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Structures of Isomeric 10b,10c-*cis*- and 10b,10c-*trans*-3a,5a,8a,10a-Tetraazaperhydropyrene

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Abstract

10b,10c-*cis*-3a,5a,8a,10a-Tetraazaperhydropyrene, $C_{12}H_{22}N_4$ (*cis*-PTAP), M_r = 222·32, is tetragonal, space group $I\bar{4}2d$, with Z = 8, a = 17·176 (4), c = 8·447 (1) Å, V = 2492·0 (7) Å^3, D_x = 1·185 Mg m^{-3}, μ(Cu $K\alpha$) = 0·502 mm^{-1}, F(000) = 976. Two independent intensity collections were averaged. Of the 637 independent reflections 536 had $I < 2\sigma_I$ and were used for the refinement. 10b,10c-*trans*-3a,5a,8a,10a-Tetraazaperhydropyrene, $C_{12}H_{22}N_4$ (*trans*-PTAP), is monoclinic, space group $P2_1/b$, with $Z = 2$, a = 5·372 (1), b = 8·015 (2), c = 14·574 (4) Å, γ = 100·78 (2)°, V = 616·4 (3) Å^3, D_x = 1·197 Mg m^{-3}, μ(Cu $K\alpha$) = 0·506 mm^{-1}, F(000) = 244. Out of a total of 1069 measured reflections, 706 with $I > 2\sigma_I$ were used in the refinement. Both structures were solved by direct methods and refined by the least-squares full-matrix procedure. The final reliability factors were: for *trans*-PTAP R = 0·064 (R_w = 0·048, $w = 1/\sigma_F^2$), and for *cis*-PTAP R = 0·068 (R_w = 0·061, $w = 1/\sigma_F^2$). Both isomers consist of fused systems of two piperazine and two hexahydropyrimidine rings with all the rings in chair conformations. The molecular point-group symmetries are exactly C_2 for *cis*-PTAP and approximately C_{2h} for *trans*-PTAP.

Introduction

cis-PTAP substituted by methyl and/or phenyl groups has been the subject of several X-ray diffraction investigations [3,8-dimethyl-1,6-diphenyl-*cis*-PTAP (Me_2-Ph_2-PTAP) (Caulkett, Greatbanks, Turner & Jarvis, 1977, 1978); 1,6-dimethyl-*cis*-PTAP (Me_2-PTAP) (Krajewski, Urbańczyk-Lipkowska, Bleidelis & Ķemme, 1977); 1,3,3,6,8,8-hexamethyl-*cis*-PTAP (Me_{gem} remote)* (Me_6-PTAP-rem) (Alcock, Moore & Mok, 1980); 1,1,3,6,6,8-hexamethyl-*cis*-PTAP (Me_{gem} close) (Me_6-PTAP-cls) (Alcock *et al.*, 1980; Gluziński, Krajewski & Urbańczyk-Lipkowska, 1980)]. These compounds appear to consist of two fused pairs of piperazine and hexahydropyrimidine rings. The rings are all in chair conformations and form folded ring systems with a twofold symmetry axis perpendicular to the 10b,10c C—C bridge (Fig. 1*b*). However, the ring systems of the molecules always deviate slightly from exact C_2 symmetry, possibly due to the asymmetric substitution.

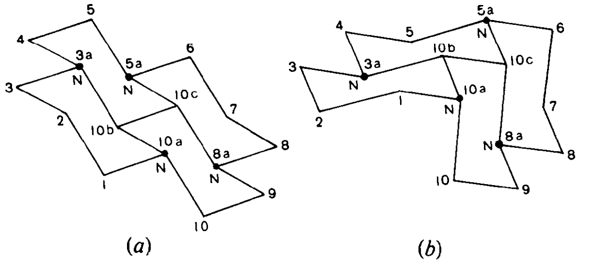

Fig. 1. Sterochemical formulae of (*a*) *trans*-PTAP and (*b*) *cis*-PTAP with conventional atomic numbering.

For the analogous *trans*-PTAP systems (Fig. 1*a*), neither chemical nor crystallographic data were available in the literature until now.

In order to investigate the unperturbed ring conformations in PTAP, an X-ray structural analysis of unsubstituted *cis* (Choiński, 1974; Choiński & Koliński, 1980; Weisman, Ho & Johnson, 1980) and *trans* (Zbieć, 1980) isomers of PTAP has been performed. It was hoped that these compounds would crystallize in space groups in which the molecular symmetry elements coincide with the crystallographic ones.

