sind grösser als die Summe der Van der Waals-Radien benachbarter Atome.

Dank gilt den Herren Kollegen des Instituts für Kristallographie der Freien Universität Berlin für die Unterstützung bei den Messungen und für die Über-lassung einiger Rechenprogramme. Dem Fonds der Chemischen Industrie danken wir für finanzielle Unterstützung.

Literatur

BONDI. A. (1964). *J. Phys. Chem.* **68**. 441–451.
BÜNGER. T.. MERREM. H. J. & ENGELHARDT. U. (1982). *Z. Anorg. Allg. Chem.* Im Druck.
CROMER. D. T. & MANN. J. B. (1968). *Acta Cryst.* A**24**. 321–324
ENGELHARDT. U. & HARTL. H. (1975a). *Acta Cryst.* B**31**. 2098–2105.

ENGELHARDT. U. & HARTL. H. (1975b). *Angew. Chem.* **87**. 541–542.
ENGELHARDT. U. & HARTL. H. (1976). *Acta Cryst.* B**32**. 1133–1138.
ENGELHARDT. U. & JÜRGENS. G. (1980). *Acta Cryst.* B**36**. 3059–3063.
ENGELHARDT. U. & VIERTEL. H. (1982). *Acta Cryst.* B**38**. 1972–1975.
GERMAIN. G.. MAIN. P. & WOOLFSON. M. M. (1971). *Acta Cryst.* A**27**. 368–376.
HAMILTON. W. C. (1959). *Acta Cryst.* **12**. 609–610.
International Tables for X-ray Crystallography (1962). Bd III. S. 213. Birmingham: Kynoch Press.
STEWART. J. M.. MACHIN. P. A.. DICKINSON. C.. AMMON. H. L.. HECK. H. & FLACK. H. (1976). *The XRAY system* – *version of March* 1976. Tech. Rep. TR-446. Computer Science Center. Univ. of Maryland. College Park. Maryland.
STEWART. R. F.. DAVIDSON. E. R. & SIMPSON. W. T. (1965). *J. Chem. Phys.* **42**. 3175–3187.

A Sixteen-Membered-Ring Organophosphorus Compound: *cis*-2,10-Di(*tert*-butyl)-1,3,6,9,11,14-hexathia-2,10-diphosphacyclohexadecane 2,10-Disulphide

BY ANDRÉ GRAND* AND JEAN MARTIN

Laboratoires de Chimie (LA CNRS n° 321), Département de Recherche Fondamentale, Centre d'Etudes Nucléaires de Grenoble, 85 X, F. 38041 Grenoble CEDEX, France

Abstract

$C_{16}H_{34}P_2S_8$. $M_r = 544.9$. is monoclinic. $P2_1/c$. with $a = 10.054$ (1). $b = 11.929$ (2). $c = 21.861$ (5) Å. $\beta = 97.38$ (1)°. $V = 2600.16$ Å³. $D_x = 1.392$. $D_m = 1.36$ Mg m⁻³. $Z = 4$. The structure was refined to $R = 0.064$ for 3009 unique diffractometer data. The molecule adopts an asymmetric conformation which does not belong to the conventional forms and displays a significant discrepancy between corresponding bond lengths and angles in the two parts of the molecule.

Introduction

Studies of large organophosphorus rings were under-taken to solve problems such as the synthesis of large heteroatomic molecules and their complexation with metal atoms, and to obtain their molecular geometry and conformation. Although the conformations of

macrocycles have been well studied from both theoretical (Dale, 1973a) and experimental (Anet & Cheng, 1975: Groth, 1976: Dutasta, Grand & Robert, 1978) points of view, many problems still remain, particularly when heteroatoms are present in the ring. Besides the conformational problems, it seems that in rings containing P atoms and having the same *R* groups attached to the P atom, a relation can be shown between the NMR parameters $|\delta^{31}P$. ^1J (P–C). ^3J (P–S–C–H)| in the liquid state and the bond angles and bond lengths determined by X-ray diffraction in the solid state (Martin & Robert. 1981: Grand. 1979: Gorenstein. 1975). The crystal structure analysis of (I) has also revealed that it is the *cis* isomer. a result not possible to determine by NMR.

