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TETRAHEDRON: *ASYMMETRY*

The first enantiomerically pure, C_2-symmetric spiroselenurane: 3,3,3′,3′-tetramethyl-1,1′-spirobi[3*H*,2,1]-benzoxaselenole

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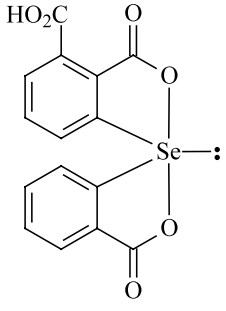
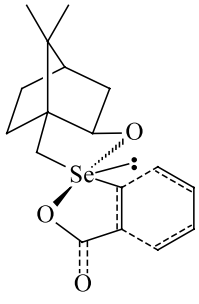
Abstract—The enantiomers of a C_2-symmetric spirobisalkoxyselenurane, 3,3,3′,3′-tetramethyl-1,1′-spirobi[3*H*,2,1]-benzoxaselenole, have been isolated for the first time via chromatographic resolution of the racemate using a chiral HPLC column. The isomers were further characterized by ^{1}H NMR and CD spectroscopic measurements.

Spiroselenuranes constitute a class of hypervalent selenium compounds which are commonly described as 10-Se-4 species.[1] They have trigonal bipyramidal geometry and may exhibit chirality due to molecular dissymmetry even in cases where they are constructed by the use of a pair of the same two-arms ligands only.[2] To date, no member of this class of C_2-symmetric spiroselenuranes has been prepared in optically active form. In this context, it is of interest to note that the first optically active, unsymmetrically substituted selenurane, 7-carboxy-3,3′-spirobi(3-selenaphthalide), **1** was partially resolved via classical resolution, although diastereomeric excess values for the free acids liberated from the diastereomeric salts were not determined.[3] Recently, the Koizumi group has prepared[4] a few diastereomerically pure bicyclic selenuranes **2** in which the 2-*exo*-hydroxy-10-bornyl group serves as a chiral ligand.



1



2

Continuing our interest in the static and dynamic stereochemistry of hypervalent compounds with a stereogenic heteroatom,[5,6] we would like to report herein the successful liquid chromatographic separation of the enantiomers of the tetramethyl substituted spiroselenurane **3** and their characterization by CD and ^{1}H NMR spectroscopy.

Racemic **3**, available by a route involving a few steps,[7] was synthesized by the one step reaction of diethyl selenite and the Grignard reagent derived from *ortho*-bromocumyl alcohol (Eq. (1)) as elaborated recently in the Łódź laboratory.[8]

The stereogenic character of the selenium atom is clearly indicated by the presence of the two well-separated methyl singlets in the ^{1}H NMR spectrum at 1.591 and 1.637 ppm and in the ^{13}C NMR spectrum at 32.898 and 33.898 ppm. The remaining absorptions in the ^{13}C NMR were observed at 82.049, 124.192, 127.671, 128.555, 131.100, 135.001 and 150.238 ppm.[9] Additional support for this structure is provided by a 2D NMR spectrum recorded with the use of a pulsed field gradient[9,10] (see Fig. 1), which shows the unsubstituted aromatic ring positions, and an X-ray analysis (see Fig. 2).[11]

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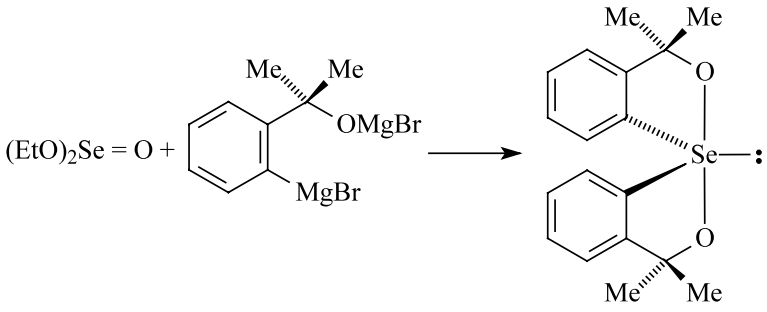

(1)

3

We have found that the enantiomers of **3** give very well resolved peaks when a solution of the racemate was passed through an analytical chiral column[12] (see Fig. 3)

A semi-preparative separation was done by repeated injection and collection of the respective fractions from the analytical column. This procedure gave a few milligrams of each enantiomer, allowing further characterization by means of polarimetry, and ^{1}H NMR and CD spectroscopy. Polarimetric measurements[13] showed that the enantiomer having negative rotation at 589 nm and $[\alpha]_{589} = -20$ (c 0.36, CH_2Cl_2) was consistently the first eluted in the system used. It is of interest to note that its optical rotation decreases in the 578–485 nm region, disappears close to 480 nm and becomes positive in the region below 480 nm. The CD spectra[14] of the isolated enantiomers are shown in Fig. 4.

