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References


Structure of Adamantanamine Hydrochloride at 143 K

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Abstract. Tricyclo[3.3.1.1^{3,7}]decano-1-aminium chloride, \( \text{C}_{15}\text{H}_{15}\text{NH}_{3}^+\text{Cl}^- \), \( M_r = 207.71 \), monoclinic, \( C2/c \), \( a = 20.549(10), b = 11.138(5), c = 9.658(6) \AA, \beta = 108.81(5)^\circ \), \( V = 2092.5 \AA^3 \) (at 143 K), \( Z = 8, D_x = 1.191 \text{Mg m}^{-3}, \lambda(\text{Cu K}) = 1.54178 \AA, \mu(\text{Cu K}) = 2.847 \text{mm}^{-1}, F(000) = 816, R = 0.065 \) for 1394 observed reflections. The structure of the high-temperature phase at 143 K has been shown to be ordered. The adamantan skeleton is not affected by the substitution. The molecules are held together by almost linear hydrogen bonds of the type N–H–Cl. All three H atoms of the NH$_3$ group are involved in hydrogen bonds and all Cl atoms form three H bonds. The d(N–Cl) distances range from 3.163 (5) to 3.219 (5) Å.

Introduction. The occurrence of order–disorder phase transitions in adamantane and its derivatives is well known (Parsonage & Staveley, 1978), and simple substitution, even though the high symmetry of adamantan itself is destroyed, does not always preclude the occurrence of the transitions (Clark, Knox, MacKle & McKervey, 1977). Stronger intermolecular interactions, such as hydrogen bonding, can affect the behaviour. For example, in 1-adamantanol (Amoureux, Bee, Gors, Warin & Baert, 1979) the phase transition occurs at 353 K with a large entropy change of 8.97 J K$^{-1}$ mol$^{-1}$ (Harvey, Gilson & Butler, 1986a), and the higher temperature phase is probably ordered.

A study of the adamantanamine hydrochloride salt showed that a sharp phase transition occurs at 124 K (Harvey, Gilson & Butler, 1986b) with enthalpy and entropy of transition of 0.32 kJ mol$^{-1}$ and 2.51 J K$^{-1}$ mol$^{-1}$ respectively. This transition is at a lower temperature than for any other adamantane derivative. The room-temperature vibrational spectra show quite narrow vibrational bands which split, usually into two or three components, in the low-temperature phase. In view of these spectral changes, the phase transition is probably first-order even though the enthalpy and entropy changes are small. An activation energy of 33.6 kJ mol$^{-1}$ obtained from proton spin-lattice relaxation time measurements was assigned to the barrier to rotation of the adamantyl group about its C$_3$ axis.

Thus adamantanamine hydrochloride is a singly substituted derivative that retains the threefold symmetry axis in the parent molecule, but has an ordered high-temperature phase. The same is probably true for the carboxylic acid compound but in this case the molecules exist as dimers. Clearly it is the hydrogen bonding in the amine hydrochloride salt that prevents the order–disorder transition from occurring, and the structure of the high-temperature phase is the subject of...
the present study. The structures of two other adamantanamine derivatives have been reported. The bisulfate salt (Khan & Pepinsky, 1969) is monoclinic at room temperature with possible space groups C2, Cm or C2/m, with one phase transition at 423 K to another monoclinic phase (Cc or C2/c) and another at 513 K to a cubic structure. No details of the molecular structure were given. The 2-amino-2-carboxylic acid hydrobromide derivative (Chacko & Zand, 1973) is monoclinic (P21/c), and the substitution appears to have little effect on the geometry of the adamantyl moiety.

Adamantanamine hydrochloride is marketed under various trade names* as an antiviral agent and for the treatment of Parkinson’s disease.