We report here the first structure of a sixteen-membered macrocycle (I) containing two P atoms. The molecule was obtained by dimerization of the eight-membered-ring monomer (II) for which the solid-state structure and synthesis were published elsewhere (Martin & Robert. 1979. 1980). Because disorder phenomena appeared during the refinement process

---

* Faculty member of the Université Scientifique et Médicale de Grenoble.

using a room-temperature data set, we collected data at 213 K.
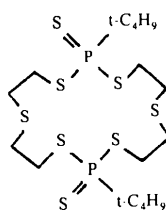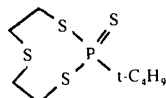
(I)   (II)

Experimental section and structure determination

Colourless crystals (m.p. 420 K) were obtained by recrystallization from benzene. Weissenberg photographs showed the monoclinic space group $P2_1/c$. Cell parameters were refined by a least-squares fitting of the angular positions of 25 reflexions. The intensities of 4850 independent reflexions ($2° < \theta < 25°$) were recorded on an automatic Enraf–Nonius CAD-4 diffractometer, using graphite-monochromatized Mo $K\alpha$ radiation, and were measured at room temperature (set 1) and at 213 K (set 2). Three standard reflexions were checked periodically and showed no discrepancy during data collection. The intensities were corrected for Lorentz and polarization factors but not for absorption. 2751 reflexions $|F_o > 3\sigma(F_o)|$ were judged observed for set 1 and 3009 for set 2. The structure was solved by direct methods, using MULTAN (Germain, Main & Woolfson, 1971).

An E map based on the phases of 288 reflexions with $E > 1·95$ revealed all the non-hydrogen atoms. The structure was refined using the full-matrix least-squares program XFLSN (Busing, Martin & Levy, 1971). With set 1, the R factors reached the values $R = \sum |F_o - F_c|/\sum F_o = 0·057$ and $R_w = [\sum w(F_o - F_c)^2/\sum wF_o^2]^{1/2} = 0·066$. In spite of these values, the atoms of the chain S(3)–C(4)–C(5)–S(6)–C(7)–C(8)–S(9) were affected by large thermal factors (7 Å^2) and examination of bond lengths and angles showed important asymmetries in equivalent molecular fragments (C—C range 1·42–1·48 Å; S—C range 1·78–1·93 Å). These results indicate a disorder phenomenon in these parts of the molecule. Such disorder has often been observed in rings of a similar or larger size (Groth, 1979; Dunitz & Ibers, 1968).

Refinements based on set 2, with anisotropic thermal factors for P, S and C, converged to R values, $R = 0·075$, $R_w = 0·085$. At this stage, a difference-Fourier map showed the positions of the H atoms. In the last refinement cycle (P, S, C varying anisotropically, H fixed isotropically with $B = 3$ Å^2) the R factors reached the final values $R = 0·064$, $R_w = 0·063$. Atomic coordinates are reported in Table 1, bond distances and

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *with their e.s.d.'s*

$$B_{eq} = 8\pi^2 (U_1 U_2 U_3)^{2/3}.$$

	x	y	z	B_{eq} (Å^2)
S(1)	1294 (2)	5970 (2)	9515 (1)	1·70
P(2)	143 (2)	7281 (2)	9076 (1)	1·32
S(3)	515 (2)	7092 (2)	8162 (1)	1·93
C(4)	22 (9)	8495 (7)	7839 (4)	2·36
C(5)	373 (8)	8624 (7)	7207 (4)	1·84
S(6)	−609 (2)	7805 (2)	6627 (1)	2·35
C(7)	553 (8)	6658 (8)	6496 (4)	2·35
C(8)	1477 (9)	7022 (8)	6054 (4)	2·23
S(9)	2674 (2)	5953 (2)	5887 (1)	1·93
P(10)	4150 (2)	6148 (2)	6646 (1)	1·45
S(11)	3524 (2)	4932 (2)	7242 (1)	1·65
C(12)	4342 (8)	5363 (7)	7996 (4)	2·26
C(13)	3577 (8)	4838 (7)	8481 (4)	1·85
S(14)	4367 (2)	5058 (2)	9246 (1)	1·76
C(15)	3942 (8)	6536 (7)	9370 (4)	1·73
C(16)	2885 (8)	6662 (7)	9792 (4)	1·96
S(17)	546 (2)	8789 (2)	9403 (1)	2·05
C(18)	−1564 (8)	6788 (7)	9137 (4)	1·43
C(19)	−1839 (8)	6922 (7)	9801 (4)	2·22
C(20)	−1735 (8)	5557 (7)	8938 (4)	1·89
C(21)	−2555 (8)	7522 (7)	8712 (4)	1·99
S(22)	4331 (2)	7644 (2)	7004 (1)	2·17
C(23)	5688 (8)	5612 (7)	6353 (4)	1·91
C(24)	6094 (8)	6438 (8)	5882 (4)	2·51
C(25)	5450 (9)	4443 (7)	6059 (5)	2·59
C(26)	6781 (8)	5512 (8)	6902 (4)	2·66