Experimental

Well shaped crystals of *trans*-PTAP (m.p. 403–405 K from *n*-heptane, dimensions 0·4 × 0·3 × 0·27 mm) and *cis*-PTAP (m.p. 356–357 K from *n*-hexane, dimensions 0·28 × 0·27 × 0·25 mm) were selected for the X-ray

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* The positions 1 and 3 are not equivalent and should be distinguished. Since it was not foreseen in IUPAC nomenclature, in further discussion the position at the folding of the molecule will be called 'close' (cls), the other 'remote' (rem).

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diffraction studies. The intensities ($2\theta_{\max} = 150°$) were collected on a single-crystal automatic diffractometer (Syntex $P2_1$) using in both cases Cu $K\alpha$ radiation ($\lambda = 1\cdot54178$ Å) and the $\omega/2\theta$ scan mode. The cell constants were refined from 20 reflections using the XTL system. Lorentz and polarization corrections were applied to all intensities but no correction for absorption was made. Crystallographic data are given in the *Abstract*.

trans-PTAP

Of the total of 1069 reflections, 706 had $I > 2\sigma_I$ and were used in further refinements. The monoclinic space group $P2_1/b$ was clearly defined by the systematic absences. The number of molecules ($Z = 2$) in a unit cell implies, as expected, that the molecule (point group C_{2h}) could be located at crystallographic symmetry centers. The structure was solved by direct methods using the *SHELX* program (Sheldrick, 1976).

The atomic parameters of the non-H atoms were then refined by the full-matrix least-squares procedure (program *CRYLSQ* in the XRAY system; Stewart, Kundell & Baldwin, 1976), initially with isotropic and then anisotropic thermal parameters using the $1/\sigma_F^2$ weighting scheme where the σ_F's were derived from counting statistics. The positions of all H atoms were calculated (program *XANADU*; Roberts & Sheldrick, 1975) and refined together with the remaining atomic parameters of the molecule. The isotropic temperature factors for H atoms were assumed to be one unit higher than the $B_{\rm eq}$ of the associated non-hydrogen atoms and held fixed during the refinement. The final reliability value was $R = 0\cdot064$ ($R_w = 0\cdot048$) and the shift/error value was below 0·02.

cis-PTAP

The number of reflections initially measured was relatively small, so it was decided to repeat the collection with another crystal of similar size and then average the data. The averaged set of data consisted of 637 independent reflections, 536 of which had $I > 2\sigma_I$ (366 of these were measured twice).

The observed restriction $h + k + l = 2n$ and the metric relation $a = b$ indicate $I4$ symmetry. The systematic absence (hhl, $2h + l \neq 4n$) limits the choice of tetragonal space groups significantly. The number of molecules in a unit cell ($Z = 8$) suggested that the molecules may lie on some twofold crystal axes, since the twofold axis is expected to be the only symmetry element in the molecule (point group C_2), suggesting space groups $I4_1cd$ or $I\bar{4}2d$. Attempts to solve the structure by direct methods (program *MULTAN* 76; Main, Woolfson, Lessinger, Germain & Declercq, 1974) failed in $I4_1cd$ and succeeded in $I\bar{4}2d$.

Refinement of the atomic parameters in $I\bar{4}2d$ was performed in the same way as for *trans*-PTAP, except that the positional H-atom parameters could not be refined together with the whole parameter set, because the number of low-angle reflections was too small. They were, therefore, refined separately with a damping factor of 0·2. The final reliability value was $R = 0\cdot068$ ($R_w = 0\cdot061$) with a shift/error value of 0·01.

The refined positional parameters for both PTAP isomers are presented in Table 1.*

Discussion

Parallel projections (*ORTEP*; Johnson, 1965) of the two isomeric molecules with the atomic labelling are shown in Fig. 2. Tables 2 and 3 give the intramolecular bond lengths and angles for both isomers. Examination of these values does not reveal any peculiarities.