Experimental. Crystal bound by (100), (101), (110), (100), (110); dimensions 0.025 × 0.182 × 0.190 mm. Unit-cell parameters from 25 well centred reflections in the range 40 ≤ 2θ ≤ 50°. Nonius CAD-4 diffractometer equipped with a modified Nonius low-reflections in the range 40 < 2θ < 50°. Nonius CAD-4 equipped with a modified Nonius low-temperature attachment, graphite-monochromatized Cu Kα radiation, 0~--2θ scan (option flat), Δθω = (1·00 + 0·14 tanθ)°, 2θmax = 140°, 0 ≤ h ≤ 24, 0 ≤ k ≤ 13, -11 ≤ l ≤ 11. Orientation monitored every 100 measurements, intensity checked every hour using seven standard reflections, largest intensity fluctuation 0.190 mm. Unit-cell parameters from 25 well centred reflections, largest intensity fluctuation 1.6%. Data collection temperature (1.00 + 0.14 tanθ)°, 2θmax = 140°, 0 ≤ h ≤ 24, 0 ≤ k ≤ 13, -11 ≤ l ≤ 11. Orientation monitored every 100 measurements, intensity checked every hour using seven standard reflections, largest intensity fluctuation of standards: 1.6%. Data collection temperature 143 (4) K. 1982 unique measured reflections of which 1394 with I ≥ 1·6σ(I) were retained for structure determination and refinement. Lp and absorption corrections (Gaussian integration, grid 10 × 10 × 10, transmission range: 0.67-0.93). Direct methods (MULTAN80),† full-matrix least squares based on F, anisotropic for all atoms but H's. H atoms located from difference Fourier syntheses, refined isotropically. Function minimized \( \sum w(\|F_o\| - \|F_c\|)^2 \). Final \( R = 0·065, wR = 0·071 \) and \( S = 2·602 \). Weights derived from the counting statistics, \( w = 1/σ^2(IV) + \left( 0·016(I_{rel}) \right)^2 \). Maximum \( (Δσ/σ) = 0·08 \), average \( (Δσ/σ) = 0·01 \), electron density extrema on final difference Fourier synthesis -0·49 and +0·69 e Å\(^{-3} \), the first peaks (0·69, 0·60 e Å\(^{-3} \)) at about 1·2 Å from the Cl atom, general background ±0·3 e Å\(^{-3} \). All attempts to identify the residual peaks as disordered Cl ions with fractional occupancies were unsuccessful (the occupancy factors always tended to values less than 1%). The scattering factors for the non-hydrogen atoms were taken from Cromer & Mann (1968), and those for H atoms from Stewart, Davidson & Simpson (1965). The anomalous-dispersion coefficients \( f' \) and \( f'' \) for Cl were those given by Cromer & Liberman (1970). The final atomic coordinates and equivalent isotropic values are given in Table 1.*

Discuss. The molecular geometry of the adamantanamine ion and the atomic numbering are given in Fig. 1. The bond distances, angles and torsion angles are given in Table 2.

The adamantane ring system

The C–C bonds of the adamantane skeleton range from 1·505 (11) to 1·540 (12) Å with a mean value of 1·522 Å which is slightly lower than the value of 1·544 Å for the C(sp\(^3\))-C(sp\(^3\)) bond in diamond. The C–C–C bond angles, with a mean value of 109·5°, are in good agreement with the value for a tetrahedral angle. The individual values vary from 107·7 (5) to 111·7 (6)°. The adamantane skeleton consists of four fused cyclohexane rings. Each ring has a nearly perfect chair conformation; the overall mean torsion angle of 60·3° is very close to the expected value of 60° for a perfectly staggered chair conformation of cyclohexane with tetrahedral bond angles. All these values agree well with the corresponding values in some related compounds such as 1-adamantan-1-ol (Amoureux et al., 1979) or 2-iodoadamantane (Wahl, Greene & Bordner, 1973). However, the distances are, on the average, slightly shorter than in adamantane itself (Donohue & Goodman, 1967) or in the theoretical calculations of Gleicher & von Schleyer (1967). The adamantane cage is quite rigid and its geometry is not affected by substitution and crystal packing forces.

Table 1. Final atomic coordinates and their e.s.d.'s (×10\(^3\) for Cl, ×10\(^4\) for N, C) and \( U_{eq} (Å^2, ×10^3) \)

| \( U_{eq} = \frac{1}{2} \sum \gamma_{ij} u_j a_i a_j \) |
|---|---|---|---|---|
| C4 | 9401 (7) | -13204 (12) | 64143 (13) | 33 |
| N | 681 (2) | 1052 (4) | 4514 (5) | 31 |
| C(1) | 1009 (3) | 2090 (5) | 5489 (5) | 31 |
| C(2) | 754 (4) | 2067 (6) | 6800 (6) | 46 |
| C(3) | 1086 (5) | 3116 (7) | 7805 (7) | 64 |
| C(4) | 873 (5) | 4298 (7) | 6970 (8) | 57 |
| C(5) | 1130 (3) | 4301 (5) | 5654 (6) | 42 |
| C(6) | 791 (3) | 3236 (5) | 4663 (6) | 31 |
| C(7) | 1785 (3) | 1943 (6) | 5949 (9) | 52 |
| C(8) | 2110 (4) | 3003 (8) | 6960 (10) | 76 |
| C(9) | 1899 (4) | 4166 (7) | 6108 (10) | 65 |
| C(10) | 1859 (6) | 2983 (8) | 8276 (9) | 105 |

* Lists of structure factors, H-atom coordinates and anisotropic temperature factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43510 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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* Amazolon, Mantadix, Mantadan, Midantan, Mydantane, Symmetrel, Virofral. Sulfate: Contenton, PK-Merz, Trivaline.

