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CONFIGURATIONAL ASSIGNMENT TO PSEUDOASYMMETRIC *GEM*-DISULPHOXIDES. X-RAY STRUCTURE OF (*s*)-1,1-BIS(METHYLSULPHINYL)-3-PHTHALIMIDOPROPANE

M. POJE* and E. F. PAULUS†
Laboratory of Organic Chemistry, Faculty of Science, University of Zagreb, P.O. Box 153, 41001 Zagreb, Yugoslavia

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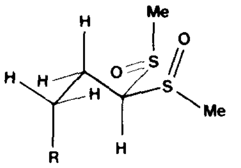
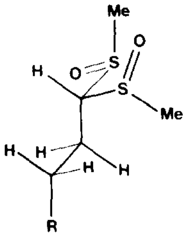
Abstract—The structure of (*s*)-1,1-bis(methylsulphinyl)-3-phthalimidopropane (2)[2] was established by X-ray crystallography. Comparison of ^{1}H and ^{13}C NMR chemical shifts with structural parameters allowed the configurational assignment to non-cyclic *gem*-disulphoxides containing a centre of pseudoasymmetry.

During an investigation of microbial oxidations of 1,1 - bis(methylthio) - 3 - phthalimidopropane (1), proton NMR correlation between configurationally related mono- and disulphoxides was used to deduce whether a particular diastereomer belonged to the (*R*, *S*)/(*S*, *R*) or (*R*, *R*)/(*S*, *S*) pair.[1] It was apparent that disulphoxides 2 and 3, containing a centre of pseudoasymmetry,[2] were particularly suited to a detailed investigation, since the NMR spectra are capable of complete analysis. In order to obtain meaningful results from more readily applied NMR methods it was necessary to be able to relate spectral parameters to certain accurately known stereochemical relationships.

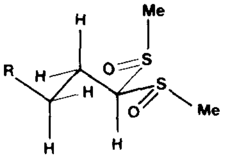


2



3

R = $C_6H_4(CO)_2N$



4 (S,S)

So far as we are aware, studies of pseudoasymmetric *gem*-disulphoxides have been restricted to cyclic systems,[3,4] and no data on conformational properties of the non-cyclic analogues were reported.[5] Since X-ray crystallographic structure determinations have played a major part in clarifying stereochemistry of *gem*-disulphoxides, we undertook to obtain similar information in a non-cyclic system with the centre of pseudoasymmetry.

Conclusive evidence in support of the structural assignment came from a single-crystal X-ray diffraction determination which clearly established the (*s*)-configuration of the pseudoasymmetric centre in 2. The atomic parameters defining the crystal structure of 2 are given, together with their associated estimated standard deviations, in Table 1. An ORTEP drawing of the molecule is shown in Fig. 1. The drawing also shows the atom labeling scheme and interatomic distances. Bond and torsion angles are presented in Table 2.

The main factors determining the stereochemistry of 2 are *gauche-gauche* relationships of C(4)–S(1)–C(1)–S(2)–C(5) and O(1)–S(1)–C(1)–S(2)–O(2), a distorted (ϕ = 18.8°) *syn*-orientation of C(4)–S(1)...S(2)–O(2), and *gauche* relationships in the O(1)–S(1)–C(1)–C(2), O(2)–S(2)–C(1)–C(2), and C(1)–C(2)–C(3)–N(1) fragments. The unit cell contains four molecules of 2 in two enantiomorphic conformations. A view of the molecular packing in the crystal is shown in Fig. 2. Intermolecular

