

different substituents in these isomers, most of the torsion angles are similar except those at the bonds related to the N(2) and N(30) atoms. The C(21)–N(2)–C(3)–N(30) and C(3)–N(30)–C(31)–C(32) torsion angles are distorted considerably by the hindrance of the substituent at N(2). Their respective values are -54.0 and -69.3° .

The short intermolecular distances, excluding those for H atoms, are given in Table 7. None of these are shorter than the sum of the van der Waals radii.

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The Structure of 3-Methyl-3-(3-methylaminopropyl)-1-phenyl-2-indolinone Hydrochloride

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Abstract

$C_{19}H_{23}N_2O^+ \cdot Cl^-$ is orthorhombic, space group *Pcab* (alternative setting of *Pbca*), with $a = 11.105$ (1), $b = 34.147$ (7), $c = 9.563$ (1) Å, $Z = 8$. Final $R = 0.078$ for 2396 observed reflections. The indoline group is nearly planar. The dihedral angle between the phenyl ring and indoline group is 49° . The N atom of the methylaminopropyl chain is protonated and forms hydrogen bonds with the Cl^- ion, the average $N \cdots Cl$ distance being 3.102 (6) Å.

Introduction

The discovery in 1957 of the therapeutic effect of imipramine in endogenous depression stimulated a search for other substances with similar properties, and several drugs which are structurally closely related to imipramine, known collectively as the tricyclic antidepressants, have become available. The spectrum of antidepressant effects of these drugs is fairly uniform, although some possess tranquillizing activity, which is useful for treating patients whose depression is complicated by agitation. But these substances have side effects which stem partly from anticholinergic and antihistaminic properties. In the past five years attempts have been made to depart from the tricyclic structures, and antidepressant activity has been claimed

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for iprindole, thiazesim and other compounds, but it is too early to assess their place in the therapy of depression.

Attempts to develop an antidepressant drug of novel structure which might display new pharmacological and clinical features were reported (Cañas-Rodríguez & Leeming, 1969). Medicinal chemical considerations led to the development of a series of aminoalkyl-substituted *N*-phenylindolines and -2-indolinones.

The compound was synthesized by treatment of 3-methyl-1-phenyl-2-indolinone with 3-(*N*-benzyl-*N*-methylamino)propyl chloride in the presence of sodium amide and subsequent hydrolysis.

Experimental

Crystals were in the form of colourless prisms. Preliminary cell dimensions and space-group information were obtained from oscillation and Weissenberg photographs taken with $Mo K\alpha$ radiation. Accurate cell dimensions (Table 1) were obtained by least squares from the θ values of 50 reflections measured on a Philips PW 1100 automated four-circle diffractometer. Intensities were also collected on this instrument with graphite-monochromated $Mo K\alpha$ radiation and the ω - 2θ step scanning mode. Intensities were collected over the range $2^\circ < \theta < 30^\circ$ to give 5199 independent reflections of which 2396 were considered as observed [$I > 2\sigma(I)$].

Table 1. *Crystal data*

$C_{10}H_{23}N_2O^+ \cdot Cl^-$, $M_r = 330.8$
 Space group: $Pcab$
 $a = 11.105(1) \text{ \AA}$ $D_c = 1.21 \text{ Mg m}^{-3}$
 $b = 34.147(7)$ $D_o = 1.22$
 $c = 9.563(1)$ $F(000) = 1408$
 $V = 3626.3 \text{ \AA}^3$ $\mu = 0.214 \text{ mm}^{-1}$
 $Z = 8$

Structure determination

The structure was solved with *MULTAN* (Main, Lessinger, Woolfson, Germain & Declercq, 1977). 400 reflections with $|E| > 1.70$ (approximately 17 reflections for each non-hydrogen atom in the asymmetric unit) were used and a choice of phasing was possible based on FOM'S; the highest combined figure of merit derived with unit weights for the components was 2.0. An *E* map computed with this phase set had distinguishable peaks for all non-hydrogen atoms.