The high enantiomeric purity of a sample of the levorotatory enantiomer of optically active spiroselenurane **3** $[\alpha]_{589} = -20$, was supported by the ^{1}H NMR technique. In the ^{1}H NMR spectrum of the mixture of this optically active selenurane and (+)-(*S*)-mandelic acid (1:10 ratio) dissolved in $CDCl_3$ only two singlets of equal intensity at 1.588 and 1.644 were observed for the magnetically nonequivalent geminal methyl groups (see Fig. 5C) and the doublet at 8.26 ppm for aromatic protons in *ortho* positions in respect to the hypervalent selenium atom. In the spectrum of racemic **3** recorded

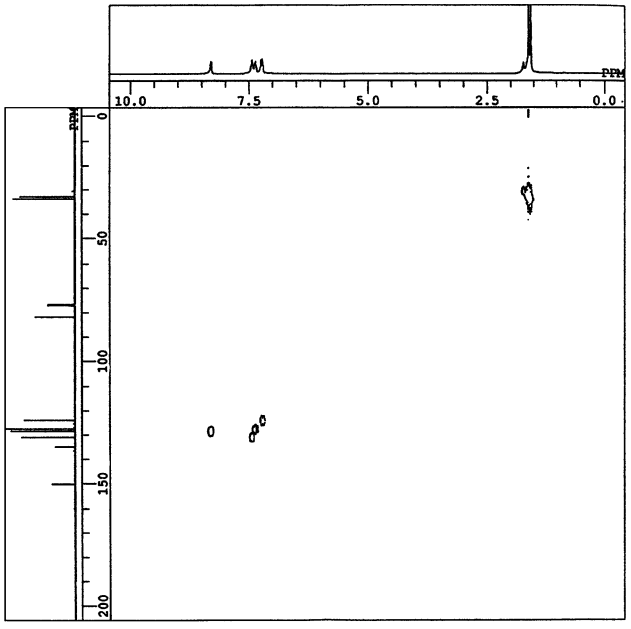

Figure 1. 2D-HMQCD NMR spectrum of **3**.

