Acta Cryst. (1980). B36, 3150–3153

Bulgarsenine (*R*:*R*)-(+)-Bitartrate: A Pyrrolizidine Alkaloid

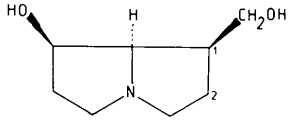
BY HELEN STOECKLI-EVANS

Institut de Chimie de l'Université, avenue de Bellevaux 51, *CH*-2000 *Neuchâtel, Switzerland*

(*Received* 26 *June* 1980; *accepted* 7 *August* 1980)

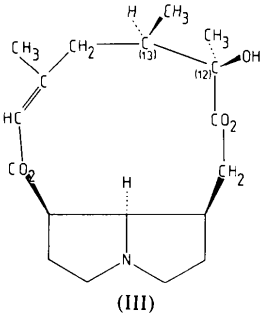
Abstract. $C_{18}H_{28}NO_5^+.C_4H_5O_6^-$, orthorhombic, $P2_12_12_1$, $a = 24{\cdot}59$ (1), $b = 13{\cdot}17$ (1), $c = 7{\cdot}490$ (8) Å, from diffractometer measurements (Mo $K\bar{\alpha}$ radiation), $V = 2425{\cdot}6$ Å^3, $M_r = 486$, $D_m = 1{\cdot}31$ Mg m^{-3}, $Z = 4$, $D_c = 1{\cdot}33$ Mg m^{-3}, μ(Mo $K\bar{\alpha}$) = 0·11 mm^{-1}. The structure was solved by multisolution direct methods and refined by the full-matrix least-squares method to $R = 0{\cdot}087$. The atomic coordinates define the correct absolute configuration for the (*R*:*R*)-(+)-tartaric acid moiety, and hence the absolute configuration of bulgarsenine has been derived. Bulgarsenine, a pyrrolizidine alkaloid derived from platynecine, has a 13-membered macro-ring with the ester carbonyls antiparallel.

Introduction. The present analysis forms part of a structural study of pyrrolizidine alkaloids (PA's) whose structure and/or toxicity is of particular interest (Stoeckli-Evans & Crout, 1976; Stoeckli-Evans, 1979*a*,*b*). Bulgarsenine, a PA derived from platynecine (I), was isolated from *Senecio nemorensis* L. var. *bulgaricus* (Vel.) Stoj. et Stef. (Nghia, Sedmera, Klásek, Boeva, Drjanovska, Dolejě & Šantavý, 1976). On the basis of NMR and MS evidence structure (III) was assigned to it. PA's derived from platynecine (I) are rare, and are not toxic as they do not possess a double bond in the pyrrolizidine nucleus (Mattocks, 1972). Bulgarsenine is the first of this type to be studied by X-ray analysis. It also contains a 13-membered unsaturated macro-ring like doronenine, the retronecine (II) derived analogue of bulgarsenine, whose structure was recently elucidated (Kirfel, Will, Wiedenfeld & Roeder, 1980).



(I) C(1)–C(2) Platynecine

(II) C(1)=C(2) Retronecine



(III)

Small crystals of bulgarsenine tartrate were grown by slow cooling of an ethanol solution. The crystals did not diffract well and data were collected for layers *hk*0–7 and *h*0–8*l* with $\theta_{max} = 21°$ on a Stoe Stadi-2 two-circle diffractometer (graphite-monochromated Mo $K\bar{\alpha}$ radiation). The ω-scan technique was used and the optimum scan width was computed for each reflection (Freeman, Guss, Nockolds, Page & Webster, 1970). The intensities were corrected for Lorentz–polarization effects only. 921 unique reflections [$I > 3\sigma(I)$] were obtained and used in subsequent calculations. The structure was solved by multisolution direct methods using the program *MULTAN* 76 (Main, Lessinger, Woolfson, Germain & Declercq, 1976). Refinement and all other calculations were carried out using the *SHELX* system (Sheldrick, 1976). Complex neutral-atom scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Weighted anisotropic full-matrix least-squares refinement converged at $R = 0{\cdot}087$ for 914 reflections (seven reflections suffering from extinction were removed from the final cycles of refinement) ($R = \sum||F_o| - |F_c||/\sum|F_o|$); $R_w = 0{\cdot}091$ [$R_w = \sum(|F_o| - |F_c||w^{1/2})/\sum(|F_o|w^{1/2})$], $w = 0{\cdot}9826/[\sigma^2(F_o) + 0{\cdot}0072F_o^2]$. In the final cycle the average parameter shift was $\leq 0{\cdot}3$ e.s.d. A final difference synthesis revealed no peaks higher than possible H atoms; no attempt was made to locate these atoms. Final positional parameters are given in Table 1.*