The structure was refined by full-matrix least squares. Scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Refinement of the non-hydrogen atoms with isotropic temperature factors and unit weights gave $R = 0.14$. With anisotropic temperature factors and the weighting scheme $w = 1/\sigma^2(F)$, R was reduced to 0.088. The positions of the H atoms were then calculated. A difference synthesis revealed most of the H atoms near their calculated positions. Further refinement with non-hydrogen atoms treated anisotropically and H atoms isotropically (the H positions were also included

in the refinement) produced convergence with $R = 0.078$.

In the last cycle the H atoms were kept fixed with isotropic temperature factors equal to 4.0 \AA^2 . The positional and isotropic thermal parameters for the

Table 3. *Atomic coordinates of the H atoms ($\times 10^3$)*

| | x | y | z |
|--------|---------|---------|---------|
| H1N(1) | 406 (6) | 238 (2) | 747 (7) |
| H2N(1) | 373 (6) | 245 (2) | 560 (7) |
| H1C(1) | 196 (6) | 271 (2) | 593 (7) |
| H2C(1) | 210 (6) | 274 (2) | 758 (7) |
| H3C(1) | 295 (6) | 298 (2) | 673 (7) |
| H1C(2) | 250 (6) | 189 (2) | 770 (7) |
| H2C(2) | 178 (6) | 207 (2) | 623 (7) |
| H1C(3) | 328 (6) | 159 (2) | 505 (7) |
| H2C(3) | 272 (6) | 137 (2) | 624 (7) |
| H1C(4) | 517 (6) | 179 (2) | 618 (7) |
| H2C(4) | 478 (6) | 153 (2) | 747 (7) |
| H1C(5) | 693 (6) | 102 (2) | 590 (7) |
| H2C(5) | 699 (6) | 142 (2) | 580 (7) |
| H3C(5) | 670 (6) | 125 (2) | 734 (7) |
| HC(9) | 364 (6) | 48 (2) | 240 (7) |
| HC(10) | 441 (6) | 97 (2) | 66 (7) |
| HC(11) | 557 (6) | 148 (2) | 103 (7) |
| HC(12) | 597 (6) | 160 (2) | 349 (7) |
| HC(14) | 203 (6) | 49 (2) | 401 (7) |
| HC(15) | 79 (6) | -4 (2) | 437 (7) |
| HC(16) | 150 (6) | -59 (2) | 578 (7) |
| HC(17) | 332 (6) | -53 (2) | 710 (7) |
| HC(18) | 455 (6) | 2 (2) | 663 (7) |

Table 2. *Final coordinates ($\times 10^4$) and equivalent isotropic temperature factors for non-hydrogen atoms*

| | x | y | z | $B_{eq} (\text{\AA}^2)$ |
|-------|----------|----------|----------|-------------------------|
| Cl | 4922 (2) | 2419 (1) | 9258 (2) | 5.9 |
| O | 4398 (4) | 780 (1) | 7583 (4) | 4.7 |
| N(1) | 3291 (5) | 2366 (1) | 6620 (5) | 4.5 |
| N(2) | 4092 (4) | 651 (1) | 5233 (4) | 3.4 |
| C(1) | 2546 (7) | 2716 (2) | 6761 (8) | 5.3 |
| C(2) | 2614 (6) | 1997 (2) | 6728 (8) | 4.9 |
| C(3) | 3264 (6) | 1656 (2) | 6016 (8) | 5.0 |
| C(4) | 4563 (5) | 1599 (2) | 6456 (6) | 3.9 |
| C(5) | 6487 (6) | 1213 (2) | 6254 (8) | 5.0 |
| C(6) | 5158 (5) | 1233 (2) | 5818 (6) | 3.7 |
| C(7) | 4519 (5) | 869 (2) | 6358 (6) | 3.7 |
| C(8) | 4360 (5) | 852 (1) | 3962 (5) | 3.2 |
| C(9) | 4107 (5) | 736 (2) | 2606 (6) | 3.8 |
| C(10) | 4500 (6) | 978 (2) | 1533 (6) | 4.7 |
| C(11) | 5102 (7) | 1321 (2) | 1805 (7) | 4.1 |
| C(12) | 5349 (6) | 1431 (2) | 3174 (7) | 4.7 |
| C(13) | 4982 (5) | 1195 (1) | 4254 (6) | 3.6 |
| C(14) | 2305 (5) | 271 (2) | 4663 (6) | 4.2 |
| C(15) | 1603 (5) | -55 (2) | 4846 (7) | 4.7 |
| C(16) | 1967 (6) | -351 (2) | 5749 (7) | 4.8 |
| C(17) | 3049 (6) | -318 (2) | 6437 (7) | 4.3 |
| C(18) | 3776 (5) | 6 (2) | 6237 (6) | 3.7 |
| C(19) | 3382 (5) | 300 (1) | 5366 (5) | 3.2 |