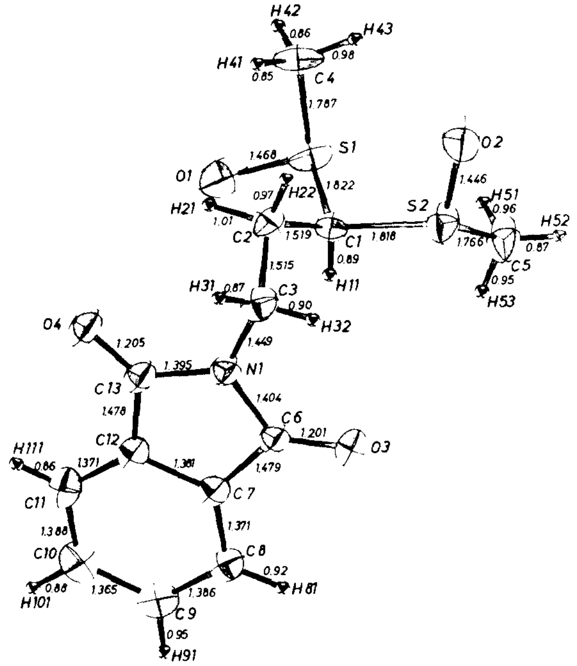


Fig. 1. ORTEP drawing of the structure of 2.

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†Angewandte Physik, Hoechst AG, P.O. Box 80 03 20, 6230 Frankfurt (M) 80, Germany.

Table 1. Positional and thermal parameters for **2**

Atom	*x*	*y*	*z*	*B*	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
S(1)	0.5982(1)	0.1126(1)	0.4511(1)	4.9(1)	5.5(1)	4.6(1)	4.8(1)	-1.6(1)	0.7(1)	0.1(1)
S(2)	0.8812(1)	0.0480(1)	0.6474(1)	5.4(1)	4.2(1)	4.5(1)	8.1(1)	-0.1(1)	2.5(1)	-0.8(1)
O(1)	0.4568(3)	0.1331(3)	0.4436(3)	7.0(2)	4.5(1)	7.5(2)	10.1(2)	-0.9(3)	0.4(3)	2.9(3)
O(2)	0.9527(3)	0.1225(2)	0.6038(4)	7.7(3)	6.3(2)	4.7(1)	16.8(3)	-0.7(3)	6.4(4)	-0.4(4)
O(3)	0.7429(3)	-0 0640(2)	0.8784(3)	5.2(2)	6.2(2)	4.5(1)	7.6(2)	1.9(2)	3.5(3)	1.1(2)
O(4)	0.4551(3)	0.2129(2)	0.7905(3)	5.8(2)	7.5(2)	3.8(1)	8.4(2)	2.0(2)	3.1(3)	0.8(2)
N(1)	0.6243(3)	0.0894(2)	0.8298(3)	3.9(2)	5.4(2)	3.4(1)	4.2(1)	0.7(2)	2.2(2)	0.2(2)
C(1)	0.7049(3)	0.0935(3)	0.6135(3)	3.5(2)	3.7(1)	3.3(1)	4.5(2)	-0.6(2)	1.7(2)	-0.1(2)
C(2)	0.7099(5)	0.1842(3)	0.6946(4)	4.2(2)	5.2(2)	3.3(1)	5.1(2)	-0.2(3)	2.3(3)	-0.1(3)
C(3)	0.7352(5)	0.1528(3)	0.8240(4)	4.6(2)	6.3(2)	3.8(2)	4.8(2)	-0.3(3)	2.1(3)	-0.8(3)
C(4)	0.6655(7)	0.2321(4)	0.4258(5)	5.3(3)	8.0(3)	5.1(2)	4.5(2)	-2.4(4)	1.8(4)	0.0(4)
C(5)	0.8464(7)	-0.0623(4)	0.5544(8)	6.8(4)	6.7(3)	4.0(2)	12.7(5)	-0.1(4)	5.2(7)	-1.7(5)
