The Crystal and Molecular Structure of 25-Isosolafloridine Hydrochloride

By Bryan M. Gatehouse and Alex J. Jozsa

Department of Chemistry, Monash University, Clayton, Victoria, Australia 3168

The steroidal alkaloid 25-isosolafloridine occurs in the species *Solanum callium*. Its hydrochloride, $C_{27}H_{45}NO_2$.HCl, crystallizes in the space group $P2_1$, with a 6·761 (2), b 30·563 (3), c 6·368 (1) Å, β 94·95 (1)°, Z 2. The structure was refined to R 0·040 for 1544 counter reflections. The cations lie along the direction of the screw axis and are linked by hydrogen bonds to the Cl⁻ ions.

Introduction

The steroidal alkaloid 25-isosolafloridine (Fig. 1) is contained in the leaves, stems and fruit of *Solanum callium* C. T. White *ex* R. J. Henderson (ms). The position of the second hydroxyl group, on C(16), and the configuration at C(25) were uncertain from chemical and spectral data.

The configuration at C(25) is different from that observed in all other C(20) imine *Solanum* steroidal alkaloids. This configuration has, however, been observed in steroidal alkaloids from the *Veratrum* species. Crystals of the free base and the hydrochloride were kindly supplied by G. J. Bird, Dr D. J. Collins and Dr F. W. Eastwood (Bird, Collins, Eastwood, Gatehouse, Jozsa & Swan, 1976).

Experimental

$C_{27}H_{45}NO_2$.HCl crystallizes as large colourless rectangular plates whereas the free base crystallizes as very small colourless rectangular plates, too thin for use; hence the former was chosen for the following work.

The systematic absences (0k0, k odd) indicate $P2_1$ or $P2_1/m$. As $Z = 2$ and the molecule possesses no symmetry, the space group must be $P2_1$. The non-centrosymmetric alternative is also indicated by the optical activity of the compound. The crystal data are summarized in Table 1.

Cell parameters were determined with a standard Philips PW 1100 X-ray diffractometer computer program from 25 high-angle, medium to strong reflections. The intensities of 1616 independent reflections with $3° \leq \theta \leq 54°$ were measured from a crystal $0.025 \times 0.025 \times 0.030$ cm, on the diffractometer with graphite-monochromated Cu $K\alpha$ radiation. Of these, only 1544 with $I \geq 3\sigma(I)$ were used in the subsequent calculations. Three standard reflections, measured at two-hourly intervals, showed no significant variations.

The data were collected by the ω-scan technique, with a symmetric scan range of $\pm 0.5°$ in ω from the calculated scattering angle, at a scan rate of $0.030°$ s⁻¹. The $11\bar{1}$ reflection was intense enough to cause insertion of the first attenuation filter. The intensities were processed with a program written specifically for the PW 1100 diffractometer (Hornstra & Stubbe, 1972). The intensities were calculated from $I = CT - (t_c/t_b)(B_1 + B_2)$ where CT is the total integrated peak count obtained in time t_c, and B_1 and B_2 are background counts, each obtained in time $\frac{1}{2}t_b$. The variance of the intensity was calculated as the sum of the variance due to counting statistics and the square of $0.04I$:

$$\sigma^2(I) = CT + (t_c/t_b)^2(B_1 + B_2) + (0.04I)^2.$$

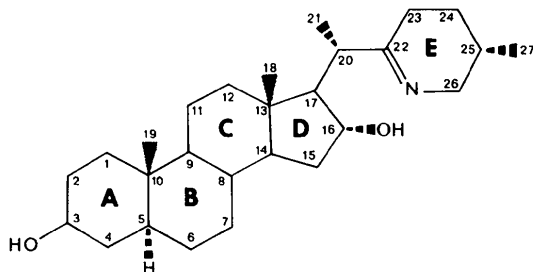The 4% uncertainty was included to allow for other sources of error and to prevent too high a weight being

Fig. 1. Diagram of 25-isosolafloridine showing atom-numbering scheme.

