structure is not a possible candidate for phase (II), but might be stable at very low temperatures. The best hypothetical structure for (II) is the disordered orthorhombic structure, as in agreement with experiment its energy is expected to be (slightly) higher than for the ordered monoclinic phase. This hypothesis gives the following picture for the phase transitions in ethane at zero pressure:

$$\begin{array}{c}\text{hypothetical (IV)}\\\text{(ordered orthorhombic)}\end{array} \underset{?}{\dashrightarrow} \begin{array}{c}\text{(III) (ordered}\\\text{monoclinic)}\end{array} \xrightarrow{89\cdot73\text{ K}}$$

$$\begin{array}{c}\text{(II) (disordered}\\\text{orthorhombic?)}\end{array} \xrightarrow[89\cdot83\text{ K}]{} \begin{array}{c}\text{(I) (plastic}\\\text{cubic)}\end{array} \xrightarrow[90\cdot35\text{ K}]{} \text{liquid.}$$

When (III) is heated, orientational disorder for the molecules sets in at 89·73 K which at an increase in temperature of only 0·1 K is followed by a much stronger (dynamical) orientational disorder. This qualitative picture agrees with NMR measurements (Schutte, 1979).

As far as its calculated powder pattern is concerned, it is not impossible that a phase (II) with the orthorhombic disordered structure corresponds to the MP powder diagram. The small stability region of this phase and the small transition energy to (III) do not make it very likely, however, that Marck & Poland have frozen-in this phase at zero pressure. Accidental crystallization of phase (II) is easier to achieve at higher pressures, as NMR data (Schutte, 1979) have shown that the stability region of (II) increases with increasing pressure, but it is doubtful whether such pressures have been realized in Marck & Poland's sample.

Table 3. *Calculated and observed data for experimental and proposed ethane structures*

	E_c (kJ mol^{-1})	H_{obs} (kJ mol^{-1})	ρ (Mg m^{-3})
Plastic cubic (I)	$1\cdot334 + \delta$	2·140	0·669
Disordered orthorhombic (*A*)	δ'		0·693
Phase (II)		0·090	
Ordered monoclinic (III)	0	0	0·719
Ordered orthorhombic (*B*)	−2·590		0·693

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The Structure of Treptilaminum: an Anticholinergic Drug

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Abstract

$C_{20}H_{28}NO^+.Cl^-$, $M_r = 333\cdot90$, monoclinic, $P2_1/c$, $a = 11\cdot267\ (2)$, $b = 31\cdot610\ (9)$, $c = 10\cdot803\ (1)$ Å, $\beta = 98\cdot71\ (1)°$, $U = 3803\cdot1$ Å^3, $Z = 8$, $D_c = 1\cdot166$ Mg m^{-3}, $F(000) = 1440$. The final $R = 0\cdot087$ for 3956 reflections. The acetylcholine-like moiety adopts a conformation similar to that of acetylcholine in crystals of the chloride and bromide, as well as in other anticholinergic drugs. Both crystallographically independent molecules have the same bond lengths and angles, but their conformations have significant differences due to packing forces. The nortricycline moiety displays non-crystallographic 3*m* symmetry. Each molecule is involved in a $N-H\cdots Cl$ salt bridge.

Introduction

Treptilaminum, 2-[α-(tricyclo[2.2.1.0^{2,6}]hept-3-ylidene)benzyloxy]triethylamine, ASTA S5521, belongs to a class of synthetic drugs closely related to

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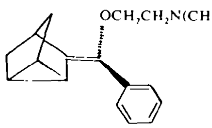
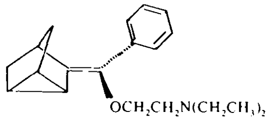
acetylcholine. It acts as an atropine-like antagonist of acetylcholine at the parasympathetic post-ganglionic (muscarinic) receptor. Its activity is approximately equal to that of atropine sulphate and *N*-bromobutylhyoscine. It has found clinical applications as an antispasmodic and does not have the undesirable side-effects of similar kinds of anticholinergic drugs.