C(6)	0.6384(4)	-0.0152(3)	0.8586(3)	4.0(2)	5.4(2)	3.7(1)	3.7(1)	1.0(3)	2.0(3)	0.3(2)
C(7)	0.5026(4)	-0.0477(3)	0.8580(3)	3.4(2)	5.2(2)	3.9(1)	2.9(1)	0.6(3)	1.4(2)	-0.2(2)
C(8)	0.4596(5)	-0.1416(3)	0.8808(4)	4.6(2)	6.3(2)	4.0(2)	4.0(2)	0.3(3)	1.9(3)	-0.2(3)
C(9)	0.3230(5)	-0.1509(4)	0.8703(4)	4.8(3)	6.0(2)	5.0(2)	4.6(2)	-0.9(4)	1.5(3)	-0.3(3)
C(10)	0.2353(5)	-0.0684(4)	0.8398(4)	5.1(3)	4.8(2)	7.5(2)	5.2(2)	-0.8(4)	1.6(3)	-1.0(4)
C(11)	0.2788(5)	0.0270(4)	0.8180(4)	5.0(3)	4.9(2)	5.7(2)	5.0(2)	1.0(4)	1.2(3)	-0.7(3)
C(12)	0.4138(4)	0.0357(3)	0.8281(3)	3.6(2)	4.9(2)	4.0(2)	3.2(1)	0.7(3)	1.2(2)	-0.2(2)
C(13)	0.4914(4)	0.1249(3)	0.8116(3)	4.1(3)	5.8(2)	3.7(2)	4.3(2)	1.2(3)	1.8(3)	0.1(3)
H(11)	0.663(3)	0.039(2)	0.628(3)	0.5(6)						
H(21)	0.620(4)	0.224(3)	0.657(3)	2.9(9)						
H(22)	0.782(4)	0.231(3)	0.694(3)	2.6(8)						
H(31)	0.730(4)	0.208(3)	0.863(4)	2.9(9)						
H(32)	0.816(4)	0.118(3)	0.856(3)	1.9(8)						
H(41)	0.655(4)	0.278(3)	0.471(4)	3.2(11)						
H(42)	0.607(5)	0.249(3)	0.354(4)	3.4(10)						
H(43)	0.758(6)	0.224(4)	0.425(5)	6.0(16)						
H(51)	0.782(7)	-0.047(5)	0.473(6)	9.2(25)						
H(52)	0.923(6)	-0.091(4)	0.557(5)	6.1(15)						
H(53)	0.790(7)	-0.102(5)	0.583(6)	8.9(20)						
H(81)	0.520(4)	-0.197(3)	0.896(3)	2.9(9)						
H(91)	0.289(4)	-0.214(3)	0.887(3)	2.2(8)						
H(101)	0.153(4)	-0.071(3)	0.844(3)	2.2(8)						
H(111)	0.231(5)	0.083(3)	0.805(4)	3.7(11)						