Table 1. *Crystal data*

$C_{27}H_{45}NO_2$.HCl	$M_r = 452·2$
Monoclinic	Space group $P2_1$
$a = 6·761$ (2) Å	$Z = 2$
$b = 30·563$ (3)	Monochromatized copper
$c = 6·368$ (1)	radiation
$\beta = 94·95$ (1)°	$\lambda = 1·5418$ Å
$D_x = 1·12$ (2) g cm⁻³	$\mu = 13·6$ cm⁻¹
$D_c = 1·14$	$F(000) = 496$

given to strong reflections. The values of I and $\sigma(I)$ so obtained were then corrected for Lorentz and polarization effects, but not for extinction or absorption.

The E statistics ($\langle |E^2 - 1| \rangle$ for the largest reflection group was 0·742) and the small number of weak reflections are consistent with the non-centrosymmetric space group.

Structure determination and refinement

The structure was determined with MULTAN (Germain, Main & Woolfson, 1971). Normalized structure factors, E, were calculated from a Wilson plot (Shiono, 1964), and 396 E's >1·22 were used in the phase determination.

An E map, calculated from the phases generated for the set with the highest figure of merit (1·19), clearly showed the whole steroidal nucleus. After two cycles of AFLS refinement* with isotropic thermal parameters and unit weights, all the non-hydrogen atoms were located. The y coordinate of the Cl⁻ ion was fixed in

---

* Accelerated full-matrix least-squares is used in place of a blocked-diagonal matrix in the SHELX program (Sheldrick, 1976).

Table 2. *Positional parameters* ($\times 10^4$) *for the non-hydrogen atoms*

	x	y	z		x	y	z
Cl	4845 (2)	6070	7663 (2)	C(16)	6325 (7)	6886 (1)	2486 (7)
C(1)	6386 (9)	9291 (2)	3355 (11)	C(17)	8012 (6)	7117 (1)	3886 (7)
C(2)	5400 (11)	9748 (2)	3197 (13)	C(18)	5875 (7)	7481 (2)	6435 (7)
C(3)	4019 (10)	9781 (2)	1169 (11)	C(19)	3678 (12)	8936 (2)	5200 (10)
C(4)	2531 (9)	9418 (2)	997 (9)	C(20)	8899 (6)	6804 (2)	5625 (8)
C(5)	3541 (8)	8969 (2)	1210 (8)	C(21)	701 (7)	7004 (2)	6993 (8)
C(6)	2119 (7)	8598 (2)	736 (9)	C(22)	9515 (6)	6379 (1)	4649 (7)
C(7)	3189 (7)	8157 (2)	690 (9)	C(23)	1213 (7)	6368 (2)	3321 (9)
C(8)	4559 (7)	8083 (1)	2689 (7)	C(24)	1338 (8)	5945 (2)	2092 (10)
C(9)	5981 (7)	8469 (2)	3185 (8)	C(25)	1003 (8)	5562 (2)	3473 (9)
C(10)	4862 (8)	8914 (2)	3288 (8)	C(26)	8936 (8)	5592 (2)	4197 (9)
C(11)	7446 (8)	8373 (2)	5114 (9)	C(27)	1215 (9)	5121 (2)	2360 (13)
C(12)	8550 (7)	7935 (2)	4995 (8)	N	8536 (5)	6038 (1)	5014 (6)
C(13)	7093 (6)	7550 (2)	4576 (7)	OC(3)	2975 (7)	184 (1)	1059 (8)
C(14)	5804 (6)	7668 (1)	2527 (7)	OC(16)	7213 (5)	6715 (1)	738 (5)
C(15)	4634 (6)	7237 (1)	1925 (7)				

Table 3. *Hydrogen positional parameters* ($\times 10^3$)

$U = 0{\cdot}05$ except for the starred hydrogens for which $U = 0{\cdot}07$ Å².