Discussion. Bond distances and angles and their standard deviations are given in Table 2. Within experimental error, the bond distances and angles in the bitartrate ion are normal (Ruble, Hite & Soares, 1976; Hite & Soares, 1973). For bulgarsenine the bond distances and angles, apart from those involving atoms C(1) and C(2), differ little from those observed in other

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35558 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0567-7408/80/123150-04$01.00

Table 1. *Final positional and thermal parameters* ($\times 10^4$) *and their standard deviations*

$$U_{eq} = (U_{11}.U_{22}.U_{33})^{1/3}.$$

	x	y	z	U_{eq} (Å^2)
C(1)	8932 (6)	7201 (13)	5470 (20)	376 (48)
C(2)	9222 (7)	7697 (14)	6983 (22)	483 (50)
C(3)	8861 (7)	7383 (13)	8654 (19)	314 (48)
N(4)	8296 (5)	7135 (10)	7857 (16)	357 (46)
C(5)	7799 (8)	7737 (14)	8560 (24)	526 (50)
C(6)	7529 (7)	8094 (13)	6881 (22)	429 (49)
C(7)	7998 (6)	8317 (12)	5576 (22)	337 (48)
C(8)	8300 (7)	7345 (12)	5850 (19)	345 (48)
C(9)	9111 (7)	7439 (12)	3530 (22)	393 (49)
O(10)	9104 (4)	8541 (9)	3106 (14)	377 (43)
C(11)	9588 (5)	9037 (11)	3041 (20)	133 (46)
C(12)	9523 (7)	10100 (12)	2428 (20)	377 (48)
C(13)	9081 (7)	10692 (13)	3414 (22)	443 (50)
C(14)	9213 (6)	10762 (12)	5387 (20)	325 (48)
C(15)	8784 (7)	11334 (12)	6421 (21)	333 (48)
C(16)	8274 (8)	11009 (13)	6676 (23)	504 (51)
C(17)	8009 (7)	10110 (12)	5958 (22)	363 (49)
O(18)	8285 (4)	9178 (8)	6169 (14)	336 (41)
O(19)	9982 (4)	8661 (9)	3721 (17)	460 (44)
O(20)	7582 (5)	10120 (10)	5210 (18)	618 (46)
C(21)	9375 (8)	10013 (12)	422 (20)	586 (46)
O(22)	10020 (4)	10631 (7)	2634 (15)	475 (38)
C(23)	8989 (6)	11798 (11)	2587 (19)	457 (44)
C(24)	8988 (7)	12370 (11)	7265 (20)	511 (45)
O(30)	9044 (4)	4807 (8)	14016 (13)	453 (41)
O(31)	8177 (3)	4339 (7)	14325 (11)	243 (37)
C(32)	8629 (6)	4515 (11)	13336 (18)	299 (45)
C(33)	8550 (6)	4223 (12)	11379 (17)	314 (44)
O(34)	9010 (4)	4553 (9)	10374 (12)	414 (41)
C(35)	8045 (5)	4807 (10)	10656 (16)	191 (43)
O(36)	8083 (4)	5849 (7)	10937 (12)	306 (38)
C(37)	7986 (5)	4521 (11)	8697 (17)	206 (43)
O(38)	8171 (4)	5085 (7)	7490 (10)	144 (37)
O(39)	7750 (4)	3680 (8)	8368 (12)	361 (40)

Table 2. *Bond distances* (Å) *and angles* (°)

