

**The Crystal Structures of Racemic
3-Benzylamino-4-hydroxypent-2-enoic Acid Lactone Hydrochloride
and of Spontaneously Resolved
3-Benzylamino-4-hydroxypent-2-enoic Acid Lactone Hydrobromide**

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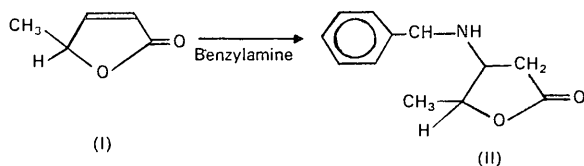
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The crystal structure of the hydrochloride of the reaction product of 4-hydroxypent-2-enoic acid lactone with benzylamine, $C_{12}H_{16}ClNO_2$, has been determined. System: monoclinic, $P2_1/c$, $a=9.183$ (7), $b=11.278$ (20), $c=12.218$ (10) Å; $\beta=101.3$ (1)° $Z=4$. The *trans* configuration of the C(12) methyl group and the N atom about C(8)–C(9) has been confirmed. Structure analysis of the spontaneously resolved (and hence non-isomorphous) hydrobromide is also reported. System: monoclinic, $P2_1$, $a=6.612$ (1), $b=10.824$ (3), $c=9.054$ (2) Å, $\beta=98.4$ °, $Z=2$. A possible reason is given for the significant difference in the conformation of the lactone ring in the two structures.

Introduction

Certain lactones are known to be moderately carcinogenic (Dickens & Jones, 1961) and their mode of action has been attributed to chemical reaction with the bases of deoxyribonucleic acid and of ribonucleic acid. Thus the reaction of such carcinogenic lactones with nitrogenous bases is of considerable biological interest and we have examined the crystal structures of both the hydrochloride and of the hydrobromide of the reaction product of 4-hydroxypent-2-enoic acid lactone (I) with benzylamine, namely 3-benzylamino-4-hydroxypent-2-enoic acid lactone (II).



Although Lukeš & Linhartová (1960) presented evidence that the product (II) had the N atom and the methyl group at C(12) disposed *trans* with respect to C(8)–C(9) [see Fig. 1(a) for numbering], this particular stereochemical feature is of biological interest and an X-ray analysis was undertaken to check it. The *trans* conformation has been confirmed and already reported in a preliminary communication from these laboratories (Jones, Koo, Mellor, Nyburg & Young, 1968)

Our original intention was to examine only the hydrobromide of (II) but preliminary X-ray examination indicated a space group at variance with that thought to be likely on chemical grounds. Accordingly the hydrochloride was first analyzed and later the hydrobromide with which it is not isomorphous.

CRYSTAL STRUCTURE OF THE HYDROCHLORIDE

Experimental

The salt was obtained as colorless columnar crystals by recrystallization from ethanol–methanol. The calculated linear absorption coefficient for Cu $K\alpha$ radiation is 26.6 cm^{-1} and all crystals were kept smaller than $2/\mu=0.75 \text{ mm}$; no absorption corrections were made.

All data were collected photographically on Weissenberg cameras and intensities eye-estimated. Cell dimensions were obtained from zero-level photographs calibrated with aluminum wire at high Bragg angles and refined by least squares.

Crystal data are:

$C_{12}H_{16}ClNO_2$, M.W. 241.7

Monoclinic, $P2_1/c$

$a=9.183$ (7), $b=11.278$ (20), $c=12.218$ (10) Å

$\beta=101.3$ (1)°. $V=1240.7 \text{ Å}^3$.

$\rho=1.290 \text{ g.cm}^{-3}$. (chloroform–benzene); Calculated for $Z=4$ molecules per cell, 1.304 g.cm^{-3} .

Since the molecule is asymmetric the crystal is clearly that of the racemate.

Equi-inclination, eye-estimated intensity data were collected on multiple-film packs: one set $h0l$ through $h.11l$, the other $0kl$ through $6kl$. Of the 2772 independent reflections lying in the Cu $K\alpha$ sphere, 2120 (76.5%) were observed and measured. After interfilm scaling and data reduction, the overall temperature factor $B=3.85 \text{ Å}^2$ and scale factor were obtained from a Wilson plot.