Table 2. *Bond distances* (Å) *and angles* (°) *and their e.s.d.'s*

|			
P(2)–S(1)	2·105 (3)	P(2)–S(3)	2·092 (3)
P(10)–S(9)	2·091 (3)	P(10)–S(11)	2·100 (3)
S(1)–C(16)	1·832 (8)	S(3)–C(4)	1·855 (9)
S(9)–C(8)	1·822 (9)	S(11)–C(12)	1·820 (8)
S(14)–C(13)	1·777 (8)	S(6)–C(7)	1·845 (9)
S(14)–C(15)	1·842 (8)	S(6)–C(5)	1·794 (9)
C(4)–C(5)	1·477 (10)	C(16)–C(15)	1·503 (10)
C(7)–C(8)	1·488 (11)	C(13)–C(12)	1·522 (10)
P(2)–S(17)	1·958 (3)	P(10)–S(22)	1·948 (3)
P(2)–C(18)	1·835 (8)	P(10)–C(23)	1·861 (8)
C(18)–C(19)	1·522 (10)	C(23)–C(24)	1·519 (11)
C(18)–C(20)	1·535 (11)	C(23)–C(25)	1·541 (11)
C(18)–C(21)	1·543 (10)	C(23)–C(26)	1·525 (11)
S(1)–P(2)–S(3)	101·6 (1)	S(9)–P(10)–S(11)	100·2 (1)
P(2)–S(1)–C(16)	102·8 (3)	P(2)–S(3)–C(4)	101·2 (3)
P(10)–S(11)–C(12)	103·3 (3)	P(10)–S(9)–C(8)	100·6 (3)
C(13)–S(14)–C(15)	101·3 (4)	C(5)–S(6)–C(7)	102·3 (4)
S(14)–C(15)–C(16)	112·5 (6)	S(6)–C(5)–C(4)	115·4 (6)
S(1)–C(16)–C(15)	114·1 (6)	S(3)–C(4)–C(5)	111·4 (6)
S(11)–C(12)–C(13)	107·7 (6)	S(6)–C(7)–C(8)	110·1 (7)
S(14)–C(13)–C(12)	112·9 (6)	S(9)–C(8)–C(7)	114·1 (6)
S(1)–P(2)–S(17)	116·1 (1)	S(11)–P(10)–S(22)	113·8 (1)
S(3)–P(2)–S(17)	113·2 (1)	S(9)–P(10)–S(22)	116·2 (1)
S(1)–P(2)–C(18)	101·2 (3)	S(11)–P(10)–C(23)	107·7 (3)
S(3)–P(2)–C(18)	108·5 (3)	S(9)–P(10)–C(23)	103·0 (3)
S(17)–P(2)–C(18)	114·8 (3)	S(22)–P(10)–C(23)	114·5 (3)
C(19)–C(18)–C(20)	110·0 (7)	C(24)–C(23)–C(25)	110·2 (7)
C(19)–C(18)–C(21)	109·4 (7)	C(24)–C(23)–C(26)	110·8 (7)
C(20)–C(18)–C(21)	109·4 (7)	C(25)–C(23)–C(26)	108·4 (7)
C(19)–C(18)–P(2)	108·8 (6)	C(24)–C(23)–P(10)	108·5 (6)
C(20)–C(18)–P(2)	111·0 (6)	C(25)–C(23)–P(10)	111·3 (6)
C(21)–C(18)–P(2)	108·2 (5)	C(26)–C(23)–P(10)	107·6 (6)
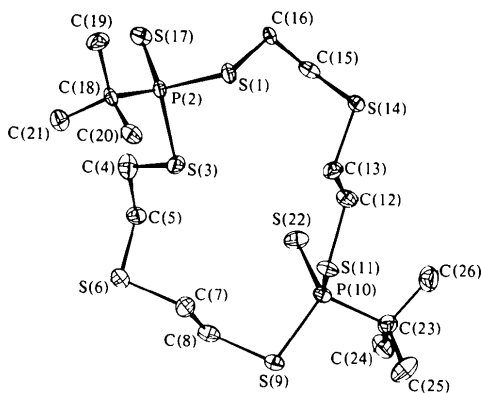
Fig. 1. Perspective view of the molecule.

