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Synthesis and Structure of 1,3-[5,5′-(1,2-Phenylenedimethylenedithio)bis-(2,3-dihydro-2-oxo-1,3,4-thiadiazol-3-yl]propane†

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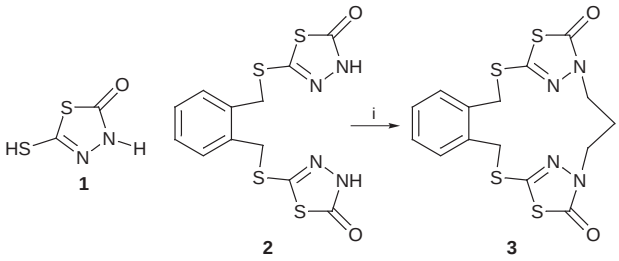
1,3-[5,5′-(1,2-Phenylenedimethylenedithio)bis(2,3-dihydro-2-oxo-1,3,4-thiadiazol-3-yl]propane is prepared and its structure clearly established from spectroscopic data (IR, ^{1}H and ^{13}C NMR, and mass spectrometry) and X-ray crystallography.

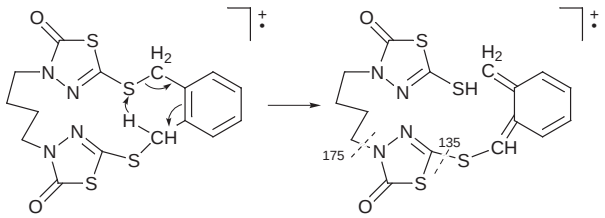
The construction of macrocyclic compounds has focused on those containing heterocyclic subunits, because they have unique chemical and biological properties.[1,2] We recently reported[3] the synthesis and tautomeric behavior of 5-mercapto-3*H*-1,3,4-thiadiazolin-2-one **1**, compound of biological and analytical interest. From compound **1**, S-bridged macrocycles can be derived, in which sulfur atoms are directly connected to the heterocyclic rings. The sulfur atom is soft and is thus useful for forming complexes with transition metals.[4] In light of the general interest in the construction of synthetic macrocycles containing heterocyclic subunits as well as the limited examples[5] that include 1,3,4-thiadiazole in a macrocyclic framework, we describe the synthesis and structural characterization of the macrocycle 1,3-5,5′-(1,2-phenylenedimethylenedithio)bis-(2,3-dihydro-2-oxo-1,3,4-thiadiazol-3-yl]propane **3**.



Scheme 1 *Reagents:* i, 1,3-dibromopropane, Et_3N, EtOH

Macrocycle **3** was prepared using the method outlined in Scheme 1. The synthesis of **2** followed a previously reported procedure.[6] The structure of **3** was firmly established by well defined ^{1}H and ^{13}C NMR, IR and mass spectra. The NH group (δ_H 13.1) of **2** is acidic enough to be alkylated in triethylamine with 1,3-dibromopropane.

The intermolecular [2 + 2] cyclization and alkylation were demonstrated by the appearance of an NCH_2 group, instead of NH, at δ_H 4.04 and δ_C 34.3 in the ^{1}H and ^{13}C NMR, respectively, and a strong carbonyl band at 1685 cm^{-1}. Mass spectra provided further structural proof with the molecular ion peak being the base peak. The second major peak was observed at *m/z* 135 ($[CH_2C_6H_4CHS]^+$, 52.6%) and another signal was found at *m/z* 175 ($[C_2HN_2OS_2CH_2CH_2CH_2]^+$, 7.3%). Scheme 2 shows that the fragmentation progresses *via* a six-membered cyclic transition state with transfer of a benzylic hydrogen to the opposite sulfur atom. Simple ring cleavage was indicated by signals at *m/z* 274 ($[C_2N_2OS_2CH_2CH_2CH_2C_2N_2OS]^+$, 53%) and 136 ($[CH_2C_6H_4CH_2S]^+$, 16.2%). In addition, signals at *m/z* 103 and 104 are identified as $[CHC_6H_4CH_2]^+$ (11.3%) and $[CH_2C_6H_4CH_2]^+$ (32.9%), respectively.



Scheme 2

In addition, the structure was clearly characterized by a single-crystal X-ray diffraction study. As shown in Fig. 1, the X-ray crystal structure shows a 15-membered macrocycle, composed of the C–N–N atoms of 1,3,4-thiadiazolone rings, a propylene chain and an S-*syn* conformation within the *o*-xylene. Two of the 1,3,4-thiazolone rings are planar, and are offset from each other in the *syn* position by an angle of 16.8°. The crystal packing arrangement of the macrocycles comprises two molecules in the *trans*-position as shown in Fig. 2. The 1,3,4-thiazolone ring and the benzene ring in the other macrocycle are almost perpendicular, at an angle of 81.8°.