The *trans*-PTAP molecules have approximate C_{2h} point-group symmetry, but the mirror plane and the

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* Lists of structure factors, anisotropic thermal parameters, torsion angles and data involving H-atoms for both *cis* and *trans* isomers have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38016 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates* (×10⁴) *and equivalent isotropic thermal parameters* (Å²), *with e.s.d.'s in parentheses*

$B_{\rm eq} = 8\pi^2(U_1U_2U_3)^{1/3}$; where U_i are the eigenvalues of the U_{ij} matrix.

	cis-PTAP				*trans*-PTAP			
	x	y	z	$B_{\rm eq}$	x	y	z	$B_{\rm eq}$
N(1)	8568 (2)	4198 (2)	8450 (6)	4·1 (2)	2371 (6)	1716 (4)	543 (2)	3·6 (2)
C(2)	8606 (3)	3538 (3)	7347 (7)	4·5 (3)	3198 (9)	2646 (6)	300 (3)	4·5 (3)
C(3)	7941 (3)	3589 (3)	6208 (6)	4·9 (2)	3394 (9)	1421 (6)	1063 (3)	4·2 (2)
N(4)	7211 (2)	3560 (2)	7037 (4)	3·6 (2)	920 (6)	329 (4)	1229 (3)	3·6 (2)
C(5)	6548 (4)	3607 (3)	5885 (6)	5·8 (3)	1108 (9)	−829 (7)	1989 (3)	4·5 (2)
C(6)	5771 (3)	3608 (4)	6749 (9)	6·6 (4)	−1428 (10)	−1927 (7)	2172 (3)	4·6 (3)
C(7)	5768 (3)	4248 (3)	8008 (9)	5·9 (3)	−2299 (9)	−2910 (6)	1298 (6)	4·6 (3)
C(8)	7163 (2)	4210 (2)	8166 (5)	3·4 (2)	103 (7)	−631 (5)	388 (3)	3·2 (2)

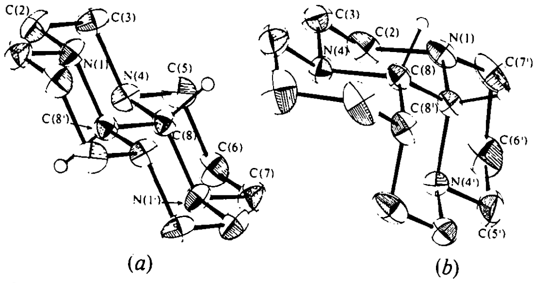

Fig. 2. Conformations of the PTAP isomers. Thermal ellipsoids are set to the 40% probability level. Geminal H atoms are not shown. (*a*) *trans*-PTAP; (*b*) *cis*-PTAP.

Table 2. *Bond lengths* (Å) *with e.s.d.'s in parentheses*

	cis-PTAP	*trans*-PTAP
N(1)–C(2)	1·469 (7)	1·463 (6)
C(2)–C(3)	1·496 (7)	1·500 (7)
C(3)–N(4)	1·437 (6)	1·469 (5)
N(4)–C(5)	1·501 (7)	1·461 (6)
C(5)–C(6)	1·521 (9)	1·501 (7)
C(6)–C(7)	1·529 (9)	1·524 (7)
C(7)–N(1^{i})	1·443 (7)	1·464 (6)
N(1)–C(8^{i})	1·461 (6)	1·463 (5)
N(4)–C(8)	1·471 (5)	1·470 (5)
C(8)–C(8^{i})	1·520 (6)	1·534 (6)

Symmetry code: for *cis*-PTAP (i) $\frac{3}{2}-x, y, \frac{7}{4}-z$; for *trans*-PTAP (i) $-x, -y, -z$.

Table 3. *Bond angles* (°) *with e.s.d.'s in parentheses*

	cis-PTAP	*trans*-PTAP
C(2)–N(1)–C(7^{i})	113·4 (4)	109·9 (3)
C(2)–N(1)–C(8^{i})	111·9 (3)	109·2 (3)
C(7^{i})–N(1)–C(8^{i})	111·5 (4)	111·9 (3)
N(1)–C(2)–C(3)	109·2 (4)	109·9 (4)
C(2)–C(3)–N(4)	110·5 (4)	110·2 (4)
C(3)–N(4)–C(5)	110·1 (4)	110·0 (3)
C(3)–N(4)–C(8)	109·8 (3)	108·8 (3)
C(5)–N(4)–C(8)	109·7 (3)	110·5 (3)
N(4)–C(5)–C(6)	110·8 (4)	110·1 (3)
C(5)–C(6)–C(7)	109·7 (5)	108·2 (4)
C(6)–C(7)–N(1^{i})	112·3 (4)	109·5 (4)
N(1^{i})–C(8)–N(4)	111·7 (3)	109·3 (3)
N(1^{i})–C(8)–C(8^{i})	108·8 (4)	109·7 (3)
N(4)–C(8)–C(8^{i})	112·2 (3)	108·7 (3)