Table 2. Bond and torsion angles in 2

Bond angles	Degrees	Bond angles	Degrees	Torsion angles	Deg.
O(1)—S(1)—C(1)	104.9(2)	H(51)—C(5)—H(52)	113. (5)	O(1)—S(1)—C(1)—S(2)	171.5
O(1)—S(1)—C(4)	106.5(3)	H(51)—C(5)—H(53)	101. (5)	O(1)—S(1)—C(1)—C(2)	-60.1
C(1)—S(1)—C(4)	100.8(2)	H(52)—C(5)—H(53)	117. (5)	O(1)—S(1)—C(1)—H(11)	61.8
O(2)—S(2)—C(1)	108.9(2)	O(3)—C(6)—N(1)	124.2(4)	C(4)—S(1)—C(1)—S(2)	-78.1
O(2)—S(2)—C(5)	109.3(3)	O(3)—C(6)—C(7)	130.0(3)	C(4)—S(1)—C(1)—C(2)	50.4
C(1)—S(2)—C(5)	101.2(2)	N(1)—C(6)—C(7)	105.8(3)	C(4)—S(1)—C(1)—H(11)	172.3
C(3)—N(1)—C(6)	124.2(3)	C(6)—C(7)—C(8)	130.3(3)	O(2)—S(2)—C(1)—S(1)	60.4
C(3)—N(1)—C(13)	124.5(3)	C(6)—C(7)—C(12)	108.5(3)	O(2)—S(2)—C(1)—C(2)	-70.4
C(6)—N(1)—C(13)	111.2(3)	C(8)—C(7)—C(12)	121.3(4)	O(2)—S(2)—C(1)—H(11)	168.1
S(1)—C(1)—S(2)	114.2(2)	C(7)—C(8)—C(9)	117.9(4)	C(5)—S(2)—C(1)—S(1)	-54.6
S(1)—C(1)—C(2)	114.8(3)	C(7)—C(8)—H(81)	119. (3)	C(5)—S(2)—C(1)—C(2)	174.6
S(1)—C(1)—H(11)	100. (2)	C(9)—C(8)—H(81)	123. (3)	C(5)—S(2)—C(1)—H(11)	53.1
S(2)—C(1)—C(2)	110.0(3)	C(8)—C(9)—C(10)	120.7(4)	C(6)—N(1)—C(3)—C(2)	109.3
S(2)—C(1)—H(11)	103. (2)	C(8)—C(9)—H(91)	121. (2)	C(6)—N(1)—C(3)—H(31)	-135.4
C(2)—C(1)—H(11)	113. (2)	C(10)—C(9)—H(91)	118. (2)	C(6)—N(1)—C(3)—H(32)	-11.1
C(1)—C(2)—C(3)	112.6(3)	C(9)—C(10)—C(11)	121.6(4)	C(13)—N(1)—C(3)—C(2)	-72.9
C(1)—C(2)—H(21)	110. (2)	C(9)—C(10)—H(101)	121. (3)	C(13)—N(1)—C(3)—H(31)	42.3
C(1)—C(2)—H(22)	108. (2)	C(11)—C(10)—H(101)	117. (3)	C(13)—N(1)—C(3)—H(32)	166.6
C(3)—C(2)—H(21)	110. (2)	C(10)—C(11)—C(12)	117.5(4)	S(1)—C(1)—C(2)—C(3)	152.2
C(3)—C(2)—H(22)	111. (2)	C(10)—C(11)—H(111)	126. (3)	S(1)—C(1)—C(2)—H(21)	29.7
H(21)—C(2)—H(22)	105. (3)	C(12)—C(11)—H(111)	116. (3)	S(1)—C(1)—C(2)—H(22)	-84.5
N(1)—C(3)—C(2)	113.0(4)	C(7)—C(12)—C(11)	121.0(4)	S(2)—C(1)—C(2)—C(3)	-77.3
N(1)—C(3)—H(31)	103. (3)	C(7)—C(12)—C(13)	108.1(3)	S(2)—C(1)—C(2)—H(21)	160.2
N(1)—C(3)—H(32)	109. (2)	C(11)—C(12)—C(13)	130.8(4)	S(2)—C(1)—C(2)—H(22)	46.0
C(2)—C(3)—H(31)	107. (3)	O(4)—C(13)—N(1)	124.0(4)	H(11)—C(1)—C(2)—C(3)	37.8
C(2)—C(3)—H(32)	108. (2)	O(4)—C(13)—C(12)	129.6(4)	H(11)—C(1)—C(2)—H(21)	-84.6
H(31)—C(3)—H(32)	117. (4)	N(1)—C(13)—C(12)	106.3(3)	H(11)—C(1)—C(2)—H(22)	161.2
S(1)—C(4)—H(41)	110. (3)			C(1)—C(3)—C(3)—N(1)	-62.7
S(1)—C(4)—H(42)	103. (3)			C(1)—C(2)—C(3)—H(31)	-175.6
S(1)—C(4)—H(43)	111. (3)			C(1)—C(2)—C(3)—H(32)	57.8
H(41)—C(4)—H(42)	104. (4)			H(21)—C(2)—C(3)—N(1)	59.7
H(41)—C(4)—H(43)	118. (4)			H(21)—C(2)—C(3)—H(31)	-53.2
H(42)—C(4)—H(43)	109. (4)			H(21)—C(2)—C(3)—H(32)	-179.8
S(2)—C(5)—H(51)	111. (4)			H(22)—C(2)—C(3)—N(1)	175.6
S(2)—C(5)—H(52)	112. (4)			H(22)—C(2)—C(3)—H(31)	62.7
S(2)—C(5)—H(53)	103. (4)			H(22)—C(2)—C(3)—H(32)	-63.9