C(1)–C(2)	1·49 (2)	C(13)–C(14)	1·52 (2)
C(1)–C(8)	1·59 (2)	C(13)–C(23)	1·60 (2)
C(1)–C(9)	1·55 (2)	C(14)–C(15)	1·51 (2)
C(2)–C(3)	1·59 (2)	C(15)–C(16)	1·34 (3)
C(3)–N(4)	1·55 (2)	C(15)–C(24)	1·59 (2)
N(4)–C(5)	1·55 (2)	C(16)–C(17)	1·46 (2)
N(4)–C(8)	1·53 (2)	C(17)–O(18)	1·41 (2)
C(5)–C(6)	1·50 (3)	C(17)–O(20)	1·19 (2)
C(6)–C(7)	1·54 (2)	O(30)–C(32)	1·20 (2)
C(7)–C(8)	1·49 (2)	O(31)–C(32)	1·36 (2)
C(7)–O(18)	1·41 (2)	C(32)–C(33)	1·53 (2)
C(9)–O(10)	1·49 (2)	C(33)–O(34)	1·43 (2)
O(10)–C(11)	1·36 (2)	C(33)–C(35)	1·56 (2)
C(11)–C(12)	1·42 (2)	C(35)–O(36)	1·39 (2)
C(11)–O(19)	1·20 (2)	C(35)–C(37)	1·52 (2)
C(12)–C(13)	1·53 (2)	C(37)–O(38)	1·26 (2)
C(12)–C(21)	1·55 (2)	C(37)–O(39)	1·27 (2)
C(12)–O(22)	1·42 (2)		
C(8)–C(1)–C(2)	106·3 (13)	O(22)–C(12)–C(21)	110·2 (12)
C(9)–C(1)–C(2)	119·1 (14)	C(14)–C(13)–C(12)	110·5 (13)
C(9)–C(1)–C(8)	114·9 (12)	C(23)–C(13)–C(12)	112·3 (13)
C(3)–C(2)–C(1)	102·5 (13)	C(23)–C(13)–C(14)	110·7 (13)
N(4)–C(3)–C(2)	104·7 (11)	C(15)–C(14)–C(13)	112·5 (13)
C(5)–N(4)–C(3)	118·0 (12)	C(16)–C(15)–C(14)	124·6 (15)
C(8)–N(4)–C(3)	109·7 (11)	C(24)–C(15)–C(14)	114·4 (13)
C(8)–N(4)–C(5)	104·3 (12)	C(24)–C(15)–C(16)	121·0 (14)
C(6)–C(5)–N(4)	103·0 (13)	C(17)–C(16)–C(15)	128·8 (16)
C(7)–C(6)–C(5)	105·2 (13)	O(18)–C(17)–C(16)	116·8 (14)
C(8)–C(7)–C(6)	97·0 (12)	O(20)–C(17)–C(16)	124·1 (16)
O(18)–C(7)–C(6)	109·2 (13)	O(20)–C(17)–O(18)	119·1 (15)
O(18)–C(7)–C(8)	113·5 (13)	C(17)–O(18)–C(7)	115·1 (12)
N(4)–C(8)–C(1)	99·2 (11)	O(31)–C(32)–O(30)	121·2 (12)
C(7)–C(8)–C(1)	124·2 (14)	C(33)–C(32)–O(30)	126·5 (13)
C(7)–C(8)–N(4)	106·6 (12)	C(33)–C(32)–O(31)	112·1 (12)
O(10)–C(9)–C(1)	113·3 (13)	O(34)–C(33)–C(32)	109·2 (11)
C(11)–O(10)–C(9)	117·8 (11)	C(35)–C(33)–C(32)	108·1 (11)
C(12)–C(11)–O(10)	111·8 (12)	C(35)–C(33)–O(34)	107·3 (11)
O(19)–C(11)–O(10)	119·5 (13)	O(36)–C(35)–C(33)	112·4 (11)
O(19)–C(11)–C(12)	127·4 (14)	C(37)–C(35)–C(33)	106·8 (10)
C(13)–C(12)–C(11)	114·1 (13)	C(37)–C(35)–O(36)	113·3 (10)
C(21)–C(12)–C(11)	104·8 (12)	O(38)–C(37)–C(35)	120·9 (12)
C(21)–C(12)–C(13)	109·8 (13)	O(39)–C(37)–C(35)	116·5 (11)
O(22)–C(12)–C(11)	109·9 (12)	O(39)–C(37)–O(38)	122·7 (11)
O(22)–C(12)–C(13)	108·0 (12)		

Table 3. *Torsion angles in the macrocyclic ring* (°)