Symmetry code: for *cis*-PTAP (i) $\frac{3}{2}-x, y, \frac{7}{4}-z$; for *trans*-PTAP (i) $-x, -y, -z$.

twofold axis are in this case non-crystallographic. The calculation of the equations for the plane and the axis by least-squares methods (*PLALIN*; Nardelli, Musatti, Domiano & Andreetti, 1978) indicates that the deviations from C_{2h} symmetry for all the non-H atom positions in the molecule are within their double e.s.d. values.

The *cis*-PTAP molecule is observed with exact C_2 point-group symmetry. As in other derivatives of *cis*-PTAP already investigated, four main least-squares planes may be distinguished in this molecule: (1) through C(7), N(1^{i}), C(8), C(8^{i}), N(1) and C(7^{i}); (2) C(2), C(3), N(4), C(5), C(6) and their C_2 symmetrical equivalents; (3) N(1), C(2), N(4), C(8), C(6) and C(7); (4) as symmetrical to (3) by C_2 symmetry (the symmetry operation here is $\frac{3}{2}-x, y, \frac{7}{4}-z$). Planes (1) and (2) are parallel and perpendicular to the twofold axis with the distance between them 1·102 (15) Å. Planes (3) and (4) form a dihedral angle of 81·7 (1)°.

However, the atoms defining both parallel planes deviate significantly from these planes. The atoms belonging to the 'backbone' of the molecule [plane (1)] form a flat saddle shape (Fig. 3*a*), the outer C atoms deviating 'upwards' by 0·050 (5) Å from plane (1), whereas the N atoms as well as the C atoms of the central bridge are 'below' plane (1).

An examination of several already known structures of substituted *cis*-PTAP derivatives reveals features very similar to those above, but even more distinctly (Fig. 3*b*,*c*,*d*,*e*). It may be seen that the presence of substituents at the outer C atoms of the 'backbone' increases the saddle conformation significantly. Additionally, the presence of an axial substituent at one end of the 'backbone' (asymmetric substitution) causes the specific deformation of the central C–C bridge. The C atom lying closer with respect to the axial substituent approximates to the least-squares plane (1) and even (as in Me_2-Ph_2-PTAP) may be found on the other side of that plane (Fig. 3*c*).

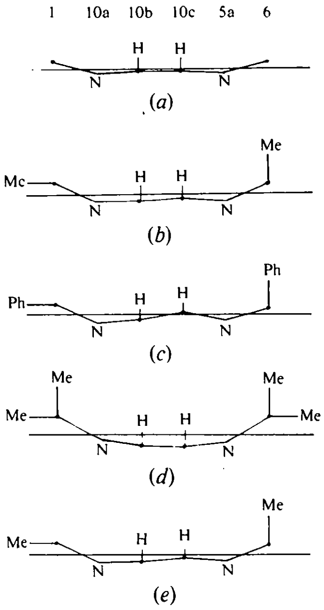

Fig. 3. The shapes of the 'backbone' for *cis*-PTAP derivatives. The horizontal lines are the traces of the least-squares planes defined by six atoms belonging to the 'backbones'. The numbers at the top of the figure refer to the IUPAC atom numbering. The vertical deviations of atoms are expanded approximately three times with respect to the horizontal scale. (*a*) *cis*-PTAP; (*b*) Me_6-PTAP-rem; (*c*) Me_2-Ph_2-PTAP; (*d*) Me_6-PTAP-cls; (*e*) Me_2-PTAP.