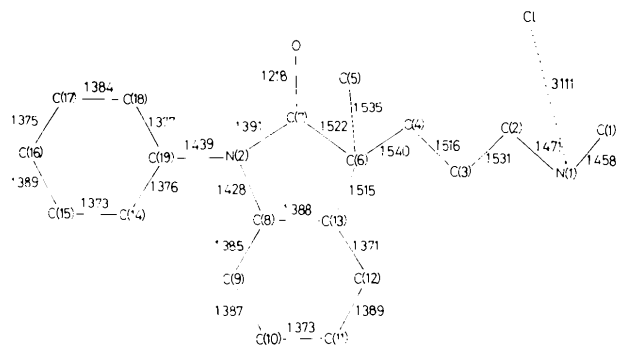


Fig. 1. Interatomic distances (\AA)

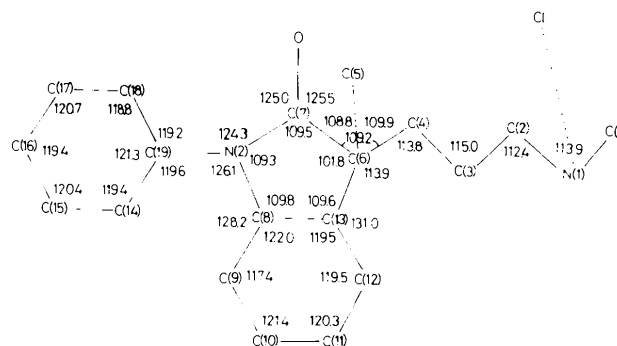


Fig. 2. Bond angles ($^\circ$). The angle C(5)-C(6)-C(13) is $112.9(5)^\circ$.

non-hydrogen atoms are given in Table 2 and those for the H atoms in Table 3. Bond distances and angles are given in Figs. 1 and 2.*

Discussion

The mean e.s.d.'s of all distances and angles not involving Cl atoms are less than 0.009 Å and 0.6°. Bond lengths and angles compare well with the corresponding parameters in analogous compounds. The phenyl C—C distances vary from 1.373 to 1.389, average 1.379 Å, and the angles from 119.4 to 121.3°. The C—C partial double bonds of the six-membered ring of the indole group vary from 1.371 to 1.389 Å and the angles from 117.4 to 122.0°. The two N—C distances of the indolinone ring are 1.391 and 1.428 Å; the C(7)—C(6)—C(13) angle is 101.8°, similar to other indole compounds (Itai, Iitaka & Kubo, 1978). In the methylaminopropyl chain the C—C lengths vary between 1.516 and 1.540 Å; the two C—N distances are 1.471 and 1.458 Å, as would be expected for C—N single bonds. Average values of C—H and N—H lengths are 1.0 and 1.1 Å, respectively. The C—C—C angles in the aminopropyl chain are 113.8 and 115.0°, the C—C—N angle is 112.4° and C—N—C is 113.9°.