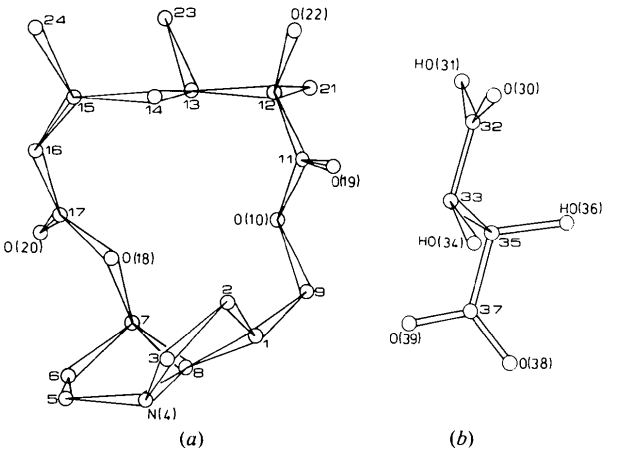
(*A*) Bulgarsenine, (*B*) doronenine.

	A	*B*
C(8)–C(1)–C(9)–O(10)	72·1 (4)	90·2
C(1)–C(9)–O(10)–C(11)	103·9 (5)	92·7
C(9)–O(10)–C(11)–C(12)	174·3 (6)	−175·5
O(10)–C(11)–C(12)–C(13)	49·8 (5)	57·3
C(11)–C(12)–C(13)–C(14)	61·3 (1)	55·7
C(12)–C(13)–C(14)–C(15)	−179·5 (1)	175·0
C(13)–C(14)–C(15)–C(16)	67·0 (2)	67·4
C(14)–C(15)–C(16)–C(17)	−4·5 (1)	3·0
C(15)–C(16)–C(17)–O(18)	50·8 (1)	42·2
C(16)–C(17)–O(18)–C(7)	175·5 (2)	169·6
C(17)–O(18)–C(7)–C(8)	−179·1 (1)	−176·8
O(18)–C(7)–C(8)–C(1)	−42·3 (3)	−39·8
C(7)–C(8)–C(1)–C(9)	−58·0 (2)	−72·6

PA's (Stoeckli-Evans, 1979*a*,*b*). The torsion angles in the macro-ring of bulgarsenine and doronenine are compared in Table 3. The numbering scheme used is apparent from Fig. 1(*a*) and (*b*). Fig. 1(*a*) also shows the configuration at asymmetric centres C(12) and C(13), which are identical to those in doronenine. As the final atomic parameters (Table 1) define the correct (Bijvoet, Peerdeman & van Bommel, 1951; Bijvoet, 1955) absolute configuration (*R*:*R*) for the (+)-tartaric acid moiety, the absolute configuration of bulgarsenine is as shown in Fig. 1(*a*).

The five-membered ring C(1), C(2), C(3), N(4), C(8) and atom C(6) are on opposite sides of the plane defined by atoms N(4), C(5) and C(7). The five-membered ring C(7), C(6), C(5), N(4), C(8) and atom C(2) are on the same side of the plane defined by atoms N(4), C(3) and C(1). Hence the pyrrolizidine nucleus has a mixed *exo–endo* conformation (Bull, Culvenor & Dick, 1968). The *exo* conformation has a puckering angle of 34·3 (4)° between planes defined by atoms C(5), C(6), C(7) and C(5), N(4), C(8). The *endo* conformation has a puckering angle of 156·2 (5)° between planes defined by atoms C(1), C(2), C(3) and C(3), N(4), C(8).

The angle between the least-squares planes defined by atoms C(1), C(8), N(4), C(3) and C(5), N(4), C(8),



(*a*) (*b*)

Fig. 1. A perspective view of the molecule showing the numbering scheme. (*a*) Bulgarsenine, (*b*) (*R*:*R*)-(+)-bitartrate.

C(7) of the pyrrolizidine nucleus is 126·8 (5)° which is similar to the average value of 126° found for retronecine (II) derived PA's (Stoeckli-Evans, 1979*a*,*b*). Within experimental error the ring fusion distance, N(4)–C(8), of 1·53 (2) Å, is close to the average value of 1·51 Å found for retronecine derived PA's.

An interesting feature in bulgarsenine and doronenine is the orientation of the C(9) ester carbonyl group. As in 12- and 14-membered macro-ring PA's (Stoeckli-Evans, 1979*a*; Gainsford, 1980; Eggers & Gainsford, 1979) the C(9) ester carbonyl group is directed above the plane of the macro-ring and antiparallel to the C(7) ester carbonyl group (see Fig. 1*a*). The same conformation of the macro-ring has recently been found for an 11-membered macro-ring PA, trichodesmine (Tashkhodzhaev, Yagudaev & Yunusov, 1979*a*). Only in the 11-membered macro-ring PA's fulvine (Sussman & Wodak, 1973), axillarine (Stoeckli-Evans & Crout, 1976), monocrotaline (Stoeckli-Evans, 1979*b*) and incanine (Tashkhodzhaev, Telezhenetskaya & Yunusov, 1979*b*) is the C(9) ester carbonyl bond directed below the plane of the macro-ring and synparallel to the C(7) ester carbonyl bond.