All the piperazine and hexahydropyrimidine rings of both isomers presently investigated adopt chair conformations. This may be proved by considering the torsion angles occurring in the rings.* The calculated asymmetry parameters (Duax & Norton, 1975) for these rings (*RING*; Párkányi, 1979) reveal small deviations $[(\Delta C_2)_{\max} = 6\cdot6\,(5)^\circ,\ (\Delta C_s)_{\max} = 5\cdot0\,(5)^\circ]$ from the ideal chair conformation. This may be partly caused by the presence of N hetero-atoms in the rings. The deviations are larger in the case of *cis*-PTAP than in *trans*-PTAP. The presence of methyl and/or phenyl substituents at the hexahydropyrimidine rings in the above known structures seems neither to influence the chair distortions in some regular way nor to increase the calculated asymmetry parameters significantly.

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* See deposition footnote.

References

ALCOCK, N. W., MOORE, P. & MOK, K. F. (1980). *J. Chem. Soc. Perkin Trans.* 2, pp. 1186–1190.

CAULKETT, P. W. R., GREATBANKS, D., TURNER, R. W. & JARVIS, J. A. J. (1977). *J. Chem. Soc. Chem. Commun.* pp. 150–151.

CAULKETT, P. W. R., GREATBANKS, D., TURNER, R. W. & JARVIS, J. A. J. (1978). *Heterocycles*, **9**, 1003–1008.

CHOIŃSKI, W. M. (1974). PhD Thesis, Institute of Organic Chemistry, Polish Academy of Sciences, Warszawa, Poland.

CHOIŃSKI, W. M. & KOLIŃSKI, R. A. (1980). Polish patent No. 101 075; *Chem. Abstr.* **92**, 94444x.

DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*, Vol. 1, pp. 18–19. New York: Plenum.

GLUZIŃSKI, P., KRAJEWSKI, J. W. & URBAŃCZYK-LIPKOWSKA, Z. (1980). *Acta Cryst.* B**36**, 2182–2184.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

KRAJEWSKI, J. W., URBAŃCZYK-LIPKOWSKA, Z., BLEIDELIS, J. & ĶEMME, A. (1977). *Cryst. Struct. Commun.* **6**, 853–858.

MAIN, P., WOOLFSON, M. M., LESSINGER, L., GERMAIN, G. & DECLERCQ, J. P. (1974). *MULTAN 74. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

NARDELLI, M., MUSATTI, A., DOMIANO, P. & ANDREETTI, G. (1978). *PLALIN*. Program for the calculation of weighted least-squares planes and lines, the angles formed by them, and e.s.d.'s. Univ. of Parma, Italy.

PÁRKÁNYI, L. (1979). *RING*. A program for ring-puckering analysis. Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, Hungary.

ROBERTS, P. & SHELDRICK, G. M. (1975). Program *XANADU*. Univ. of Cambridge, England.

SHELDRICK, G. M. (1976). *SHELX* 76. Program for crystal structure determination. Univ. of Cambridge, England.

STEWART, J. M., KUNDELL, F. A. & BALDWIN, J. C. (1976). The XRAY 76 system. Computer Science Center, Univ. of Maryland, College Park, Maryland.

WEISMAN, G. R., HO, S. C. H. & JOHNSON, V. (1980). *Tetrahedron Lett.* pp. 335–338.

ZBIEĆ, M. A. (1980). PhD Thesis, Institute of Organic Chemistry, Polish Academy of Sciences, Warszawa, Poland.

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The Structure of 4-(2-Chlorodibenz[*b,f*][1,4]oxazepin-11-yl)-1-methyl-1*H*⁺-piperazinium Succinate Monohydrate (Loxapine Succinate Monohydrate)

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Abstract

The X-ray crystal structure of the psychoactive agent loxapine succinate monohydrate has been determined. $C_{18}H_{19}ClN_3O^+.C_4H_5O_4^-.H_2O$ is triclinic, space group $P\bar{1}$, with $a = 9{\cdot}702\,(3)$, $b = 14{\cdot}237\,(4)$, $c = 9{\cdot}436\,(4)$ Å, $\alpha = 92{\cdot}80\,(3)$, $\beta = 115{\cdot}82\,(3)$ and $\gamma = 76{\cdot}89\,(2)^\circ$. The structure was solved by direct methods using *MULTAN* and refined by standard least-squares methods to $R = 0{\cdot}050$ for 2484 reflections with $I > 3\sigma(I)$. The central seven-membered heterocyclic ring is in a boat conformation while the piperazine ring is in the normal chair conformation. The dihedral angle between the planes of the benzene rings is 121°. There are two half-succinate molecules per asymmetric unit,

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