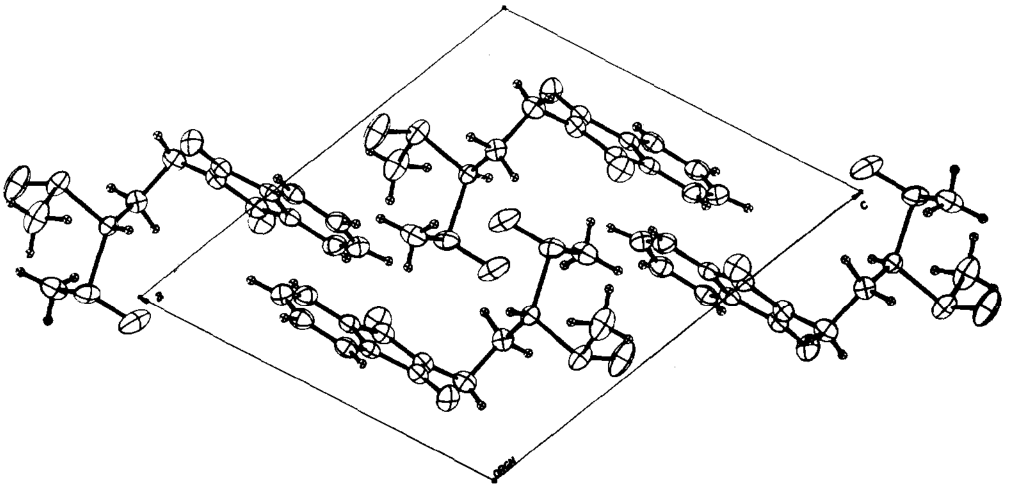

Fig. 2. Packing diagram. The direction of projection is down *b*.

Table 3. ^1H and ^{13}C chemical shifts of diastereomeric *gem*-disulphoxides **2–4**

Group†	**2**		**3**		**4**	
	$\delta\ ^1H$	$\delta^{13}C$	$\delta\ ^1H$	$\delta^{13}C$	$\delta\ ^1H$	$\delta^{13}C$
$SOCH_3$	2.88*s*	36.8*q*	2.83*s*	37.4*q*	2.70*s* 2.90*s*	36.0*q* 39.5*q*
CH (1)	3.83*t* *J 7.0*	71.6*d*	4.05*t* *J 6.0*	74.3*d*	3.88*t* *J 5.5*	76.1*d*
CH_2(2)	2.55*q*	20.8*t*	2.24*q*	21.9*t*	2.45*q*	20.3*t*
CH_2(3)	4.03*t* *J 6.5*	35.4*t*	3.98*t* *J 7.0*	36.5*t*	4.00*t* *J 6.0*	36.6*t*

† The phthalimido group showed no significant chemical shift differences: $\delta\ ^1H$, 7.81±0.01; $\delta^{13}C$ ±0.1, 168.6, 134.3, 131.9, 123.5.

contacts are effected at distances exceeding the corresponding sums of van der Waal's radii.

Comparisons of ^{13}C NMR chemical shifts (Table 3) with structural parameters available from X-ray crystallography allowed a simple configurational assignment to diastereomeric disulphoxides **2–4**. It is evident that (*s*)-**2** experiences more *gauche* interactions than those in (*r*)-**3**. This is consistent with the higher shielding observed for all carbons in the (*s*)-diastereomer.

