Intramolecular macrocyclization of bis(5-methylthio-1,2-dithiole-3-thione)s with triethyl phosphite. A stereoselective route to macrocyclic (*Z*)-thioxodesaurines

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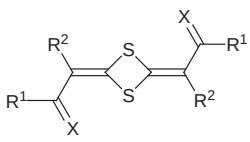
Intramolecular macrocyclizations of [oligo(oxyethylene)-ethylenedithio]bridged bis(5-methylthio-1,2-dithiole-3-thione)s 5a and b with $P(OEt)_3$ in *p*-xylene furnished the macrocyclic thioxodesaurin (*Z*)-6, thioxodesaurin (*E*)-7 and 1,3-dithiafulvene (*E*)-8, respectively.

2,4-Bis(2-oxoethylidene)-1,3-dithietanes are well-known as desaurines.[1,2] In these compounds, the electron-withdrawing groups at the 2,4-dimethylene-1,3-dithietane unit can be (*E*)- or (*Z*)-configured. (*E*)-Configuration was determined for the desaurines **1a**–**d** by X-ray analysis.[3] The well-known desaurin



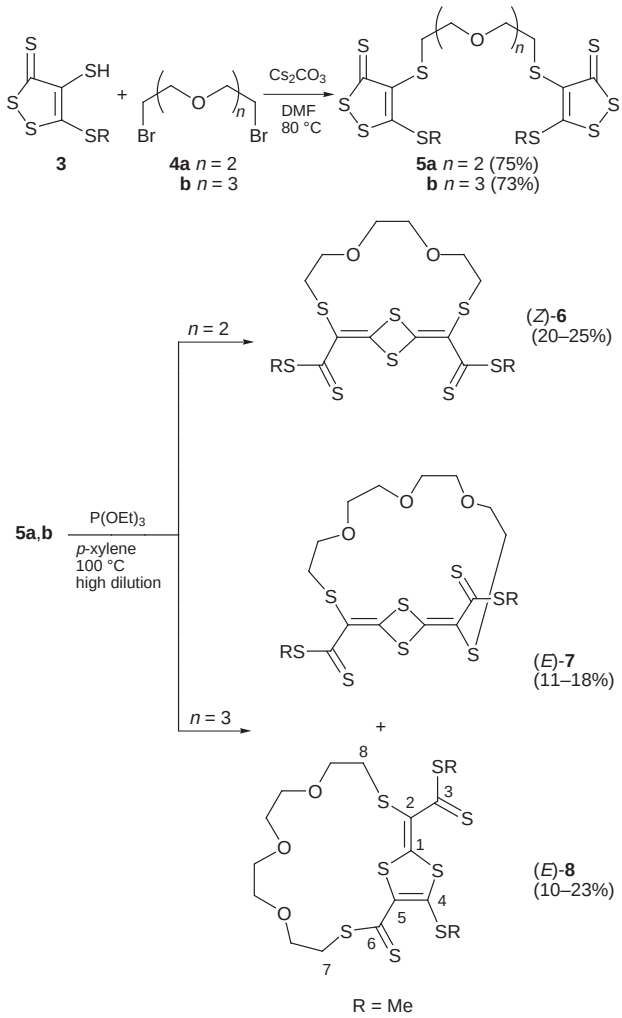
	X	R^1	R^2	ref.
1a	O	Ph	H	3(*a*)
1b	O	Me	Me	3(*b*)
1c	O	MeO	NC	3(*c*)
1d	O	Et	Ph	3(*d*)
(*E*)-**2**	S	MeS	MeS	5,7(*a*)

syntheses lead predominately to the thermodynamically stabilized (*E*)-isomer, or an (*E*)-/(*Z*)-mixture.[4] To the best of our knowledge the stereoselective synthesis of a (*Z*)-desaurin has not yet been reported.

Thioxoanalogous desaurines can be synthesized by reductive dimerization of 1,2-dithiole-3-thione derivatives containing an alkylthio substituent in the 5-position with $P(OEt)_3$.[5] Reaction of 4,5-bis(methylthio)-1,2-dithiole-3-thione[6] with $P(OMe)_3$, in refluxing benzene, yielded the (*E*)-thioxodesaurin (*E*)-**2** (35%) and its (*Z*)-isomer (*Z*)-**2** (15%).[5] We confirmed the stereochemistry of (*E*)-**2** by X-ray analysis.[7a] In (*E*)-**2** the eight sulfur and the six central carbon atoms lie almost in-plane. (*E*)-Isomers were formed exclusively by the dimerization of dodecylthio-substituted 1,2-dithiole-3-thiones and crowned 4,5-dithio-1,2-dithiole-3-thiones.[7b]

Here, we describe a novel macrocyclization reaction using bridged bis(5-methylthio-1,2-dithiole-3-thione)s **5** as precursors. Intramolecular cyclization of **5a** and **b** with $P(OEt)_3$ yielded the macrocyclic thioxodesaurin (*Z*)-**6**, thioxodesaurin (*E*)-**7** and 1,3-dithiafulvene (*E*)-**8**, respectively (Scheme 1). The length of the [oligo(oxyethylene)ethylene]dithio bridge in **5** determines the stereochemistry of the thioxodesaurin formed. With **5a** the crowned (*Z*)-thioxodesaurin (*Z*)-**6** was stereoselectively synthesized.