† The programs used here are modified versions of NRC2, data reductions, NRC10, bond distances and angles, NRC22, mean planes (Ahmed, Hall, Pippy & Huber, 1973), FORDAP, Fourier and Patterson maps (A. Zalkin), MULTAN, multi-solution program (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), NUCLS, least-squares refinement (Doedens & Ibers, 1967), and ORTEP, stereodrawings (Johnson, 1965).
All C–H bond distances are normal. Their extreme values are 0.85 (5) and 1.06 (7) Å and their average 0.96 Å. All C–C–H or H–C–H bond angles are nearly tetrahedral [range 96 (6) to 120(4) ° with average 110°].

The N atom is at 1.506 (7) Å from C(1) and the three nearly equal C–C–N bond angles average 108.4 °. The adamantanamine ion has almost threefold symmetry. It also has non-crystallographic mirror planes. One of them is formed by C(1), C(7), C(8), C(4) and N. The atoms C(2), C(3), C(10) are -1.246 (6), -1.249 (7), -1.259 (8) Å away from this plane and the corresponding deviations of C(6), C(5), C(9) are +1.232 (5), +1.233 (6), +1.241 (7) Å. It is the presence of the chlorine atom at 2.799 (1) Å from the above plane which destroys the mirror symmetry.

Packing arrangement and hydrogen bonding
A stereoscopic view of the packing is shown in Fig. 2. The N atom has a nearly perfect tetrahedral coordination. The NH$_2$ group forms almost linear hydrogen bonds with the chloride ions with N···Cl distances of 3.163 (5), 3.219 (5) and 3.173 (5) Å. Two of these distances are among the shortest for N···Cl hydrogen bonds (Table 2).

The successive molecules, held together by three N–H···Cl interactions, form pleated ribbons extending in the e direction. The ribbons consist of two types of planes defined by pairs of hydrogen bonds. One plane is nearly parallel to ac while the other is 011 (or 022). The angle between two consecutive planes is 151° (Fig. 3b).

There are no other contacts between non-hydrogen atoms shorter than 3.69 Å. It is easy to visualize (Fig. 3) that the molecules are strung by hydrogen bonds along a chain of chloride ions. Thus it is not too
surprising that atoms C(3), C(4) and C(8) to C(10) have relatively high thermal parameters. Indeed, the further an atom is from N or C(1) the larger is its thermal parameter. Ueq for N or C(1) is 0.031 Å², while the average of the Ueq's of C(2), C(6) and C(7) increases to 0.043 Å² and reaches 0.068 Å² for C(3), C(4), C(5), C(8), C(9) and C(10). The H-atom Uiso's follow the same trend (except for those on N which are H-bonded). This observation is also consistent with a slight oscillation or disorder about the C3 axis of the molecule. These results are in agreement with those of the vibrational spectroscopic and spin-relaxation time studies, in that the hydrogen bonding of the NH3 group holds this part of the molecule in place and the hydrocarbon portion undergoes hindered rotation about the molecular threefold axis (Harvey et al., 1986b), i.e. the symmetry is maintained and the high-temperature phase is ordered. Since the entropy of transition is quite small, it seems probable that only a minor change in crystal structure occurs at the transition, perhaps a doubling of one of the unit-cell dimensions.

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References


Triterpenoids. III. Structure of 3β-Acetoxy-11-oxo-18α-olean-12-en-28-oic Acid Methyl Ester

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Abstract. C33H50O5, Mr= 526.40, monoclinic, P21, a = 7.748 (1), b = 16.370 (2), c = 12.099 (2) Å, β = 102.50 (1)°, V = 1498.1 (4) Å³, Dm = 1.17 (1), Dx = 1.17 Mg m⁻³, Z = 2, λ(Cu Kα) = 1.54178 Å, μ(Cu Kα) = 0.529 mm⁻¹, F(000) = 576, room temperature, final R = 0.054 for 1893 observed reflections. The molecule consists of five trans fused six-membered rings. Ring C has a sofa conformation distorted towards a half chair. The H atom at the C(18) asymmetric centre takes an axial position relative to the D and E rings.

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