In bulgarsenine the angle between the planes defined by C(7)–O(18)–C(17)–O(20) and C(9)–O(10)–C(11)–O(19) is 24·7 (4)° compared to 25·2° in doronenine. The intramolecular distance O(10)···O(18) is 3·17 Å, compared to 3·34 Å in doronenine. This difference is explained by the slightly different conformation of the macro-ring, the dihedral angle C(9)–O(10)–C(11)–C(12) being 174·3 (6)° in bulgarsenine and −175·5° in doronenine.

Short inter- and intramolecular distances are given in Table 4. Molecules of bulgarsenine are not hydrogen bonded to symmetry-related molecules but rather are linked to the bitartrate ion principally through atom N(4), with N(4)–O(38) 2·73 Å. The bitartrate ions are linked by hydrogen bonds and form helices about the screw axes perpendicular to the *ab* plane.

Table 4. *Short intra- and intermolecular distances* (Å)

Symmetry code: (i) $\frac{1}{2}-x, -y, \frac{1}{2}+z$; (ii) $-x, \frac{1}{2}+y, \frac{1}{2}-z$.

O(10)–O(18)	3·17 (2)	N(4)–O(36)	2·91 (2)
O(19)–O(22)	2·72 (2)	O(30)–O(22^{ii})	2·83 (1)
O(30)–O(34)	2·75 (1)	O(34)–O(22^{ii})	3·15 (1)
O(34)–O(36)	2·88 (1)	O(31)–O(38)[$z+1$]	2·57 (1)
O(19)–O(34^{ii})	2·83 (2)	O(36)–O(39^{i})	2·81 (1)
N(4)–O(38)	2·73 (2)		

There is a short intramolecular hydrogen bond between the C(12) hydroxyl substituent and the carbonyl oxygen O(19), the distance O(22)···O(19) being 2·72 Å. In doronenine the same distance is shorter, 2·62 Å. Such a variation in this distance has been observed previously in jacobine (Pérez-Salazar, Cano & Garcia-Blanco, 1978) with a distance of 2·71 Å, and parsonsine (Eggers & Gainsford, 1979) with a distance of 2·64 Å.

Torsion angles around the macro-ring differ little in magnitude from those in doronenine, apart from those involving C(1).

The author wishes to thank Dr A. Klásek (Czechoslovakia) for supplying the sample of bulgarsenine tartrate, also Dr D. H. G. Crout (Exeter) for the continued interest he has shown in this work, and finally the Swiss National Science Foundation for financial support.

References

BIJVOET, J. M. (1955). *Endeavour*, pp. 71–77.

BIJVOET, J. M., PEERDEMAN, A. F. & VAN BOMMEL, A. J. (1951). *Nature (London)*, **168**, 271–272.

BULL, L. B., CULVENOR, C. C. J. & DICK, A. T. (1968). *The Pyrrolizidine Alkaloids*. Amsterdam: North-Holland.

EGGERS, N. J. & GAINSFORD, G. J. (1979). *Cryst. Struct. Commun.* **8**, 597–603.

FREEMAN, H. C., GUSS, J. M., NOCKOLDS, C. E., PAGE, R. & WEBSTER, A. (1970). *Acta Cryst.* A**26**, 149–152.

GAINSFORD, G. J. (1980). *Cryst. Struct. Commun.* **9**, 173–180.

HITE, G. & SOARES, J. R. (1973). *Acta Cryst.* B**29**, 2935–2938.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

KIRFEL, A., WILL, G., WIEDENFELD, H. & ROEDER, E. (1980). *Cryst. Struct. Commun.* **9**, 353–361.

MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J.-P. (1976). *MULTAN 76. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MATTOCKS, A. R. (1972). *Phytochemical Ecology*, edited by J. B. HARBORNE, pp. 180–200. New York: Academic Press.