The Cl^- ion forms two hydrogen bonds with the protonated N(1) atoms (Borkakoti, Lindley, Moss &

Palmer, 1978). The $Cl \cdots N(1)$ distances are 3.111 (6) Å ($Cl \cdots H = 1.95$, $H-N = 1.18$ Å and $N-H \cdots Cl = 163.6^\circ$) and 3.092 (6) Å ($Cl \cdots H = 2.02$, $H-N = 1.12$ Å, and $N-H \cdots Cl = 158.6^\circ$). There is a short contact of 3.40 Å between C(15) and C(17) of molecules related by the symmetry operation $-x + \frac{1}{2}, y, z - \frac{1}{2}$.

The planarities of the different parts of the molecule, the indoline and phenyl ring and the aminopropyl chain, were examined. The results are listed in Table 4.

The indoline group is nearly planar (Sakaki, Sogo, Wakahara, Kanai, Fujiwara & Tomita, 1976), since the six-membered ring is planar and the five-membered ring quasi-planar. The dihedral angle between them is 1.5°. The phenyl ring is planar as expected (maximum atomic deviation from the mean plane 0.012 Å). The dihedral angle between this plane and that of the indoline group is 49°. The aminopropyl chain is not planar.

Torsion angles defining the configuration and conformation are listed in Table 5. The major factors determining the molecular packing are van der Waals forces and hydrogen bonding (Fig. 3).

All calculations were carried out on a DCT 2000 terminal of the Centro de Calculo of this University,

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35487 (37 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 4. Deviations of atoms from least-squares planes (Å) (average e.s.d. is 0.010 Å)

Equations of the planes in the form $m_1x + m_2y + m_3z = d$ in orthogonal space

| Plane | m_1 | m_2 | m_3 | d |
|------------------------|---------|----------|----------|----------|
| Indoline group (A) | 0.86674 | 0.49833 | 0.04928 | 2.58237 |
| Five-membered ring (B) | 0.86548 | -0.49737 | -0.05966 | 2.52074 |
| Six membered ring (C) | 0.86730 | -0.49634 | -0.03794 | 2.61402 |
| Phenyl ring (D) | 0.46126 | -0.45180 | -0.76361 | -2.64165 |

Deviations from planes

| | A | B | C | D |
|-------|---------|---------|---------|---------|
| N(2) | 0.006* | 0.008* | | -0.088 |
| C(6) | 0.019* | 0.011* | | |
| C(7) | 0.005* | 0.016* | | |
| C(8) | 0.019* | -0.004* | -0.003* | |
| C(9) | 0.001* | | -0.001* | |
| C(10) | 0.019* | | 0.006* | |
| C(11) | 0.004* | | -0.005* | |
| C(12) | -0.009* | | -0.003* | |
| C(13) | 0.013* | -0.004* | 0.005* | |
| O | -0.030 | 0.052 | | |
| C(5) | 1.309 | 1.296 | | |
| C(14) | | | | -0.001* |
| C(15) | | | | 0.011* |
| C(16) | | | | 0.006* |
| C(17) | | | | -0.007* |
| C(18) | | | | 0.012* |
| C(19) | 0.088 | -0.086 | | 0.007* |

* Atoms defining the plane.

Table 5. Torsion angles (°)

| | |
|-----------------------|------------|
| C(1)—N(1)—C(2)—C(3) | 156.9 (5) |
| N(1)—C(2)—C(3)—C(4) | 51.9 (7) |
| C(2)—C(3)—C(4)—C(6) | 175.0 (5) |
| C(3)—C(4)—C(6)—C(13) | 48.9 (7) |
| C(4)—C(6)—C(7)—O | -57.1 (7) |
| C(5)—C(6)—C(7)—O | 62.8 (7) |
| C(13)—C(6)—C(7)—O | -177.8 (6) |
| C(8)—N(2)—C(7)—O | 177.7 (5) |
| C(19)—N(2)—C(7)—O | 3.8 (8) |
| C(8)—N(2)—C(19)—C(14) | -45.7 (7) |
| C(7)—N(2)—C(19)—C(14) | 127.2 (6) |
| C(8)—N(2)—C(19)—C(18) | 136.7 (5) |
| C(7)—N(2)—C(19)—C(18) | -50.4 (7) |