A powder sample was kindly provided by Asta Werke Laboratories (Federal Republic of Germany). The compound is a mixture of two isomers: *trans* (I), m.p. 420–422 K, and *cis* (II), m.p. 401–402 K. (II) could not be crystallized, while (I) formed colourless transparent crystals (m.p. 421 K).



(I)



(II)

A crystal (0·2 × 0·2 × 0·3 mm) of (I) was used for data collection. Intensities were measured on a four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation. Cell dimensions were obtained by least squares from 30 reflections. Systematic absences fixed the space group as $P2_1/c$. 6814 independent reflections were measured to a limit of $\theta = 25°$ and 3956 with $I > 2\sigma(I)$ were used to refine the structure. The data were corrected for Lp effects but not for absorption. No intensity decay was observed. The structure was solved by *MULTAN* (Main, Lessinger, Woolfson, Germain & Declercq, 1977). Most of the remaining calculations were performed with XRAY 70 (Stewart, Kundell & Baldwin, 1970).

Positional and anisotropic thermal parameters were refined. All H atoms, except those attached to the N atoms, which were located on a difference map, were placed at their expected positions and included as fixed contributors. For the last cycles the weighting scheme was $w = w_1 w_2$, where $w_1 = 1/(a + b|F_o|)^2$ and $w_2 = 1/(c + d\sin\theta/\lambda)$, with coefficients calculated by *PESOS* (Martinez-Ripoll & Cano, 1975). The final $R = 0{\cdot}087$ and $R_w = 0{\cdot}101$.*

Table 1. *Atomic coordinates* (×10⁴) *and isotropic thermal parameters* (×10³)

$$U_{\rm eq} = \tfrac{1}{3}U_{ij}a_i^*a_j^*a_ia_j\cos(a_i,a_j).$$

	x	y	z	$U_{\rm eq}$ (Å²)
Cl*A*	3308 (2)	2930 (1)	5131 (2)	69 (1)
O*A*	1953 (3)	3732 (1)	1598 (4)	40 (1)
N*A*	1144 (4)	2923 (1)	3013 (4)	34 (1)
C(1)*A*	2747 (5)	4049 (2)	1319 (5)	38 (2)
C(2)*A*	2927 (5)	4065 (2)	−6 (5)	39 (2)
C(3)*A*	2053 (7)	3924 (2)	−936 (6)	55 (3)
C(4)*A*	2245 (8)	3916 (3)	−2183 (7)	68 (3)
C(5)*A*	3320 (8)	4051 (3)	−2499 (7)	70 (3)
C(6)*A*	4198 (9)	4195 (3)	−1586 (8)	78 (3)
C(7)*A*	4019 (7)	4198 (3)	−337 (7)	63 (3)
C(8)*A*	3200 (5)	4310 (2)	2239 (6)	43 (2)
C(9)*A*	3077 (6)	4285 (2)	3615 (6)	49 (2)
C(10)*A*	4409 (7)	4312 (3)	4198 (7)	70 (3)
C(11)*A*	4755 (7)	4694 (3)	3510 (7)	59 (3)
C(12)*A*	3662 (7)	4970 (2)	3299 (7)	62 (3)
C(13)*A*	3977 (6)	4690 (2)	2256 (6)	51 (2)
C(14)*A*	2694 (7)	4746 (3)	3847 (8)	70 (3)
C(15)*A*	2518 (6)	3325 (2)	1774 (6)	45 (2)
C(16)*A*	1592 (6)	2981 (2)	1782 (5)	40 (2)
C(17)*A*	346 (6)	3279 (2)	3282 (6)	44 (2)
C(18)*A*	114 (7)	3274 (2)	4636 (7)	62 (3)
C(19)*A*	489 (6)	2506 (2)	3032 (6)	48 (2)
C(20)*A*	1303 (9)	2130 (2)	3118 (8)	69 (3)
Cl*B*	8317 (1)	2802 (1)	10187 (1)	49 (1)
O*B*	7066 (3)	3666 (1)	7295 (4)	38 (1)
N*B*	6133 (4)	2808 (2)	8039 (4)	35 (2)
C(1)*B*	7900 (5)	3989 (2)	7474 (5)	35 (2)
C(2)*B*	8341 (6)	4138 (2)	6320 (5)	37 (2)
C(3)*B*	7597 (6)	4095 (2)	5174 (6)	48 (2)
C(4)*B*	7972 (8)	4236 (3)	4078 (7)	66 (3)
C(5)*B*	9076 (11)	4420 (3)	4129 (8)	81 (4)
C(6)*B*	9845 (8)	4454 (3)	5232 (8)	74 (3)
C(7)*B*	9478 (6)	4315 (2)	6340 (6)	49 (2)
C(8)*B*	8174 (6)	4164 (2)	8610 (5)	40 (2)
C(9)*B*	7726 (6)	4019 (2)	9811 (5)	43 (2)
C(10)*B*	8933 (7)	3982 (2)	10675 (6)	54 (2)
C(11)*B*	9426 (6)	4411 (2)	10463 (6)	53 (2)
C(12)*B*	8351 (7)	4710 (2)	10184 (6)	53 (2)
C(13)*B*	8928 (6)	4528 (2)	9101 (6)	46 (2)
C(14)*B*	7261 (6)	4445 (2)	10269 (6)	53 (2)
C(15)*B*	7578 (6)	3262 (2)	7072 (6)	42 (2)
C(16)*B*	6623 (6)	2929 (2)	6856 (6)	42 (2)
C(17)*B*	5204 (6)	3126 (2)	8303 (6)	43 (2)
C(18)*B*	4962 (7)	3091 (3)	9644 (7)	64 (3)
C(19)*B*	5582 (6)	2367 (2)	7914 (6)	50 (2)
C(20)*B*	6528 (8)	2025 (2)	8042 (7)	65 (3)