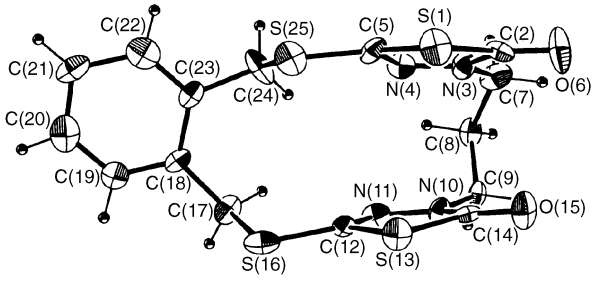


Fig. 1 The molecular structure of macrocycle **3** showing the atomic numbering used for the crystallographic analysis

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

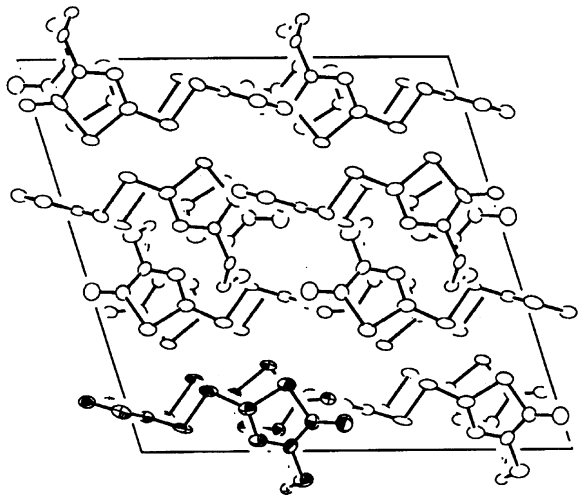

Fig. 2 Crystal packing of macrocycle **3** projected along the *b* axis

Experimental

The preparation of **2** was *via* a previously reported procedure.[6]

Macrocycle **3**.—Compound **2** (0.63 g, 1.7 mmol) was dissolved in ethanol (20 cm^3) with triethylamine (1.21 mL, 8.5 mmol) and to this solution was added 1,3-dibromopropane (0.53 g, 2.6 mmol) with stirring. The resulting mixture was heated under reflux until compound **2** disappeared (TLC). The solvent was evaporated under reduced pressure to leave a solid residue, which was washed with water. The crude product was recrystallized from $CHCl_3$–DMSO (1 : 1). Yield: 0.13 g, 32% from $CHCl_3$–DMSO (1 : 1), mp 237–239, $R_f = 0.4$ [ethyl acetate–*n*-hexane (3 : 7)]. ν_{max}(KBr)/cm^{-1}: 2925 (CH), 1685 (C=O), 1488, 1448, 1287; δ_H (400 MHz $CDCl_3$) 7.34 (4H, m, C_6H_4), 4.58 (4H, s, $CH_2C_6H_4CH_2$), 4.04 (4H, t, 2 × NCH_2), 2.44 (2H, m, CH_2); δ_C(100 MHz, $CDCl_3$) 170.0 (C=O), 148.1 (C–S), 135.1, 131.5, 129.5 (C_6H_4), 46.2 (SCH_2), 34.3 (NCH_2), 26 (CH_2); *m/z* 410 (M^+ 100%), 274 (5.3), 175 (7.3), 136 (16.2), 135 (52.6), 104 (32.9), 103 (11.3).

X-Ray Crystal Structure of Macrocycle **3**.—$C_{15}H_{14}N_4O_2S_4$, $M_r = 410.54$, monoclinic, space group $C2/c$, $a = 17.217(4)$, $b = 12.921(2)$, $c = 16.231(2)$ Å, $\beta = 107.36(2)°$, $V = 3446(1)$ $Å^3$, $Z = 8$, $D_c = 1.582$ g cm^{-3}, μ(Mo-Kα) = 5.69 cm^{-1}. The experimental data were collected at 293 K on an Enraf-Nonius Cad-4 diffractometer using a graphite monochrometor with Mo-Kα radiation ($\lambda = 0.71069$ Å). The structure was determined by direct methods (SHELX86)[7] (all non-H atoms) and refined by full-matrix least-squares refinement (SHELX97).[8] Hydrogen atoms were located from a ΔF synthesis and positionally refined. A total of 3039 independent reflections were measured in the range $2 < \theta < 25°$. Final $R[F_o > 4\sigma(F_o)]$ for 2018 unique observed reflections and *wR* (all data) were 0.0941 and 0.2372 for 226 refined parameters with $(\Delta/\sigma)_{max} = 0.000$, respectively; ρ_{max} and ρ_{min} are 0.749 and -0.923 $Å^{-3}$, respectively, in the final electron difference map; $S = 3.046$, $R_{int} = 0.000$ (intensity data collected only for the asymmetric unit[9]).

Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Research (S)*, 1999, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 423/30.

See http://www.rsc.org/suppdata/jc/1999/730/ for crystallographic files in .cif format.

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