	x	y	z		x	y	z
H(1A)	749 (8)	930 (2)	460 (9)	H(18A)*	532 (8)	745 (2)	697 (8)
H(1B)	745 (8)	922 (2)	218 (9)	H(18B)*	682 (8)	745 (2)	758 (8)
H(2A)	445 (8)	978 (2)	437 (9)	H(18C)*	458 (7)	720 (2)	600 (8)
H(2B)	678 (8)	996 (2)	296 (9)	H(19A)*	464 (7)	890 (2)	647 (8)
H(3)	508 (8)	976 (2)	16 (10)	H(19B)*	286 (6)	941 (2)	563 (7)
H(4A)	170 (8)	941 (2)	222 (9)	H(19C)*	312 (7)	876 (2)	542 (8)
H(4B)	190 (8)	941 (2)	963 (9)	H(20)	794 (8)	671 (2)	667 (9)
H(5)	454 (8)	893 (2)	27 (9)	H(21A)*	24 (6)	725 (2)	783 (7)
H(6A)	112 (8)	856 (2)	203 (9)	H(21B)*	147 (7)	678 (2)	798 (7)
H(6B)	114 (8)	868 (2)	928 (9)	H(21C)*	−50 (7)	688 (2)	619 (7)
H(7A)	398 (8)	812 (2)	949 (9)	H(23A)	120 (8)	662 (2)	256 (9)
H(7B)	218 (8)	796 (2)	26 (9)	H(23B)	267 (8)	633 (2)	446 (9)
H(8)	379 (8)	803 (2)	383 (9)	H(24A)	279 (8)	589 (2)	153 (9)
H(9)	674 (8)	847 (2)	200 (9)	H(24B)	34 (8)	595 (2)	85 (9)
H(11A)	845 (8)	859 (2)	522 (9)	H(25)	218 (8)	563 (2)	455 (9)
H(11B)	683 (8)	839 (2)	622 (9)	H(26A)	866 (8)	537 (2)	530 (9)
H(12A)	925 (8)	794 (2)	369 (9)	H(26B)	796 (8)	556 (2)	281 (9)
H(12B)	959 (8)	790 (2)	615 (10)	H(27A)*	28 (7)	511 (2)	113 (8)
H(14)	694 (8)	772 (2)	141 (9)	H(27B)*	107 (7)	486 (2)	333 (8)
H(15A)	429 (8)	725 (2)	33 (9)	H(27C)*	247 (7)	510 (1)	178 (8)
H(15B)	331 (8)	718 (2)	285 (9)	H|N···Cl|*	743 (7)	605 (2)	587 (8)
H(16)	595 (8)	665 (2)	321 (9)	H|OC(3)···Cl|*	630 (8)	542 (2)	877 (9)
H(17)	903 (8)	719 (2)	295 (9)	H|OC(16)···Cl|*	647 (8)	653 (2)	999 (9)

order to define the origin. With all these atoms anisotropic and a counting-statistics weighting scheme, R was 0·084. Several strong reflections which were affected by extinction were removed from the subsequent refinement, and successive difference syntheses revealed all but two of the H atoms. At this stage, with all H atoms having an isotropic temperature factor of $U = 0.05$ Å², refinement gave $R = 0.043$. The last two H atoms were located with the geometrical-constraint–rigid-group refinement capability of *SHELX*. On the last cycle, the isotropic temperature factor on the nine methyl H atoms and the three H atoms involved in hydrogen-bonding was raised to 0·07 Å². The final refinement gave $R = 0.040$ and $R_w = \Sigma w^{1/2}(||F_o| - |F_c||)/\Sigma w^{1/2}|F_o| = 0.043$ ($R_w = 0.045$ including unobserved data). A difference map showed no peak higher than ~0·25 e Å⁻³. Maximum shifts for non-hydrogen atoms in the final cycle were <0·2σ. $|\Sigma w(||F_o| - |F_c||)^2/N|^{1/2}$, where N is the fraction of reflections in the group, showed no significant variation with sin θ, $(F/F_{max})^{1/2}$ or l (slowest moving index). The scattering factors were those of Cromer & Mann (1968) with the anomalous scattering terms from Cromer & Liberman (1970). Tables 2 and 3 list the atomic parameters with their standard deviations.*

Results and discussion

The interatomic distances and angles (Fig. 2) are normal. The average $C(sp^3)$–$C(sp^3)$ length is 1·532 (8) and the range is 1·493 to 1·560 Å. The average C–H length is 1·03 (5); almost all lie within the range 0·95 to 1·05 Å.