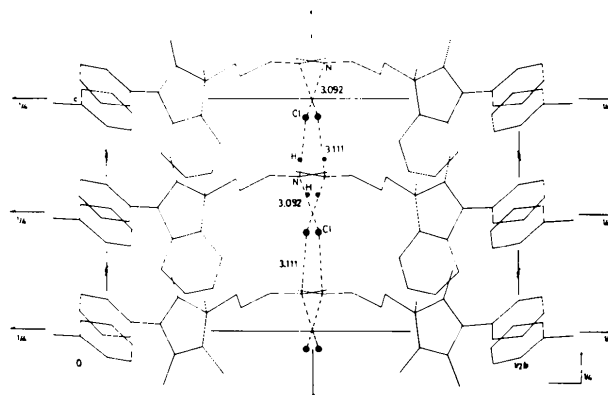


Fig. 3. Unit-cell contents and hydrogen-bonding contacts projected along *a*.

connected to a Univac 1108 computer, with the XRAY system (1970).

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Structures de Trois Nouveaux Limonoïdes Cytotoxiques: Aphanastatine, Amoorastatine, Hydroxy-12 Amoorastatine

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Abstract

The crystal structures of three novel compounds extracted from *Aphanamixis grandifolia* Bl. have been determined from three-dimensional X-ray diffraction data. Crystal data are as follows: for aphanastatin, $C_{35}H_{46}O_{13}$, $a = 19.233$ (5), $b = 14.207$ (5), $c = 12.364$ (5) Å, space group $P2_12_12_1$, $Z = 4$, $V = 3378.38$ Å³, $d_x = 1.32$ Mg m⁻³, for amoorastatin, $C_{28}H_{36}O_9$, $a = 7.781$ (6), $b = 12.81$ (1), $c = 12.99$ (2) Å, $\beta = 91.5$ (1)°, space group $P2_1$, $Z = 2$, $V = 1294.3$ Å³, $d_x = 1.37$ Mg m⁻³ and, for 12-hydroxyamoorastatin, $C_{28}H_{36}O_{10}$, $a = 7.781$ (8), $b = 12.85$ (1), $c = 12.98$ (2) Å, $\beta = 92.1$ (1)°, space group $P2_1$, $Z = 2$, $V = 1311.2$ Å³, $d_x = 1.39$ Mg m⁻³. The final R values are respectively 0.050, 0.052 and 0.068. The three molecules belong to the triterpene group with a furan ring and a hemiacetal bridge between C(19) and C(28). All three compounds show significant anti-neoplastic activity.

Introduction

On a pu extraire d'une plante de la famille des Méliacées *Aphanamixis grandifolia*, quatre substances

amères. Trois de ces composés possèdent une forte activité cytotoxique: l'aphanastatine (Polonsky, Varon, Arnoux, Pascard, Pettit, Schmidt & Lange, 1978), l'amoostatine (Polonsky, Varon, Arnoux, Pascard, Pettit & Schmidt, 1978), et l'hydroxy-12 amoorastatine (Polonsky, Varon, Marazano, Arnoux, Pettit, Schmidt & Ochi, 1979). La très faible quantité de produit isolé empêchait toute étude structurale par les voies spectroscopiques habituelles ou par voie chimique. Nous avons donc entrepris la détermination par diffraction des rayons X des structures des trois composés actifs.

Partie expérimentale

Les cristaux des différents composés ont été obtenus avec beaucoup de difficultés par Polonsky *et al.* (1978). Les principales données expérimentales sont résumées dans l'Abstract et le Tableau 1. Les intensités ont été mesurées sur un diffractomètre automatique Philips PW1100 par la méthode de balayage $\omega/2\theta$ et corrigées des facteurs de Lorentz et de polarisation. Aucune correction d'absorption n'a été effectuée.