The precursors **5a**,**b** are obtainable in yields of up to 75% by alkylation of 4-mercapto-5-methylthio-1,2-dithiole-3-thione **3**‡ (2 equiv.) with 1,8-dibromo-3,6-dioxaoctane **4a** and 1,11-dibromo-3,6,9-trioxaundecane **4b**, respectively, in the presence of Cs_2CO_3 in DMF. Correct spectral data were obtained for both compounds. Compounds **5a**,**b** were intramolecularly cyclized under high dilution conditions with $P(OEt)_3$ in *p*-xylene. Compound **5a** provides one macrocyclic reaction product (*Z*)-**6** (20–25 %) as well as unidentified polymeric material. The ^{13}C NMR spectrum of (*Z*)-**6** revealed that this macrocycle contains the expected thioxodesaurin unit.§ The configuration of the thioxodesaurin unit in (*Z*)-**6** was determined by X-ray crystallographic analysis.¶ The crystal structure of (*Z*)-**6** shows a (*Z*)-configured planar thioxodesaurin moiety which is incorporated in a macrocyclic framework by a [bis(oxyethylene)ethylene]dithio chain [Fig. 1(*a*)]. Attempts to build CPK models of the (*E*)-isomer of (*Z*)-**6** revealed that the [bis(oxyethylene)ethylene]dithio chain is too short to bridge a planar (*E*)-thioxodesaurine unit. This is possibly the reason why the intramolecular cyclization of **5a** furnishes the (*Z*)-isomer stereoselectively. In the (*Z*)-thioxodesaurin moiety of (*Z*)-**6** the



Scheme 1

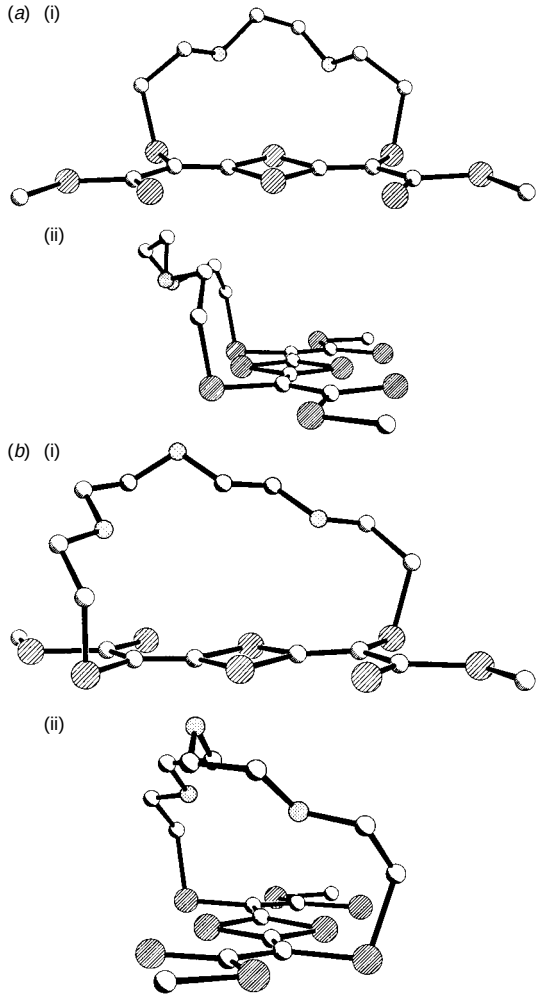


Fig. 1 Structures of the macrocyclic thioxodesaurines (*a*) (*Z*)-**6** and (*b*) (*E*)-**7** in the crystal: view of the molecules (i) orthogonal and (ii) parallel to the central 2,4-dimethylene-1,3-dithietane moiety

two carbon–carbon double bonds do not lie in line, as it is observed for the bonds in the (*E*)-thioxodesaurin units of (*E*)-**2**[7a] and (*E*)-**7** [Fig. 1(*b*)]. This deviation from 180° amounts to 9°.

In comparision to **5a**, bis(1,2-dithiole-3-thione) **5b** has a bridging chain with one more oxyethylene moiety. This chain is long enough to enable the intramolecular cyclization to form the (*E*)-thioxodesaurine (*E*)-**7** (11–18%). X-Ray analysis of crowned (*E*)-**7**¶ shows an *ansa*-compound-like molecular structure. The [tris(oxyethylene)ethylene]dithio chain, bridges the planar (*E*)-configurated thioxodesaurin unit like a handle. Since rotation of the (*E*)-thioxodesaurin moiety around the axis along the H_2C–S bonds is not possible, (*E*)-**7** has planar chirality. No (*Z*)-isomer was detected at the intramolecular cyclization of **5b**. On the contrary, we obtained the crowned 1,3-dithiafulvene (*E*)-**8** (10–23%). The molecular structure of (*E*)-**8** was determined *via* an X-ray structural investigation.[7b]

