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The Crystal and Molecular Structure of 10-Methyl-5-phenyldibenzo[*b*,*e*]phosphorinan-10-ol 5-Oxide (5,10-Dihydro-10-methyl-5-phenylacridophosphin-10-ol 5-Oxide)

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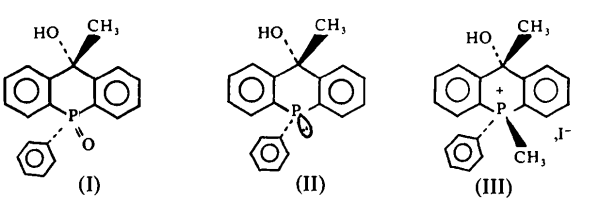
Abstract

The crystal structure of the title compound, $C_{20}H_{17}O_2P$, has been determined and refined using three-dimensional X-ray diffraction data. The molecule crystallizes in space group $P2_1/n$ with a = 11·6512 (5), b = 12·1150 (3), c = 11·7471 (4) Å and β = 90·90 (1)°. The phenyl group was found to occupy a pseudo-equatorial position in the butterfly conformation, as was the case for two similar compounds previously reported. The fold angle was found to be 161·6°. The final R value for all 3413 data was 5·0%. The derived geometrical parameters are compared with similar compounds.

Introduction

The title compound (I) is an example of a substituted derivative of anthracene which possesses a folded or 'butterfly' conformation. The compound was synthesized by addition of H_2O_2 to 5,10-dihydro-10-methyl-5-phenylacridophosphin-10-ol (II), for which the solid-state structure has been reported (Chen, Ealick, van der Helm, Barycki & Berlin, 1977). The structure of a third related compound, 5,10-dihydro-10-hydroxy-5,10-dimethyl-5-phenylacridophosphonium iodide (III), which was prepared by addition of methyl iodide to (II), has also been reported (Wu, Nunnery, van der Helm & Berlin, 1977). Together these three compounds represent all the known X-ray structures of 5-phosphanthrene systems. Because the P atom exists in



(I) (II) (III)

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a different valence state in each of the three compounds, interesting comparisons can be made regarding the effect of electronic and steric factors on the geometrical parameters. It is also important to establish which isomer exists in the solid state (*i.e.* which substituents occupy axial and equatorial positions).

Experimental

Large single crystals of the title compound were obtained by cooling a solution of 10% ethanol and 90% benzene. Preliminary examination of the data crystal (0·10 × 0·13 × 0·41 mm) revealed the space group to be $P2_1/n$ with four molecules per unit cell. Integrated intensity data and crystallographic data (Table 1) were measured on a Nonius CAD-4 automatic diffractometer at 296 ± 1 K. For the unit-cell constants Cu $K\alpha_1$ radiation (λ = 1·54051 Å) was used and for the intensity data Cu $K\bar{\alpha}$ radiation (λ = 1·54178 Å) was used. 3413 intensities with $2\theta \leq 150°$ were measured using θ–2θ scans. For each reflection a variable scan width $(0{\cdot}8 + 0{\cdot}08 \tan\theta)°$ and receiving aperture, $(4{\cdot}0 + 0{\cdot}86 \tan\theta)$ mm with a constant height of 6 mm, were used. The maximum time spent on each measurement was 60 s. Less than 60 s was used if 40 000 counts could be obtained with a faster scan speed. 552 intensities were considered indistinguishable from the background on the basis that the intensity was less than $2\sigma(I)$. A monitor intensity for the reflection 172 was recorded after every 25 intensities and did not show a significant variation during the data collection. Other experimental details have been described previously (van der Helm & Poling, 1976). Lorentz, polarization and absorption corrections (μ = 1·512 mm^{-1}) were applied and individual structure factor amplitudes were derived. For the absorption correction the program of Coppens, Leiserowitz & Rabinovich (1965) was used. The program employs a Gaussian integration, and, in this case, 216 sampling points were used. Each amplitude was assigned an experimental weight, W_F, based on counting statistics using a weighting scheme which has been previously described (van der Helm & Poling, 1976).

Table 1. *Crystallographic data*

Formula: $C_{20}H_{17}O_2P$
M_r = 320·31
Space group: $P2_1/n$

Unit-cell dimensions at 296 ± 1 K*

a = 11·6512 (5) Å	V = 1657·9 Å^3
b = 12·1150 (3)	Z = 4
c = 11·7471 (4)	D_{calc} = 1·283 Mg m^{-3}
β = 90·90 (1)°	D_{obs} = 1·292

* Determined from the 2θ values of 58 reflections distributed throughout reciprocal space.