angles in Table 2. The molecular conformation is represented by an *ORTEP* view in Fig. 1.*

Discussion

Bond lengths and angles

Bond lengths are in good agreement with values generally found in 1,3,2-dithiaphospha ring compounds (Grand, Martin & Robert, 1976; Martin & Robert, 1979), but further examination shows that differences between the corresponding bond lengths in each of the four P—S—C—C—S parts of the molecule are slightly outside the error limits (3σ). This could be interpreted as a slight disorder in the chains, which could be explained by the easy mobility of such fragments and/or by the numerous allowed conformations energetically close for this kind of molecule. However, in the present case, this asymmetry in units of energy would not exceed $6\cdot2$ kJ mol^{-1} (Allinger & Hickey, 1975).

The bond angles show some interesting features when compared with values in rings of smaller size. By comparing the S—P—S intracyclic angles in the five- ($100\cdot5$, $98\cdot5°$) (Lee & Goodacre, 1971), the six- ($100\cdot6$, $107\cdot8°$) (Grand, Martin & Robert, 1976), the eight- ($108\cdot9°$) (Martin & Robert, 1979) and the sixteen-membered ring ($101\cdot5$, $100\cdot2°$) it is found that the variation is not monotonic and shows a maximum for the eight-membered ring. In the same rings, a similar evolution is observed for the P—S—C angle, for which the mean values are $97\cdot7$, $100\cdot0$, $105\cdot0$ and

$102\cdot0°$ respectively. The variations of these two angles (S—P—S and P—S—C) with ring size are different from those observed in homologous rings where S atoms are substituted by O atoms, compounds in which the O—P—O and P—O—C angles vary continuously from the five- to the twelve-membered ring (Dutasta, Grand & Robert, 1978).

Ring conformation

For the cyclohexadecane system, experiments (Anet & Cheng, 1975) and calculations (Dale, 1973a) have shown that the ring could adopt two energetically favourable conformations, separated by only $5\cdot0$ kJ mol^{-1}: first the square 4-4-4-4 and next the rectangular 3-5-3-5 conformation. The introduction of *gem*-dimethyl substituants does not perturb the ring conformation, but the substituted C atoms are restricted to corner positions in the ring as a result of steric requirements (Groth, 1974; Björnstad, Borgen, Dale & Gudmund, 1975; Dale, 1973b). Similarly, tetraoxacyclohexadecane rings (Groth, 1971, 1975; Borgen, Dale & Teien, 1979) adopt the same conformation with O atoms placed across the corners. On this basis, in our molecule (I), the substituted P atoms should be at the corners with the intracycle heteroatoms S(6) and S(4) across the corners, which agrees with the requirements outlined above. Thus, the square 4-4-4-4 conformation is excluded by this scheme and the rectangular 3-5-3-5 form is expected.

Examination of the torsion angles (Fig. 2) shows that the ring cannot be depicted as the 3-5-3-5 form. The ring conformation is asymmetric and belongs neither to the lower-, nor to the higher-energy forms proposed by Dale. A possible explanation is the existence of short intermolecular distances, and the presence in the ring of S···C distances in the range of the sum of the van der Waals radii.
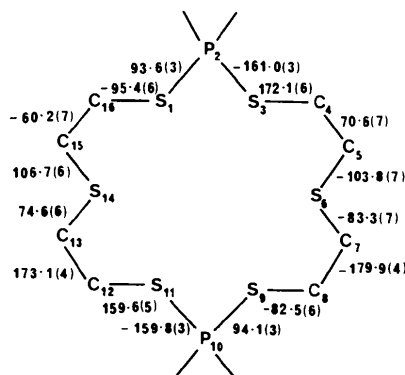
Fig. 2. Torsion angles (°) across the ring.

References

ALLINGER, N. L. & HICKEY, M. J. (1975). *J. Am. Chem. Soc.* **97**, 5167–5177.

ANET, F. A. L. & CHENG, A. K. (1975). *J. Am. Chem. Soc.* **97**, 2420–2424.

BJÖRNSTAD, S. L., BORGEN, G., DALE, J. & GUDMUND, G. (1975). *Acta Chem. Scand. Ser. B*, **29**, 320–324.

BORGEN, G., DALE, J. & TEIEN, G. (1979). *Acta Chem. Scand. Ser. B*, **33**, 15–21.

BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1971). *ORXFLS*-3. Report ORNL 59-4-37. Oak Ridge National Laboratory, Tennessee.

