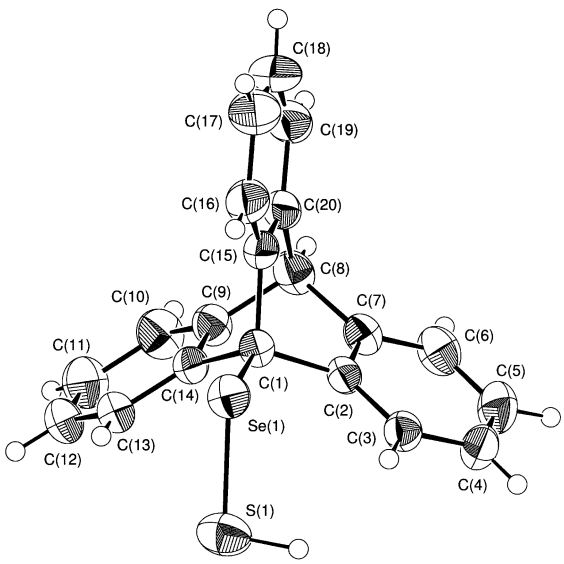


Fig. 1 ORTEP drawing of triptycene-9-thioselenenic acid (**2**) (50% ellipsoidal probability). Relevant bond lengths (Å) and angles (deg) data: Se1–C1 1.975(2); Se1–S1 2.1796(9); C1–C14 1.536(3); C1–C2 1.537(3); C1–C15 1.538(3); S1–H1 1.24(6); C1–Se1–S1 103.85(7); C14–C1–C2 106.19(17); C14–C1–C15 105.15(17); C2–C1–C15 105.31(17); C14–C1–Se1 115.62(15); C2–C1–Se1 115.27(15); C15–C1–Se1 108.37(15).

† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b2/b207810d/

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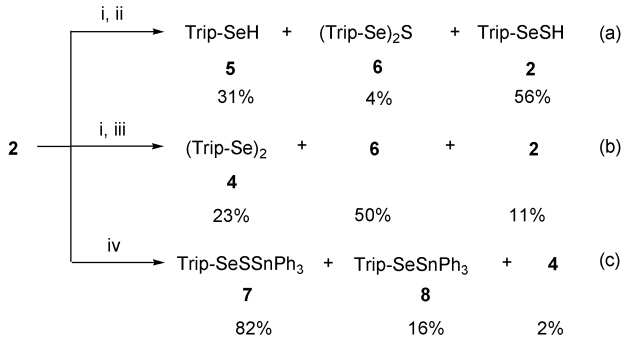

Scheme 2 *Reagents and conditions*: i, Et_3N, PhH, rt, 5 min; ii, aq. NH_4Cl; iii, evaporation in the presence of Et_3N; iv, Ph_3SnCl, Et_3N, PhH, rt, 1 h. Yields are calculated from ^1H NMR integral ratios.

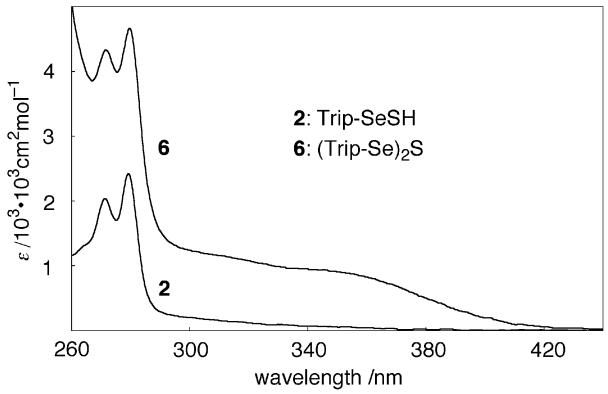

Fig. 2 UV-vis spectra of triptycene-9-thioselenenic acid (**2**) and di-(triptycene-9-selenenyl) sulfide (**6**).

methane. The absorption of **2** ceased approximately at 360 nm, while **6** has a broad absorption from 285 to 360 nm with the molecular absorption coefficient ($\varepsilon/10^3$ cm^2 mol^{-1}) ≈ 1000. Anyway, we did not observe an explicit absorption maximum around 375 nm. This might be attributed to the contrasting character of the substituents: the more sterically demanding, hydrophobic 9-tripycyl group and the much less sterically demanding, hydrophilic 2-amino-3-propionyl (Cys) group. We are therefore now investigating the preparation of thioselenenic acids having groups derived from the Cys group or alkyl substituents structurally simpler than the 9-triptycyl group.

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10 **3**: mp 177–180 °C (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$, 400 MHz) δ 2.50 (s, 3H), 5.37 (s, 1H), 6.98–7.05 (m, 6H), 7.35–7.40 (m, 3H), 7.47–7.51 (m, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 29.8, 54.1, 64.9, 123.5, 123.7, 125.0, 125.9, 144.1, 145.2, 192.1; IR (KBr) 1700 (C=O) cm^{-1}. Anal. Calc. for $C_{22}H_{16}OSSe$: C, 64.86; H, 3.96. Found: C, 64.80; H, 3.92%.