For the enantiomorphous configuration, refinement converged to $R = 0.048$ and $RG = |\Sigma w(||F_o| - |F_c||)^2/\Sigma w|F_o|^2|^{1/2} = 0.059$ (RG was 0·053 for the original configuration). Application of Hamilton's R-ratio test (Hamilton, 1965) showed that this difference is highly significant and that the second configuration can be rejected at less than the 0·005 level. This is
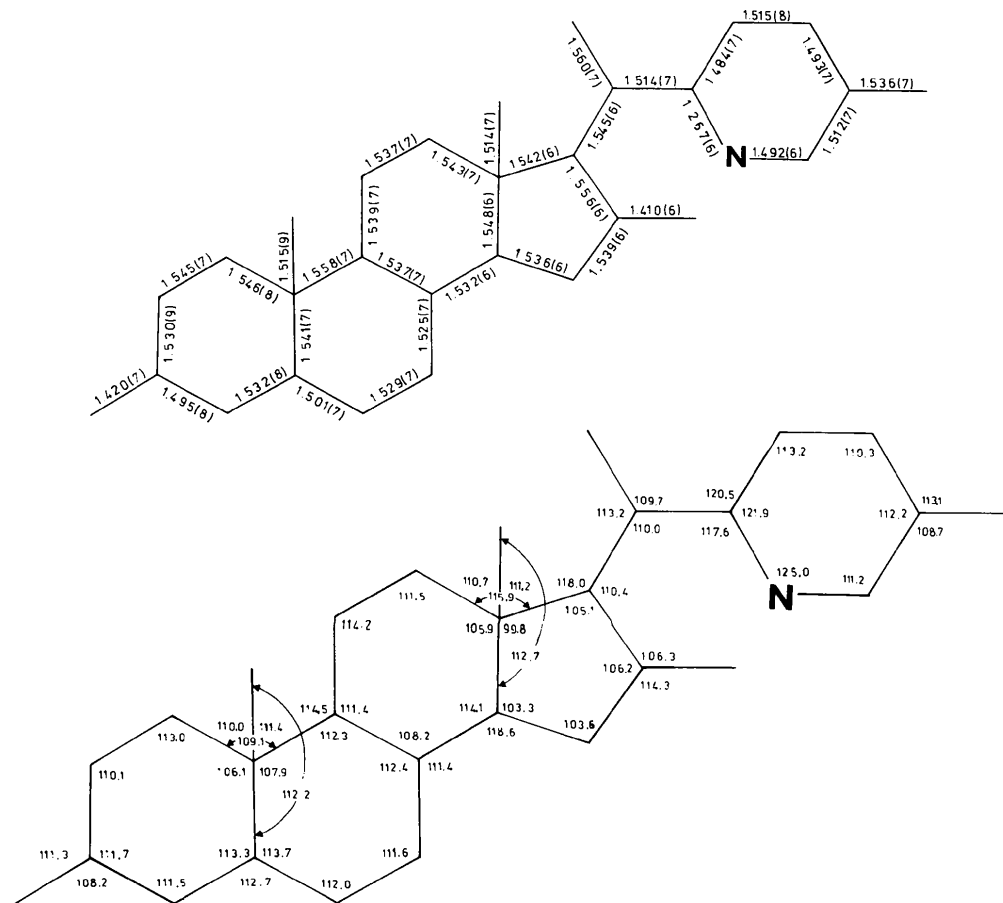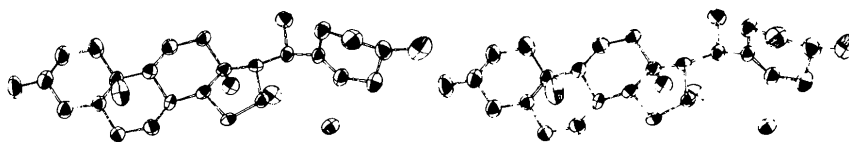
Fig. 2. Bond distances (Å) and angles (°) (e.s.d.'s 0·4 to 0·5°).

Fig. 3. A stereoscopic view of the molecule with 50% probability ellipsoids (*ORTEP*, Johnson, 1965).

supported by the observation that all known steroids isolated from natural sources have the configuration [at C(10) and C(13)] shown in Fig. 3. The ring junctures A/B, B/C and C/D are all *trans*.