Results and discussion

Atomic parameters and molecular dimensions are listed in Tables 1–4. Fig. 1 shows the shapes of the two independent molecules in the crystal with the atom labelling. The independent molecules in the asymmetric unit are related by a pseudo translational vector (0·5, 0·0, 0·5) which causes a pseudo *B*-centred lattice. This implies strong atomic parameter correlations, which account for difficulties in the refinement and the relatively high *R* obtained. Bond lengths and angles in the two molecules are similar. A half-normal probability plot (Abrahams & Keve, 1971) calculated from a comparison of all intramolecular distances <2·70 Å (between non-H atoms) gave a linear array, with a correlation coefficient of 0·995. Table 2 shows the mean bond lengths and angles and several selected intramolecular distances. However, molecules *A* and *B* show significant differences in their torsion angles, Table 3. Mechanical molecular-energy calculations (Garcia-Garcia, 1978), including repulsion, attraction

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35474 (47 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Average bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

Mean values and their standard errors have been calculated from: $x_m = \sum(x_i/\delta_i^2)/\sum(1/\delta_i^2)$; $\sigma_m = 1/\sum(1/\delta_i^2)$. Selected intramolecular distances for molecules *A* and *B* are also included. Ph is the centroid of the phenyl ring.

C(1)–C(2)	1·482 (6)	C(2)–C(1)–C(8)	126·4 (4)
C(1)–C(8)	1·335 (6)	C(2)–C(1)–O	114·9 (3)
C(1)–O	1·394 (5)	C(8)–C(1)–O	118·6 (4)
C(2)–C(3)	1·383 (6)	C(1)–C(2)–C(3)	119·7 (4)
C(2)–C(7)	1·396 (7)	C(1)–C(2)–C(7)	121·7 (4)
C(3)–C(4)	1·393 (7)	C(3)–C(2)–C(7)	118·5 (4)
C(4)–C(5)	1·372 (9)	C(2)–C(3)–C(4)	120·6 (5)
C(5)–C(6)	1·366 (8)	C(3)–C(4)–C(5)	120·0 (5)
C(6)–C(7)	1·395 (8)	C(4)–C(5)–C(6)	120·4 (6)
C(8)–C(9)	1·525 (6)	C(5)–C(6)–C(7)	119·9 (6)
C(8)–C(13)	1·482 (6)	C(2)–C(7)–C(6)	120·4 (5)
C(9)–C(10)	1·536 (7)	C(1)–C(8)–C(9)	127·2 (4)
C(9)–C(14)	1·553 (7)	C(1)–C(8)–C(13)	132·8 (4)
C(10)–C(11)	1·497 (8)	C(9)–C(8)–C(13)	99·9 (3)
C(11)–C(12)	1·516 (7)	C(8)–C(9)–C(10)	99·6 (4)
C(11)–C(13)	1·518 (6)	C(8)–C(9)–C(14)	100·3 (4)
C(12)–C(13)	1·525 (7)	C(10)–C(9)–C(14)	100·0 (4)
C(12)–C(14)	1·498 (8)	C(9)–C(10)–C(11)	98·8 (4)
C(15)–C(16)	1·502 (6)	C(10)–C(11)–C(12)	106·4 (4)