The largest difference in chemical shift involves C(1). The chemical shifts of C(2) are sensitive to the stereochemistry of sulphoxide groups. The methylene carbon C(2) in **2** and **4** is *gauche* to both sulphoxide oxygens, whereas in **3** it is *gauche* to only one. The observed shielding differences for **2** ($\Delta\delta$ −1.1) and for **4** ($\Delta\delta$ −1.6) are consistent with similar γ-effects. The upfiled shift of *Re*(*S*) or *Si*(*R*) sulphoxide methyls in **4** due to a *gauche* interaction with C(2) can also be used in assignment to diastereotopic ligands. It is noteworthy that a shielding contribution of the same sign is characteristic of such topic relations in pseudoasymmetric diastereomers; the *Re*(*S*)/(*Si*(*R*) arrangement of enantiotopic ligands in **2** is more shielded than that of *Re*(*R*)/*Si*(*S*) in **3**.

The results appear to indicate that the general trend of ^{13}C NMR results should be considered reliable enough to assign configurations in related *gem*-disulphoxides. The relatively small, but characteristic, ^1H NMR shift differences (Table 3) for diastereomers **2–4** should provide a valuable complement to ^{13}C NMR spectra.

EXPERIMENTAL

M.ps are uncorrected. NMR spectra were recorded in deuteriochloroform (20% w/v) on Varian T-60 and XL-100 instruments. Chemical shifts are given in ppm (δ) from internal tetramethylsilane and coupling constants are expressed in Hz (s, singlet; d, doublet; t, triplet; q, quartet). Off-resonance decoupling served to distinguish between the primary, secondary, tertiary, and quaternary carbons. Integration showed that precise quantitative data for the composition of diastereomeric mixtures purpose of this study diastereomeric disulphoxides were prepared on a 0.01 mol scale and separated by preparative TLC procedure described previously.[1] Recrystallizations from ethanol gave pure isomers: **2** (24%), m.p. 162–163°, R_f 0.54; **3** (20%), m.p. 153–154°. R_f 0.45; and **4** (50%), m.p. 174–175°, R_f 0.34. ^1H and ^{13}C NMR spectral data are given in Table 3. Four further recrystallizations from ethanol provided a sample of (*s*) - 1,1 - bis(methylsulphinyl) - 3 - phthalimidopropane (**2**), m.p. 163–165°, for single crystal X-ray diffraction studies.

Crystallography

A parallelepiped-shaped crystal (0.42 × 0.56 × 0.19 mm) of **2** was used for the X-ray analysis. The crystal specimen was in a glass capillary during the data collection. Lattice dimensions were determined by an automatic Siemens AED diffractometer, using MoK_α (λ 0.7107 Å) radiation.

Crystal data. Crystals of **2**, $C_{13}H_{15}NO_4S_2$, M = 313.4, are monoclinic, space group $P2_1/n$, with $a = 10.451(4)$, $b = 13.081(5)$, $c = 11.929(6)$ Å, $\beta = 113.85(3)°$, $V = 1491\ 6$ Å^3, $Z = 4$. The measured crystal density (flotation in i-C_8H_{18}/CCl_4) is identical with that calculated (1.40 gcm^{-3}) assuming four molecules in the unit cell.

Intensity data were measured using MoK_α (λ 0.7107 Å, θ_{max} = 28°) radiation. A total of 3550 independent reflexions were collected of which 2683 showed intensity significantly above background ($I > \sigma I$). No absorption corrections were made and the data were converted to structure amplitudes in the usual way. The structure was solved using the program MULTAN[9] and refined by full-matrix least-squares procedure. Anisotropic thermal parameters were used for non-hydrogen atoms. All hydrogen atoms were identified from difference electron-density maps and included in the refinement with isotropic B values assumed. At convergence no calculated shift in any parameter exceeded 0.1 σ. The final values $R_1 = 0.0655$ and $R_2 = 0.0546$ were obtained for the observed reflections.

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