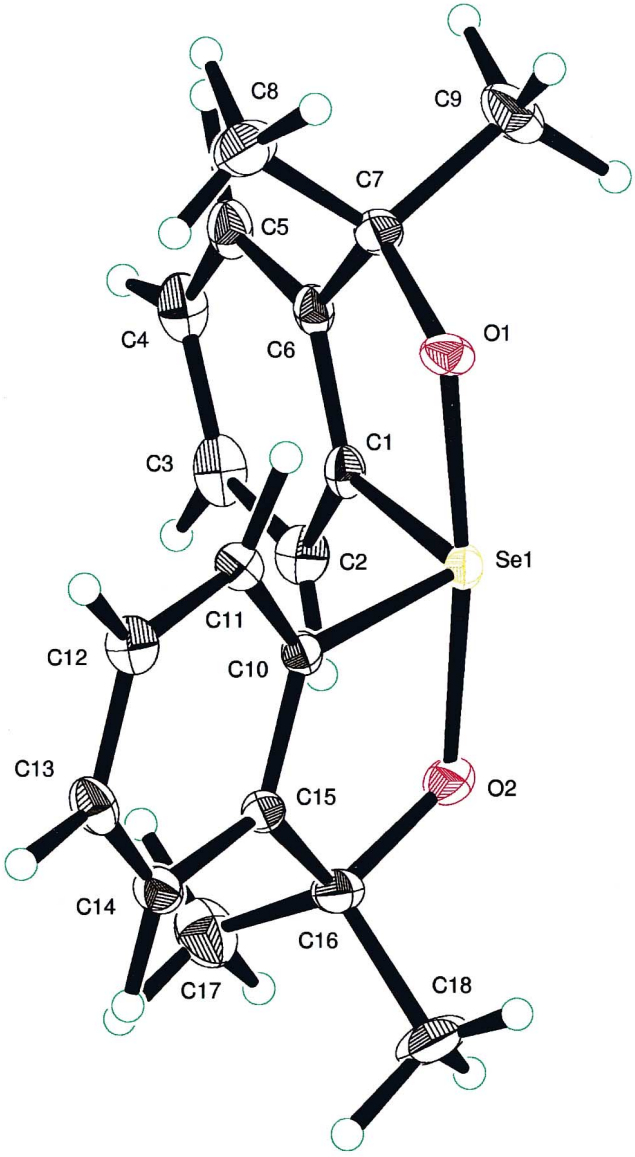

Figure 2. ORTEP drawing of **3** (one enantiomer) showing the numbering scheme adapted.

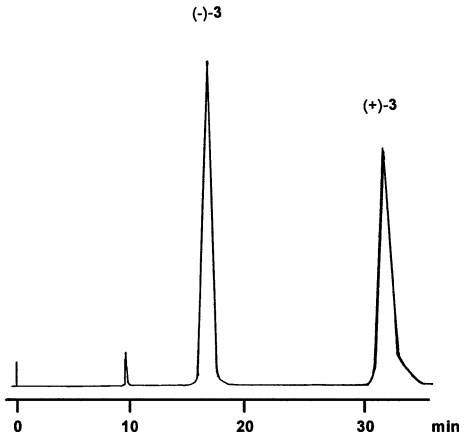

Figure 3. Chromatogram showing the separated enantiomers of **3**. Mobile phase 1.4% 2-propanol in hexane.

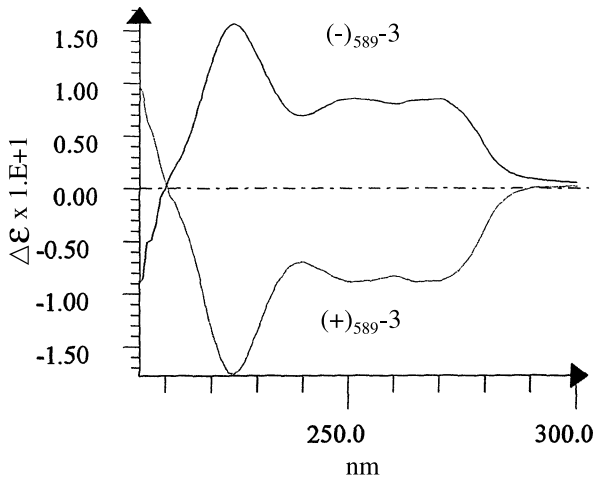

Figure 4. CD spectra of the (+) and (–) enantiomers of **3**.

in the presence of (+)-(*S*)-mandelic acid, two singlets for one of the magnetically non-equivalent methyl groups and the singlet for another methyl group (see Fig. 5B) as well as two doublets for the aromatic *ortho* protons, were observed. This observation evidently indicates that this sample of the optically active selenurane **3** is enantiomerically pure. The absolute configuration of the isolated enantiomers has not yet been determined. The preparation of a single crystal suitable for an X-ray crystallographic structure determination is under current study.