DALE, J. (1973a). *Acta Chem. Scand.* **27**, 1115–1129.

DALE, J. (1973b). *Acta Chem. Scand.* **27**, 1149–1158.

DUNITZ, J. D. & IBERS, J. A. (1968). Editors *Perspectives in Structural Chemistry*, Vol. 2. New York: John Wiley.

DUTASTA, J. P., GRAND, A. & ROBERT, J. B. (1978). *Acta Cryst.* B**34**, 3820–3822.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

GORENSTEIN, D. G. (1975). *J. Am. Chem. Soc.* **97**, 898–900.

GRAND, A. (1979). These d'Etat, Grenoble.

GRAND, A., MARTIN, J. & ROBERT, J. B. (1976). *Acta Cryst.* B**32**, 1244–1247.

GROTH, P. (1971). *Acta Chem. Scand.* **25**, 725–734.

GROTH, P. (1974). *Acta Chem. Scand. Ser. A*, **28**, 808–810.

GROTH, P. (1975). *Acta Chem. Scand. Ser. A*, **29**, 642–643.

GROTH, P. (1976). *Acta Chem. Scand. Ser. A*, **30**, 294–296.

GROTH, P. (1979). *Acta Chem. Scand. Ser. A*, **33**, 503–513.

LEE, J. D. & GOODACRE, G. W. (1971). *Acta Cryst.* B**27**, 1055–1061; 1841–1845.

MARTIN, J. & ROBERT, J. B. (1979). *Acta Cryst.* B**35**, 1623–1626.

MARTIN, J. & ROBERT, J. B. (1980). *Nouv. J. Chim.* **11**, 515–521.

MARTIN, J. & ROBERT, J. B. (1981). *Org. Magn. Reson.* **15**, 87–93.

Structural Studies of Substituted 6,7-Benzomorphan Compounds. VI.* (−)-(1R,5R,9R,13R)-2'-Hydroxy-5,9α-dimethyl-2-(tetrahydrofurfuryl)-6,7-benzomorphan and (−)-(1R,5R,9R,13S)-2'-Hydroxy-5,9-dimethyl-2-(tetrahydrofurfuryl)-6,7-benzomorphan Tartrate Monohydrate

By O. M. PEETERS, C. J. DE RANTER† AND N. M. BLATON

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, KU Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

Abstract

(−)-(1R,5R,9R,13R)-N-(Tetrahydrofurfuryl)normetazocine [2'-hydroxy-5,9α-dimethyl-2-(tetrahydrofurfuryl)-6,7-benzomorphan], $C_{19}H_{27}NO_2$, $M_r = 301 \cdot 43$, crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 9 \cdot 0022$ (5), $b = 12 \cdot 2825$ (3) and $c = 14 \cdot 840$ (1) Å, $V = 1640 \cdot 9$ Å^3, $D_m = 1 \cdot 23$, $D_c = 1 \cdot 22$ Mg m^{-3}, $Z = 4$, λ(Cu $K\alpha$) = $1 \cdot 5418$ Å, $\mu = 0 \cdot 623$ mm^{-1}. The final R value is 0·046 for 1524 observed reflections. (−)-(1R,5R,9R,13S)-N-(Tetrahydrofurfuryl)normetazocine tartrate monohydrate, $C_{19}H_{28}NO_2^+.C_4H_5O_6^-.H_2O$, $M_r = 469 \cdot 54$, has monoclinic symmetry, space group $P2_1$, with $a = 9 \cdot 033$ (4), $b = 16 \cdot 106$ (7), $c = 7 \cdot 821$ (3) Å, $\beta = 92 \cdot 58$ (4)°, $V = 1136 \cdot 7$ Å^3, $D_m = 1 \cdot 38$, $D_c = 1 \cdot 37$ Mg m^{-3}, $Z = 2$,

λ(Mo $K\alpha$) = $0 \cdot 71069$ Å, $\mu = 0 \cdot 113$ mm^{-1}. The structure was refined to $R = 0 \cdot 038$ for 1689 observed reflections. Both structures were solved using direct methods of phase determination. Potential-energy calculations, using the structural data, suggest that the different action profiles of the diastereomers could be the result of an additional drug–receptor binding.

Introduction

Since it was shown (Merz & Stockhaus, 1979) that some N-[tetrahydrofuryl(alkyl)]normetazocines‡ possess action profiles distinctly different from that of morphine and other classical opiates, it seemed worthwhile, as part of our investigation into the relationship between molecular structure and physio-

---