Structure determination and refinement

The position of the P atom was obtained from the three Harker peaks of a sharpened Patterson synthesis. Further analysis of the Patterson map revealed the positions of the 22 C and O atoms as derived from the phosphorus–light-atom vectors. After several cycles of block-diagonal least-squares refinement, all P, C and O atoms were given anisotropic thermal parameters. When the anisotropic model converged, a difference Fourier map was calculated from which the positions of

Table 2. *Fractional coordinates* (× 10^5) *for* P, C *and* O *atoms*

Standard deviations are given in parentheses.

	x	*y*	*z*
C(1)	40824 (18)	11685 (16)	6485 (15)
C(2)	52028 (18)	14778 (18)	8815 (18)
C(3)	54794 (17)	20170 (18)	18836 (19)
C(4)	46297 (15)	22299 (17)	26582 (16)
C(4a)	34950 (14)	19125 (13)	24318 (13)
P(5)	24577 (3)	22150 (3)	34947 (3)
C(5a)	12596 (13)	13692 (13)	31037 (13)
C(6)	4116 (15)	12033 (16)	39160 (15)
C(7)	−5655 (16)	6055 (19)	36518 (18)
C(8)	−6987 (17)	1650 (18)	25807 (19)
C(9)	1375 (17)	3126 (16)	17732 (16)
C(9a)	11332 (14)	9179 (13)	20146 (13)
C(10)	19698 (15)	11170 (13)	10514 (13)
C(10a)	32047 (14)	13805 (13)	14137 (13)
C(11)	15243 (19)	21006 (17)	3432 (17)
C(12)	30438 (13)	16417 (14)	47959 (13)
C(13)	33018 (16)	23208 (16)	57137 (14)
C(14)	37861 (18)	18810 (19)	67036 (16)
C(15)	40173 (18)	7729 (19)	67730 (16)
C(16)	37587 (20)	900 (18)	58688 (18)
C(17)	32740 (17)	5190 (16)	48800 (15)
O(5)	21804 (10)	34070 (10)	36209 (10)
O(10)	19595 (12)	1987 (11)	2942 (10)

Table 3. *Fractional coordinates* (× 10^3) *and isotropic thermal parameters* (Å^2) *for* H *atoms*

Estimated standard deviations are given in parentheses.

	x	*y*	*z*	*B*
H(1)	388 (2)	80 (2)	−6 (2)	5·7 (5)
H(2)	579 (2)	134 (2)	34 (2)	6·2 (5)
H(3)	628 (2)	226 (2)	207 (2)	5·7 (5)
H(4)	481 (2)	263 (2)	336 (2)	5·4 (5)
H(6)	51 (2)	154 (2)	466 (2)	4·6 (4)
H(7)	−111 (2)	50 (2)	424 (2)	5·9 (5)
H(8)	−135 (2)	−27 (2)	233 (2)	5·8 (5)
H(9)	5 (2)	−2 (2)	100 (2)	6·5 (5)
H(13)	317 (2)	311 (2)	566 (2)	4·6 (4)
H(14)	395 (2)	236 (2)	734 (2)	6·8 (6)
H(15)	435 (2)	47 (2)	748 (2)	6·7 (5)
H(16)	394 (2)	−75 (2)	591 (2)	8·7 (7)
H(17)	311 (2)	1 (2)	422 (2)	5·5 (5)
H(11)*A*	76 (2)	195 (2)	9 (2)	5·6 (5)
H(11)*B*	203 (2)	222 (2)	−35 (2)	6·6 (6)
H(11)*C*	152 (2)	276 (2)	81 (2)	6·0 (5)
H(10)	225 (2)	−40 (2)	71 (2)	9·1 (7)

all H atoms were located. The least-squares refinement using anisotropic thermal parameters for P, C and O atoms and isotropic thermal parameters for H atoms was terminated when all shifts were less than the corresponding estimated standard deviation. The R value based on final parameters (Tables 2 and 3) is 5·0% for all 3413 data. The standard error in an observation of unit weight, $[\sum w|kF_o - F_c|^2/(m-n)]^{1/2}$, was 1·69 e where w is the experimental weight, m is the number of observations and n is the number of parameters.