NGHIA, T. H., SEDMERA, P., KLÁSEK, A., BOEVA, A., DRJANOVSKA, L., DOLEJĚ, L. & ŠANTAVÝ, F. (1976). *Collect. Czech. Chem. Commun.* **41**(10), 2952–2963.

PÉREZ-SALAZAR, A., CANO, F. H. & GARCÍA-BLANCO, S. (1978). *Cryst. Struct. Commun.* **7**, 105–109.

RUBLE, J. R., HITE, G. & SOARES, J. R. (1976). *Acta Cryst.* B**32**, 136–140.

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

STOECKLI-EVANS, H. (1979*a*). *Acta Cryst.* B**35**, 2798–2800.

STOECKLI-EVANS, H. (1979*b*). *Acta Cryst.* B**35**, 231–234.

STOECKLI-EVANS, H. & CROUT, D. H. G. (1976). *Helv. Chim. Acta*, **59**, 2168–2178.

SUSSMAN, J. L. & WODAK, S. J. (1973). *Acta Cryst.* B**29**, 2918–2926.

TASHKHODZHAEV, B., TELEZHENETSKAYA, M. V. & YUNOSOV, S. YU. (1979*b*). *Khim. Prir. Soedin.* No. 3, pp. 363–367.

TASHKHODZHAEV, B., YAGUDAEV, M. R. & YUNUSOV, S. YU. (1979*a*). *Khim. Prir. Soedin.* No. 3, pp. 368–373.

Acta Cryst. (1980). B**36**, 3153–3155

Structure of 3α-Bromotropane Hydrobromide Monohydrate*

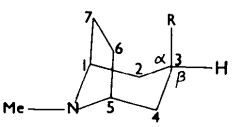
BY T. A. HAMOR AND IN PART N. KINGS†

Department of Chemistry, University of Birmingham, Birmingham B15 2TT, England

(*Received* 2 *July* 1980; *accepted* 11 *August* 1980)

Abstract. $C_8H_{15}BrN^+.Br^-.H_2O$, M_r = 303·0, orthorhombic, *Pbca*, a = 7·01 (1), b = 13·51 (1), c = 23·64 (2) Å, U = 2239 Å^3, Z = 8, D_c = 1·80 Mg m^{-3}, $F(000)$ = 1200, Mo $K\alpha$ radiation, λ = 0·71069 Å, μ(Mo $K\alpha$) = 7·05 mm^{-1}. R = 7·1% for 401 observed counter amplitudes with anisotropic temperature factors for Br and isotropic for the lighter atoms. The presence of the 3α-bromo substituent appears to cause a flattening of the piperidinium ring at C(3), so that the C(3)–Br bond is tilted outwards, away from the C(6)–C(7) bridge.

Introduction. The 3α-substituted tropane ring system (I) occurs in a number of alkaloids, such as atropine and scopolamine which are potent anticholinergic agents. Following earlier studies of 3α-halogenotropanes in solution by dipole-moment and NMR spectroscopic methods (Scheiber, Kraiss & Nádor, 1970) and crystal structure analysis of 3α-chlorotropane (II) (Vooren, Schenk & MacGillavry, 1970), the structure of the hydrobromide of 3α-bromotropane (III) has been determined to assess the effect of a large 3α substituent on the solid-state conformation of the ring system.



(I) R = X (IV) R = OCOPh

(II) R = Cl (V) R = $OCHPh_2$

(III) R = Br

Thin plate-like crystals were obtained from butanone. Cell dimensions and intensities were measured on a Stoe two-circle computer-controlled diffractometer with graphite-monochromated Mo $K\alpha$ radiation. The crystal, 1·0 × 0·4 × 0·05 mm, was mounted about the direction of elongation (*a*). The ω-scan technique was employed with a stepping interval of 0·02° and a step time of 1 s. Backgrounds were measured for 30 s at each end of the scan. The intensities of three 0*kl* reflexions were remeasured after each layer of data collection to monitor the stability of the system. There was some loss of intensity, and appropriate layer scale factors ranging from 1·0 to 1·09 were applied to the intensities.

Reflexions were scanned within the range 0·1 < $\sin\theta/\lambda$ < 0·59 Å^{-1} and 401 having $I > 3\sigma(I)$ were used

* Stereochemistry of Anticholinergic Agents. XIV. Part XIII: Hamor (1980).

† Sixth form pupil at King Edward's School, Birmingham, participating in a joint project.

0567-7408/80/123153-03$01.00