The molecules lie approximately parallel to the screw axis and each Cl⁻ ion is linked to three steroid

Table 4. *Hydrogen-bond distances* (Å)

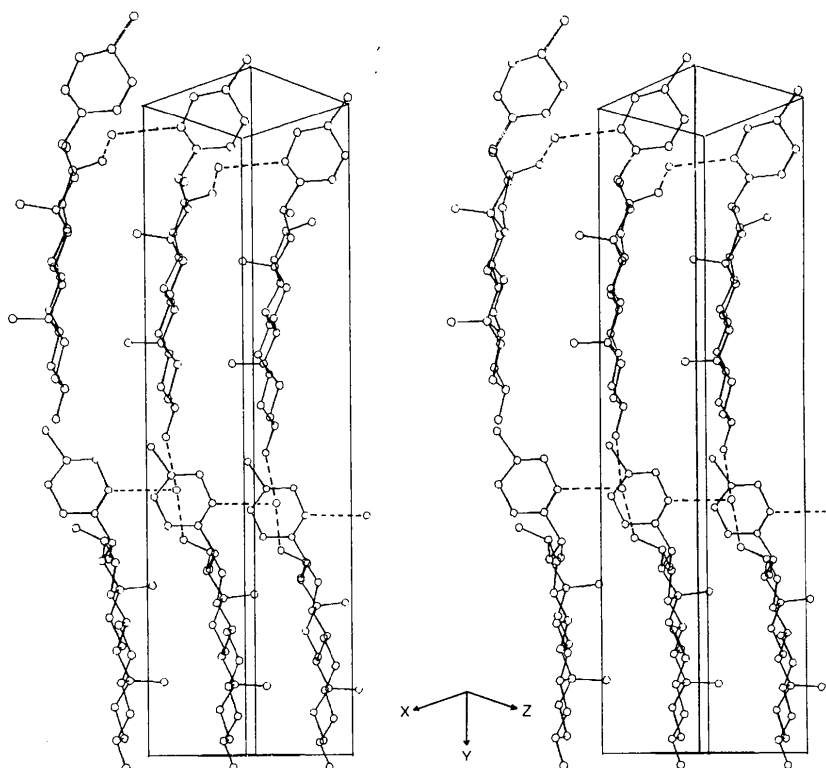| A−B−C	A−B	B−C	A−C
Cl−H−OC(16)	2·33 (5)	0·80 (5)	3·123 (8)
Cl−H−N	2·17 (4)	0·97 (4)	3·134 (8)
Cl−H−OC(3)	2·33 (5)	0·84 (5)	3·156 (8)

Fig. 4. A stereoscopic view showing packing and hydrogen bonds (dashed lines).

Table 5. *Torsion angles in the rings*

φ_{A-B} is the torsion angle about the A−B bond, and has the sense given by Klyne & Prelog (1960).

Ring A Bond	φ_{A-B}	Ring B Bond	φ_{A-B}	Ring C Bond	φ_{A-B}	Ring D Bond	φ_{A-B}	Ring E Bond	φ_{A-B}
C(1)−C(2)	−55·1°	C(10)−C(5)	56·2°	C(11)−C(9)	51·5°	C(13)−C(14)	46·7°	C(22)−N	0·3°
C(2)−C(3)	53·1	C(5)−C(6)	−56·9	C(9)−C(8)	−52·9	C(14)−C(15)	−38·0	N−C(26)	18·5
C(3)−C(4)	−54·1	C(6)−C(7)	53·7	C(8)−C(14)	61·1	C(15)−C(16)	14·0	C(26)−C(25)	−48·6
C(4)−C(5)	57·3	C(7)−C(8)	−53·0	C(14)−C(13)	−61·7	C(16)−C(17)	15·1	C(25)−C(24)	−62·8
C(5)−C(10)	−55·7	C(8)−C(9)	54·7	C(13)−C(12)	56·7	C(17)−C(13)	−37·2	C(24)−C(23)	−45·0
C(10)−C(1)	55·5	C(9)−C(10)	−54·4	C(12)−C(11)	−54·4			C(23)−C(22)	13·7

molecules by hydrogen bonds, so that in each steroid molecule the N and the two O atoms are linked to different Cl⁻ ions (Fig. 4). The hydrogen-bond lengths are shown in Table 4, and are within the sum of the van der Waals radii for H (1·2 Å) and Cl (1·8 Å). The length of the molecule from OC(3) to C(27) is 15·5 Å.