Mollier[5] and Pedersen[8] postulated thioacyl thioketenes as intermediates for the reaction of 5-alkylthio-1,2-dithiole-3-thiones with trialkyl phosphite, which dimerize in [2+2] cycloadditions to the thioxodesaurines. In a similar way bis(thioketene) intermediates of **5a**,**b** should form intramolecular macrocyclic thioxodesaurines (*Z*)-**6** und (*E*)-**7**. Compound (*E*)-**8**, which in its turn furnishes the thioxodesaurin (*E*)-**7,** cannot be formed by an intramolecular [2+3] cycloaddition of the bis(thioketene) intermediate. Therefore other thioketene intermediates must exist, at least in the reaction solution of **5b** with $P(OEt)_3$. The formation of a thioxodesaurin and a 1,3-dithiafulvene from α-thioxothioketene intermediates was recently proposed by Hartke *et al*.[9] A desaurin and a 1,3-dithiafulvene were obtained from α-oxothioketenes earlier by Voronkov.[10]

The intramolecular macrocyclization of bridged bis(5-methylthio-1,2-dithiole-3-thione)s with $P(OEt)_3$ is a simple synthetic route to macrocyclic (*Z*)- and (*E*)-thioxodesaurines and 1,3-dithiafulvenes.

We are synthesizing macrocyclic (*Z*)- and (*E*)-thioxodesaurines and 1,3-dithiafulvenes since we are interested in their redox properties and coordination chemistry. We would like to use these new macrocyclic and sulfur-rich ligands containing both endocyclic and exocyclic donor sites for the preparation of dinuclear metal complexes comprising simultaneously hard and soft metal centers, and as new components for supramolecular compounds. Full results will be reported in a full paper.

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Notes and References

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‡ Synthesized from 4-benzoylthio-5-methylthio-1,2-dithiole-3-thione (ref. 6) by saponification with NaOMe in MeOH and reaction of the corresponding sodium thiolate with dilute HCl [ref. 7(*c*)].

§ *Selected data* for (*Z*)-**6**: δ_C(75.48 MHz, $CDCl_3$) 20.70 (SCH_3), 35.82 (SCH_2), 67.22 (SCH_2CH_2O), 70.42 (OCH_2CH_2O), 124.58 (*C*=CS_2), 163.79 (CS_2), 219.22 (C=S); For (*E*)-**7**: δ_C 20.70 (SCH_3), 35.78 (SCH_2), 69.96–71.11 (m, $SCH_2CH_2OCH_2CH_2O$), 72.27 ($OCH_2CH_2OCH_2CH_2O$), 124.79 (*C*=CS_2), 162.27 (CS_2), 218.90 (C=S); For (*E*)-**8**: δ_C 18.18 (C=CS*C*H_3), 21.05 (SCS*C*H_3), 36.64 (C-8), 38.11 (C-7), 67.08–71.66 (m; OCH_2), 117.48 (C-2), 129.92 (C-5), 149.60 (C-4), 166.75 (C-1), 204.96 (C-6), 211.53 (C-3).

¶ *Crystal data* for (*Z*)-**6**·$(CHCl_3)_{0.3}$: $C_{14.3}H_{18.3}Cl_{0.9}O_2S_8$, M = 514.56 g·mol^{-1}, trigonal, space group $R\bar{3}$, $a = b = c$ = 1689.0(1) pm, $\alpha = \beta = \gamma$ = 112.044(4)°, V = 3.3092(3) nm^3, D_c. = 1.532 Mg m^{-3}, Z = 6, F(000) = 1574.7, μ = 0.92 mm^{-1}, 3150 reflections collected in the scan range of $4.36 \leqslant 2\theta \leqslant 43.00°$, 2480 independent reflections, 2079 observed reflections, R1 [$2\sigma(I)$] = 0.0453, $R1$ (all data) = 0.0558, $wR2$ (all data) = 0.0773, GoF = 1.079 for 242 parameters and 3 restraints. On the three-fold axis 0.3 disordered molecules of $CHCl_3$ per molecule (*Z*)-**6** are found.

For (*E*)-**7**: $C_{16}H_{22}O_3S_8$, M = 518.82 g·mol^{-1}, triclinic, space group $P\bar{1}$, a = 960.0(3), b = 1066.1(4), c = 1221.2(5) pm, α = 70.16(2), β = 82.33(2), γ = 72.82(3)°, V = 1.1224(7) nm^3, D_c. = 1.535 Mg m^{-3}, Z = 2, F(000) = 540, μ = 0.81 mm^{-1}, 3324 reflections collected in the scan range of $3.54 \leqslant 2\theta \leqslant 44.00°$, 2724 independent reflections, 1573 observed reflections, $R1$ [$2\sigma(I)$] = 0.0566, $R1$ (all data) = 0.1155, $wR2$ (all data) = 0.1120, GoF = 1.329 for 244 parameters.

Siemens P4 diffractometer, Mo-Kα radiation (λ = 71.073 pm), room temperature. CCDC 182/908.

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