All structure factor refinement was done using the block-diagonal least-squares program of Ahmed (1966*a*) in which the quantity $\sum w(|kF_o| - |F_c|)^2$ was minimized. All Fourier maps were calculated using the program of Ahmed (1966*b*). Atomic scattering factors for C and O atoms were taken from *International Tables for X-ray Crystallography* (1962) and those for H atoms from Stewart, Davidson & Simpson (1965). A final difference Fourier map was calculated which showed no peak greater than 0·26 e Å^{-3}. In a structure factor analysis, the average value of $\overline{W_F \Delta F^2}$ did not vary with either $\sin^2\theta$ or $|F_o|$, thus validating the weighting scheme which was used.*

Results and discussion

A stereoview of the title compound (I) is shown in Fig. 1; bond distances and the numbering scheme are in Fig. 2 and bond angles in Fig. 3. The structure consists of a central six-membered ring existing in a flattened boat conformation with two benzo groups attached at the sides to give a folded 'butterfly' conformation. The internal torsion angles for the six-membered heterocycle are P(5)–C(4a) = 15·7, C(4a)–C(10a) = 6·7, C(10a)–C(10) = −29·5, C(10)–C(9a) = 26·8, C(9a)–C(5a) = −1·6, and C(5a)–P(5) = −18·2°, as compared with 60, 0, −60, 60, 0 and −60° for the corresponding torsion angles in the boat conformation of cyclohexane. The pseudo-axial position at the P atom is occupied by the O atom while the pseudo-equatorial position is occupied by the phenyl group. At C(10) the pseudo-axial position is occupied by the methyl group and the pseudo-equatorial position is occupied by the hydroxyl group. This configuration is consistent with the configurations observed for the related phosphine (II) and the phosphonium salt (III). The P–C(4a) and P–C(5a) bond distances are 1·789 and 1·786 Å, respectively, which are shorter than the average value of 1·818 Å for the phosphine (II) and slightly larger than the average value of 1·776 Å reported for the phosphonium salt (III).

Fig. 4 provides a comparison of the fold angle in compounds (I), (II) and (III). The fold angle (*i.e.* the dihedral angle formed by the least-squares planes passing through each benzene ring) has the values of 161·6, 137·4 and 170·1° for the oxide, phosphine and phosphonium salt respectively. One explanation for the variation in fold angle comes through consideration of the 1,4-axial–axial interaction. The 1-axial position is occupied by a lone pair of electrons in the phosphine, by an O atom in the oxide and by a methyl group in the phosphonium salt. In all three cases, the 4-axial position is occupied by a methyl group. One would

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34128 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

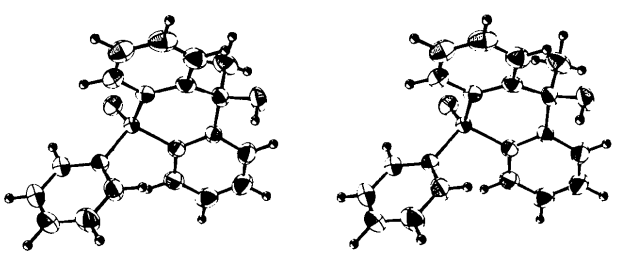

Fig. 1. Stereoview of a single molecule of (I) (Johnson, 1965).

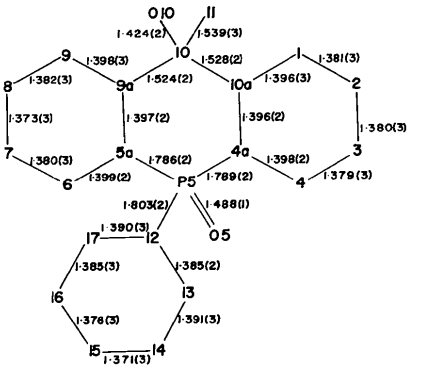

Fig. 2. Bond distances (Å) for (I).