The torsion angles are shown in Table 5. Rings A, B and C have the chair conformation while ring D has almost the ideal half-chair, $C_2(16)$, conformation as shown by the parameters $\Delta = 0·2°$ and $\varphi_m = 46·7°$ (Altona, Geise & Romers, 1968).

References

ALTONA, C., GEISE, H. J. & ROMERS, C. (1968). Tetrahedron, 24, 13–32.

BIRD, G. J., COLLINS, D. J., EASTWOOD, F. W., GATEHOUSE, B. M. K. C., JOZSA, A. J. & SWAN, J. M. (1976). Tetrahedron Lett. 40, 3653–3656.

CROMER, D. T. & LIBERMAN, D. (1970). J. Chem. Phys. 53, 1891–1898.

CROMER, D. T. & MANN, J. B. (1968). Acta Cryst. A24, 321–324.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). Acta Cryst. A27, 368–376.

HAMILTON, W. C. (1965). Acta Cryst. 18, 502–510.

HORNSTRA, J. & STUBBE, B. (1972). PW 1100 Data Processing Program. Philips Research Laboratories, Eindhoven, Holland.

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

KLYNE, W. & PRELOG, V. (1960). Experientia, 16, 521–523.

SHELDRICK, G. M. (1976). SHELX. Program for crystal structure determination. University Chemistry Laboratory, Cambridge Univ., England.

SHIONO, R. (1964). A Program to Prepare Normalized Structure Factors. Department of Crystallography, Univ. of Pittsburgh, PA 15213, USA.

La Structure Cristalline et Moléculaire du Tribenzamide, N(COC6H5)3

PAR AIMERY CARON,* CLAUDE RICHE ET CLAUDINE PASCARD-BILLY

Cristallochimie, Institut de Chimie des Substances Naturelles, CNRS, 91190 Gif-sur-Yvette, France

ET JEAN-CLAUDE GRAMAIN

Chimie et Biochimie des Substances Naturelles, Université de Clermont-Ferrand, 63 Aubière, France

Crystalline tribenzamide is monoclinic, $P2_1$, $Z = 2$, with $a = 5·388$ (4), $b = 16·053$ (8), $c = 9·987$ (7) Å and $\beta = 102·1$ (2)° at 20°C. The structure at −45°C was solved by the Patterson method and refined by the least-squares method to a final R index of 4·8% for 1360 observed intensities measured on a diffractometer. The molecule adopts a propeller conformation with pseudosymmetry 3. The N atom is not quite planar with an average C−N−C angle of 117·5 (6)°. The peptidic N−C bonds are unusually long at 1·440 (2) Å.

Introduction

De récentes études ont montré que les triamides symétriques, N(COR)₃, possèdent un moment dipolaire élevé (Avedikian, Besserre & Gramain, 1976). Cette propriété implique, soit que la molécule est plane mais non de symétrie ternaire, soit qu'elle n'est pas plane, ou soit qu'elle n'est ni plane ni ternaire. Afin de préciser la géométrie de cette classe de molécules, nous avons choisi comme modèle le tribenzamide, N(COC₆H₅)₃, que nous avons étudié à l'état cristallin par la méthode de diffraction des rayons X.

* Adresse permanente: College of the Virgin Islands, St Thomas, US Virgin Islands 00801.

Partie expérimentale

Des cristaux de tribenzamide ont été préparés selon la méthode de Kaiser & Yon (1970) et recristallisés dans l'acétonitrile. Les données cristallines sont résumées dans le Tableau 1. Un cristal en forme d'aiguille de dimensions approximatives 0,2 × 0,3 × 0,6 mm a été utilisé, et les données ont été enregistrées sur un diffractomètre automatique, Nonius CAD-4, muni d'un monochromateur au graphite avec la radiation Cu $K\alpha$. Nous avons choisi d'opérer à basse température (−45 ± 2°C) afin de réduire les mouvements thermiques et afin d'augmenter le nombre de mesures. Le système de refroidissement utilisé est celui de Nonius à l'azote liquide. Les variations d'intensités des trois réflexions de