C(15)–O	1·437 (5)	C(10)–C(11)–C(13)	106·1 (4)
C(16)–N	1·510 (6)	C(12)–C(11)–C(13)	60·3 (3)
C(17)–C(18)	1·522 (7)	C(11)–C(12)–C(13)	60·0 (3)
C(17)–N	1·502 (6)	C(11)–C(12)–C(14)	106·5 (4)
C(19)–C(20)	1·503 (8)	C(13)–C(12)–C(14)	106·5 (4)
C(19)–N	1·518 (6)	C(8)–C(13)–C(11)	105·7 (4)
O–N	3·122 (6)	C(8)–C(13)–C(12)	106·1 (4)
O–C(17)	3·068 (8)	C(11)–C(13)–C(12)	59·7 (3)
N–Ph	6·494 (11)	C(9)–C(14)–C(12)	98·3 (4)
		C(16)–C(15)–O	110·7 (3)
		C(15)–C(16)–N	113·9 (3)
		C(18)–C(17)–N	111·6 (4)
		C(20)–C(19)–N	112·7 (4)
		C(1)–O(1)–C(15)	113·1 (3)
		C(16)–N–C(17)	110·9 (3)
		C(16)–N–C(19)	110·5 (3)
		C(17)–N–C(19)	110·0 (3)

and conformational terms, were performed taking the torsion angles ω_1, ω_2, ω_3, and ω_4 (Fig. 1) as variables. The minima of the energy function correspond to the same values for both molecules and are included in Table 3. Departures of experimental from theoretical torsion angles are interpreted as being due to packing forces, which produce two crystallographically independent molecules, transforming a hypothetical *B*-centred lattice into the primitive actual one.

The overall shape of the acetylcholine-like moiety of the cation is described by the torsion angles ω_1, ω_2, ω_3 and ω_4 (Fig. 1). The internal torsion angles ω_2 and ω_3 of the group have been summarized for several acetylcholine compounds (Jagner & Jensen, 1977; Guy & Hamor, 1974; Baker, Chothia, Pauling & Petcher, 1971). These values concentrate in some areas, the more populated one being defined by $\omega_2 = \pm 80°$ and $\omega_3 = 180°$ with a range of $\pm 20°$. ω_2 and ω_3 in the present compound (Table 3) lie in this area. These

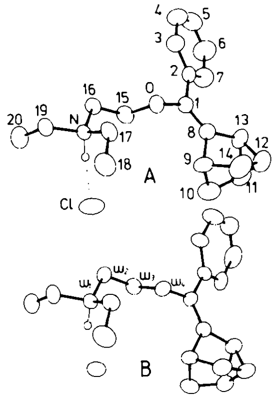

Fig. 1. The molecular structure of the two crystallographically independent molecules, related by a pseudo translational vector (0·5, 0·0, 0·5).

structural results for ASTA S5521 are, therefore, consistent with the model for the blocking action of anticholinergic agents related to acetylcholine. The mean C—N$^+$ length of 1·510 (6) Å is, as usual, longer than the accepted value for the C(sp^3)—N single bond of 1·47 Å.

Table 3. *Selected torsion angles* (°)

Observed values are given with their e.s.d.'s. Calculated values corresponding to the minimum of mechanical molecular energy are also included, with the half-width of the distributions.