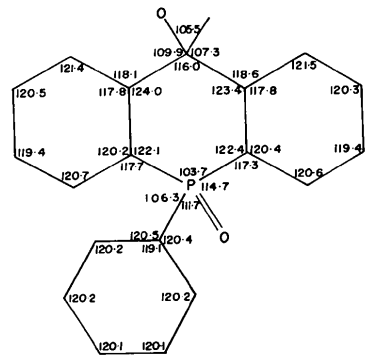

Fig. 3. Bond angles (°) for (I). Standard deviations are between 0·07° and 0·20°. Additional bond angles are O(5)–P(5)–C(5a) = 114·4, C(4a)–P(5)–C(12) = 105·2, C(9a)–C(10)–C(11) = 108·0 and C(10a)–C(10)–O(10) = 109·6°.

expect the repulsion to increase as the size of the substituent increases at the 1-axial position thus giving an order of (II), (I), (III) in terms of increasing 1,4-axial–axial repulsion. To minimize the repulsion, the axial substituents at positions 1 and 4 move apart; this is accompanied by a corresponding flattening of the molecule and, therefore, an increase in fold angle. Alternative explanations might be based on consideration of the hybridization of the P atom. In the phosphine (II) one expects more *p* character in the σ bonds than in the phosphine oxide (I); this would result in longer P—C bonds and a smaller value for the bond angle C(4a)—P—C(5a), as is observed. The smallest P—C distances and largest bond angle are observed for the phosphonium salt (III). It is clear from the comparison in Table 4 that smaller P—C distances correspond to a larger C(4a)—P—C(5a) bond angle, a larger fold angle and a more flattened boat conformation for the central ring. All P—C distances in the three compounds involve sp^2-hybridized C atoms. Table 4 also shows that the P—C(phenyl) distance in all three compounds is always slightly longer than the P—C distances in the same molecule in the tricyclic system, but that it still follows the order (II), (I), (III) in decreasing length. This lengthening is most likely caused by steric hindrances, while the consistency in order argues in favor of a hybridization effect for the P as being the cause of the systematic differences observed for the three compounds. One cannot eliminate the influence of packing forces in determining, to some extent, the fold angle in systems of this type, as can be seen from the observation that this angle for the two independent molecules of *N*-isopropylphenothiazine differs by 10° (Chu & van der Helm, 1976) and 7·4° for the two molecules of trifluopromazine (Phelps & Cordes, 1974). The possible existence of a double energy minimum in these cases cannot be eliminated, but seems unlikely. An experiment to evaluate the influence of temperature was performed for the phosphine derivative (II) by taking the diffraction data at 138 K. The fold angle changed by only 1° to 136·3°.

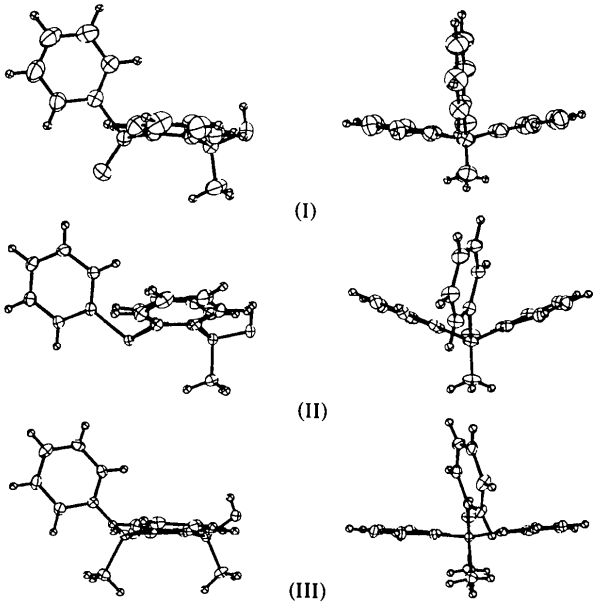

Fig. 4. Side views (left) illustrating the 1,4-axial–axial interaction and end views (right) illustrating the fold angles for (I), (II) and (III).

Table 4. *Comparison of the geometries of* 5,10-*dihydro*-10-*methyl*-5-*phenylacridophosphin*-10-*ol* (II) (*Chen et al.*, 1977), 5,10-*dihydro*-10-*methyl*-5-*phenylacridophosphin*-10-*ol* 5-*oxide* (I) (*present structure*) *and* 5,10-*dihydro*-10-*hydroxy*-5,10-*dimethyl*-5-*phenylacridophosphonium iodide* (III) (*Wu et al.*, 1977)

	(II)	(I)	(III)
P—C(4a)	1·816 Å	1·789 (2) Å	1·777 Å
P—C(5a)	1·820	1·786 (2)	1·775
P—C(Ph)	1·829	1·803	1·795
C(4a)—P—C(5a)	98·0°	103·7°	106·2°
α*	137·4	161·6	170·1
T(C4a—P)†	−35	−16‡	−12
T(P—C5a)†	38	18	8
T(5a—9a)†	−2	2	6
T(9a—10)†	−44	−27	−18
T(10—10a)†	47	30	14
T(10a—4a)†	4	−7	2

* The fold angle is the angle between the two benzo groups of the tricyclic system. Estimated standard deviations are less than 0·5°.