11 In this one-pot reaction, we have prepared (1-Ad)CH_2SeSAc and (1-Ad)CH(CH_3)SeSAc (1-Ad = 1-adamantyl).

12 **2**: pale yellow plates, mp 170–172 °C decomp (CH_2Cl_2–hexane). ^1H NMR ($CDCl_3$, 400 MHz) δ 2.64 (s, 1H, SH), 5.38 (s, 1H), 7.00–7.08 (m, 6H), 7.36–7.42 (m, 3H), 7.49–7.54 (m, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 54.0, 61.1, 123.6, 123.8, 125.0, 125.7, 144.1, 145.8; IR (KBr) 2520 cm^{-1}. Anal. Calc. for $C_{20}H_{14}SSe$: C, 65.75; H, 3.86. Found: C, 65.73; H, 3.89%. Crystal data: $C_{20}H_{14}SSe$, M_w 365.36, pale yellow plate, 0.24 × 0.16 × 0.08 mm^3, triclinic, space group $P\bar{1}$, a = 8.181(2), b = 8.217(1), c = 13.175(3) Å, α = 82.53(1), β = 72.58(1), γ = 67.82(1)°, V = 782.4(2) Å^3, Z = 2, ρ_{calc} = 1.551 g cm^{-3}, μ(CuKα) = 4.42 mm^{-1}. Mac Science MXC3KHF diffractometer with graphite-monochromated CuKα radiation (λ = 1.54178 Å), $\theta/2\theta$ scans method in the range 3° < 2θ < 140° ($-9 \leqslant h \leqslant 9$, $0 \leqslant k \leqslant 10$, $-15 \leqslant l \leqslant 16$), 2994 independent reflections. The structure was solved with direct methods (SIR92[13]), and refined with full-matrix least-squares (SHELXL-97[14]) using all independent reflections for 256 parameters. Absorption correction was done by a psi-scan method. The non-hydrogen atoms were refined anisotropically: $R1$ = 0.0303 ($I > 2\sigma(I)$, 2822 reflections), $wR2$ = 0.0860 (for all), GOF = 1.05; max/min residual density = 0.454/−0.452 e Å^{-3}. CCDC reference number 191691. See http://www.rsc.org/suppdata/cc/b2/b207810d/ for crystallographic data in CIF or other electronic format.

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15 **6**: pale yellow crystals, mp 345–346 °C decomp (hexane–CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz) δ 5.46 (s, 2H), 7.11 (pseudo d of quintet, J = 1.5, 7.4 Hz, 12H), 7.46 (dd, J = 1.5, 7 Hz, 6H), 7.76 (dd, J = 1.5, 8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 54.2, 65.2, 123.7, 124.4, 125.1, 125.9, 144.7, 145.6. Anal. Calc. for $C_{40}H_{22}SSe_2$: C, 68.96; H, 3.76. Found: C, 68.31; H, 3.68%.

16 The structures of **7** and **8** were determined by X-ray crystallography. CCDC reference numbers 191692 (**7**) and 191693 (**8**). **7**: yellow crystals, mp 176–178 °C decomp (Et_2O–hexane). ^1H NMR ($CDCl_3$, 200 MHz) δ 5.29 (s, 1H), 6.74 (dt, J = 1, 8 Hz, 3H), 6.93 (dt, J = 1, 7 Hz, 3H), 7.30 (dd, J = 1, 7 Hz, 3H), 7.43–7.55 (m, 12H), 7.74–7.84 (m, 6H, accompanying satellite signals, J = 55 Hz, due to ^{117}Sn and ^{119}Sn); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.0, 61.7, 123.1, 124.6, 124.8, 125.4, 129.1, 130.2, 137.0, 137.1, 144.4, 145.4. Anal. Calc. for $C_{38}H_{28}SSeSn$: C, 63.89; H, 3.95. Found: C, 63.71; H, 3.90. **8**: colorless cubes, mp 253–255 °C (hexane–CH_2Cl_2). ^1H NMR ($CDCl_3$, 400 MHz) δ 5.28 (s, 1H), 6.64 (dt, J = 1, 8 Hz, 3H), 6.87 (dt, J = 1, 8 Hz, 3H), 7.20—7.34 (m, 12H), 7.40 (dd, J = 1, 8 Hz, 6H, accompanying satellite signals, J = 55 Hz, due to ^{117}Sn and ^{119}Sn), 7.79 (d, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 54.1, 61.7, 122.6, 124.5, 125.36, 125.41, 128.6, 129.4, 136.8, 138.2, 144.8, 146.4. Anal. Calc. for $C_{38}H_{28}SeSn$: C, 66.89; H, 4.14. Found: C, 66.65; H, 4.04%.