Acknowledgements

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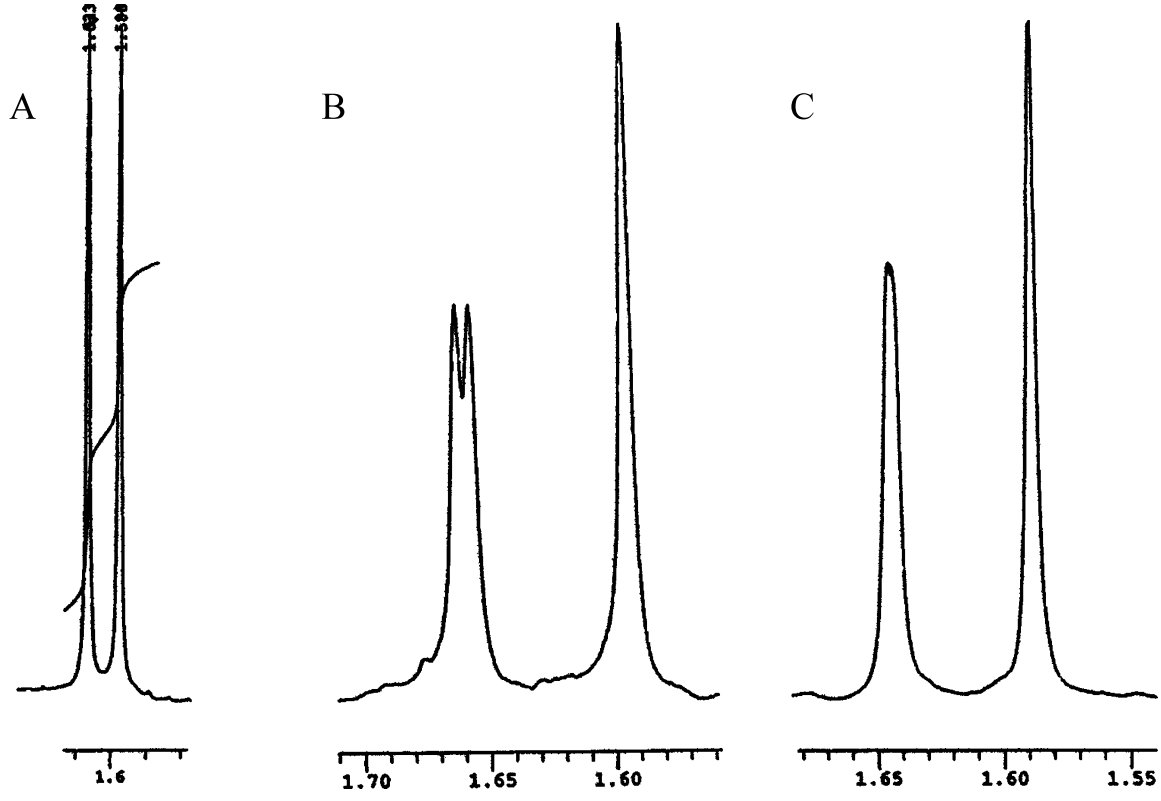

Figure 5. ^{1}H NMR absorptions of the non-equivalent methyl groups of racemic and enantiomerically pure spiroselenurane **3**; $[\alpha]_{589} = -20.0$ (CH_2Cl_2) alone and in the presence of (+)-(*S*)-mandelic acid. A: the racemate alone; B: the racemate in the presence of the acid; C: the pure enantiomer in the presence of the acid.

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11. **Crystal data for 3**: The single-crystal growth was carried out in a dichloromethane–ethyl acetate mixed solvent at room temperature. Crystal data for $(o\text{-}C_6H_4CMe_2O)_2Se$: $C_{18}H_{20}O_2Se$, colorless, crystal dimensions 0.40×0.35×0.58 mm, monoclinic, space group $P21/a$, $a=11.7740(2)$, $b=13.8830(2)$, $c=20.2610(3)$ Å, $V=3241.64(9)$ Å^3, $Z=8$, $D_{calcd}=1.423$ g cm^{-3}, $\lambda(MoK_\alpha)=0.71073$ Δ, $T=190$ K. From 7944 total reflections 7618 were unique, and 6736 with $I>3\sigma(I)$ ($2\theta_{max}=56.00$) were used for the solution of the structure. $R=0.0445$, $wR=0.0737$. No. of parameters refined 379. Goodness of fit (obsd) = 1.078. Selected bond lengths [Δ] bond angles [°], torsion angles [°]: Se1–O1 1.933(2), Se1–O2 1.958(2), Se1–C1 1.940(2), Se1–C10 1.949(2); O1–Se1–O2 172.55(8), O1–Se1–C1 83.75(10), O1–Se1–C10 92.30(10), Se1–O1–C7–C6 74(3), S1–O1–C7–C8 128.7(2), Se1–C1–C2–C3 178.5(2), Se1–C1–C6–C5 179.5(2).
12. The chromatographic resolutions were carried out on a 4.6 mm ID×250 mm analytical column. Chiral pack AS, available from Daicel Chemical Industries Ltd., Japan. using a JASCO PH-980 HPLC pomp, a JASCO UV–vis-970 detector and a Shimadzu C-RA chromatopic recorder. The mobile phases used were hexane +1.0 to 20% of 2-propanol. UV detection at 225 nm. There was no resolution when hexane containing 2.5–10% of ethanol as the mobile phases were used. Very poor resolutions were observed on a 4.6 mm ID×250 mm analytical column, Chiralpack OP.
13. Polarimetric measurements were carried out on a Perkin–Elmer 241 photopolarimeter.
14. The CD spectra were recorded in hexane solutions on a CD 6 dichrograph (Jobin–Yvon) using cells with 5 mm path length.