† Endocyclic torsion angles of the heterocyclic ring. Calculated standard deviations are less than 0·6° for (III) and less than 0·3° for (I) and (II).

‡ The crystal structure is a racemic mixture, and the angles given are for the centrosymmetrically related molecule with respect to the coordinates in Table 2 for convenience in the comparison.

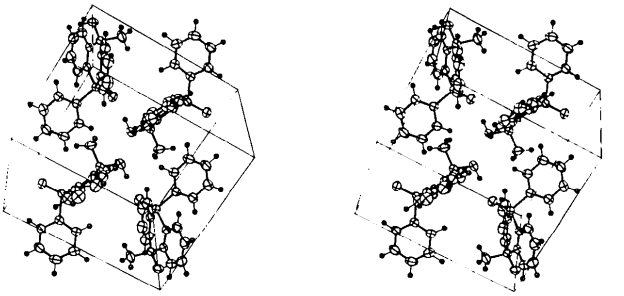

Fig. 5. Stereoview of the crystal packing of (I) (Johnson, 1965).

The crystal structure of (I) is represented by an *ORTEP* drawing in Fig. 5. The structure is stabilized by the formation of strong hydrogen bonds between molecules related by a twofold screw axis. The hydrogen-bond dimensions are O(5)···O(10) = 2·702, O(5)···H(10) = 1·777, O(10)—H(10) = 0·927 Å and ∠O(5)···H(10)—O(10) = 175·4° [where O(10) and H(10) are transformed by $\frac{1}{2}-x, \frac{1}{2}+y, 1-z$].

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Structural Studies of Substituted 6,7-Benzomorphan Compounds. II. Absolute Configurations of (−)-2-Cyclobutylmethyl-5-ethyl-2′-hydroxy-9,9-dimethyl-6,7-benzomorphan Hydrobromide (NCBME) and (−)-5-Ethyl-2′-hydroxy-2,9,9-trimethyl-6,7-benzomorphan Hydrobromide Dihydrate (NME)

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Abstract

NCBME, $C_{21}H_{32}NO.Br$, crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 11{\cdot}379$ (1), $b = 15{\cdot}314$ (1), $c = 11{\cdot}657$ (1) Å and $Z = 4$. The structure was solved from a Patterson synthesis and refined to $R = 0{\cdot}036$ for 1808 independent reflections. NME, $C_{17}H_{26}NO.Br.2H_2O$, has orthorhombic symmetry, $P2_12_12_1$, with $a = 7{\cdot}146$ (1), $b = 12{\cdot}867$ (1), $c = 19{\cdot}899$ (1) Å and $Z = 4$. The structure was solved from a Patterson synthesis and refined to $R = 0{\cdot}039$ for 1561 independent reflections. The absolute configuration of the two compounds was determined by coordinate inversion. Hydrogen bonds between Br, O and N atoms link the molecules in the crystal. In NME an extensive network of hydrogen bonds is built up by the presence of the two water molecules.

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Introduction

The title structures were solved as part of a study on the structure–activity relationship in the 6,7-benzomorphan series. (−)-2-Cyclobutylmethyl-5-ethyl-2′-hydroxy-9,9-dimethyl-6,7-benzomorphan hydrobromide (US Patent 3764606, 1970), hereafter abbreviated as NCBME,† appears to be an active agonist/antagonist of the narcotic analgesics, whilst (−)-5-ethyl-2′-hydroxy-2,9,9-trimethyl-6,7-benzomorphan hydrobromide dihydrate, abbreviated as NME,† is an active morphinomimetic, with about 20 times the analgesic potency of morphine, and having only weak

† *Chemical Abstracts* name for NCBME: (−)-3-cyclobutylmethyl-6-ethyl-1,2,3,4,5,6-hexahydro-11,11-dimethyl-2,6-methano-[3]-benzazocin-8-ol hydrobromide; for NME: (−)-6-ethyl-1,2,3,4,5,6-hexahydro-3,11,11-trimethyl-2,6-methano-[3]-benzazocin-8-ol hydrobromide dihydrate.

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