Molecule	ω_1	ω_2	ω_3	ω_4
A	72·1 (6)	278·3 (6)	192·7 (5)	81·4 (6)
B	81·4 (6)	287·7 (6)	181·4 (5)	74·5 (6)
Theoretical	90 (18)	297 (25)	175 (23)	85 (18)

Table 4. *Nortricyclene geometry compared with previously reported results*

Average bond distances (Å) and angles (°) are assigned to a representative moiety.

	(1)	(2)	(3)	(4)
C(9)–C(8)	1·525	1·507	–	–
C(9)–C(10)	1·545	1·552	1·538	1·537
C(13)–C(8)	1·482	1·488	–	–
C(10)–C(11)	1·499	1·511	1·525	1·535
C(11)–C(12)	1·519	1·519	1·527	1·510
C(8)–C(9)–C(10)	99·9	100·2	102·6	103·0
C(9)–C(8)–C(13)	100·0	100·5	–	–
C(9)–C(10)–C(11)	98·6	98·0	96·2	95·6
C(8)–C(13)–C(11)	106·3	106·2	106·6	107·0

(1) Present work; average e.s.d.'s are 0·007 Å and 0·4°.

(2) Nelsen & Calabrese (1973); X-ray results; average e.s.d.'s are 0·01 Å and 0·7°.

(3) Laurie & Stigliani (1973); microwave results; e.s.d.'s are not reported.

(4) Chiang, Wilcox & Bauer (1969); electron diffraction results; average e.s.d.'s for distances are 0·01 Å.

A geometrical analysis of the nortricyclene moiety gives the following results. Nortricyclene has non-crystallographic $3m$ symmetry for both molecules. The planes defined by C(9)—C(8)—C(13), C(9)—C(14)—C(12) and C(9)—C(10)—C(11) form an average interplanar angle of 120 ± 1°, and form with the threefold axis, defined by C(9) and the cyclopropane centre, an average angle of 0·2 ± 0·2° (0·2° being the r.m.s.d.). Planes C(11)—C(12)—C(13) and C(10)—C(14)—C(8) are parallel and are normal to the threefold axis, with a deviation of 0·5 ± 0·2°. All these values indicate no significant deviation from $3m$ symmetry, which is not distorted by the substitution at C(8). Table 4 shows the nortricyclene geometry compared with previously reported results.

The Cl$^-$ ions are hydrogen bonded to the positively charged N atoms at distances of 3·080 (4) and 3·116 (4) Å for molecules A and B, respectively. There are no contacts between non-H atoms less than 3·4 Å.

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The Structure of the Sesquiterpene Aplysistatin

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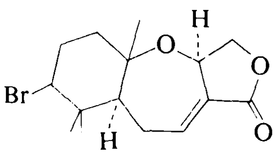
Abstract

A crystal structure analysis of the sesquiterpene aplysistatin has established the absolute configuration of the molecule. The molecular structure consists of a 6–7–5 set of fused rings, all with equatorial ring junctions. The seven-membered ring has a heterocyclic O atom in the bridging position and the five-membered ring is formed by a cyclic ester. The structure was solved by heavy-atom analysis of data from a crystal with $a = 9{\cdot}982\,(9)$, $b = 7{\cdot}182\,(2)$, $c = 20{\cdot}586\,(9)$ Å, $Z = 4$ and $\rho_c = 1{\cdot}482$, $\rho_o = 1{\cdot}469$ Mg m^{-3} in the space group $P2_12_12_1$. An automated diffractometer was used to collect the 1967 reflections available within the range $2\theta \leq 55°$ for monochromated Mo $K\alpha$ radiation. Anisotropic least-squares refinement converged to a conventional residual $R = 0{\cdot}0945$ ($R_w = 0{\cdot}0649$) for 1701 unique non-zero reflections and the best enantiomer.

Introduction

During the course of an evaluation of a chloroform extraction of a South Pacific Ocean sea hare (sp. *Aplysia angasi*) for antineoplastic activity, the sesquiterpene aplysistatin (I) had been isolated and an



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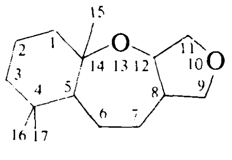

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