The unsharpened Patterson function could be interpreted in terms of either of two sets of Cl⁻ positions but sharpening did not resolve the ambiguity. Accord-

Table 1. Fractional coordinates and anisotropic thermal parameters of non-hydrogen atoms of the hydrochloride

Temperature factor in the form: $10^{-4} \exp [-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

| | <i>x</i> | <i>y</i> | <i>z</i> | β_{11} | β_{22} | β_{33} | β_{12} | β_{13} | β_{23} |
|-----------------|-------------|-------------|-------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Cl ⁻ | -0.0433 (2) | -0.4022 (1) | 0.1801 (1) | 153 (2) | 75 (29) | 57 (1) | -6 (1) | 28 (1) | -5 (1) |
| N | -0.0584 (4) | 0.3202 (4) | 0.1828 (3) | 79 (4) | 77 (29) | 57 (1) | -1 (3) | 22 (3) | -0 (2) |
| O(1) | 0.2433 (4) | 0.2160 (4) | 0.0556 (4) | 96 (5) | 111 (30) | 45 (3) | 10 (3) | 29 (3) | -21 (3) |
| O(2) | 0.1456 (6) | 0.0914 (4) | -0.0818 (5) | 188 (8) | 120 (30) | 84 (3) | -3 (4) | 59 (5) | -46 (3) |
| C(1) | -0.3075 (5) | 0.3206 (5) | 0.2364 (4) | 68 (5) | 100 (30) | 104 (5) | 7 (3) | 10 (3) | 4 (3) |
| C(2) | -0.3812 (6) | 0.2169 (6) | 0.2586 (6) | 109 (7) | 114 (30) | 57 (3) | 1 (4) | 18 (5) | 10 (4) |
| C(3) | -0.4636 (7) | 0.2163 (7) | 0.3421 (7) | 121 (8) | 133 (31) | 89 (5) | -8 (5) | 38 (6) | 25 (5) |
| C(4) | -0.4739 (7) | 0.3180 (7) | 0.4039 (6) | 98 (7) | 181 (31) | 107 (6) | 11 (6) | 32 (5) | 20 (5) |
| C(5) | -0.3999 (7) | 0.4209 (7) | 0.3831 (6) | 100 (7) | 161 (31) | 88 (5) | 18 (5) | 38 (5) | -23 (4) |
| C(6) | -0.3165 (6) | 0.4214 (5) | 0.2998 (5) | 85 (5) | 114 (30) | 83 (5) | 6 (4) | 24 (4) | 0 (4) |
| C(7) | -0.2225 (6) | 0.3205 (6) | 0.1414 (5) | 81 (6) | 142 (30) | 77 (4) | 2 (4) | 12 (3) | 1 (4) |
| C(8) | 0.0225 (5) | 0.3073 (4) | 0.0879 (4) | 76 (5) | 82 (30) | 60 (4) | -3 (3) | 18 (3) | 1 (2) |
| C(9) | 0.1921 (5) | 0.2992 (4) | 0.1326 (4) | 72 (5) | 89 (30) | 42 (3) | 3 (3) | 10 (3) | 0 (3) |
| C(10) | 0.1256 (6) | 0.1584 (5) | -0.0108 (5) | 118 (6) | 96 (30) | 56 (3) | -7 (4) | 30 (4) | -3 (3) |
| C(11) | -0.0146 (5) | 0.1949 (4) | 0.0223 (4) | 98 (6) | 96 (30) | 64 (4) | -13 (4) | 22 (3) | -12 (3) |
| C(12) | 0.2752 (6) | 0.4124 (5) | 0.1301 (6) | 93 (6) | 109 (30) | 52 (3) | -16 (4) | 7 (5) | 2 (4) |

ingly electron densities, phased on both sets, were computed. For every peak *X* on these maps the corresponding vectors of Cl⁻-*X* were verified on the sharpened Patterson function. Every such verified *X* position gave an intelligible molecular skeleton for the 15 non-hydrogen 'light' atoms for one Cl⁻ set but not for the other. The former proved to be the true set.

Full-matrix anisotropic least-squares refinement was carried out on the sixteen non-hydrogen atomic parameters with scattering factors taken from *International Tables for X-ray Crystallography* (1962) and using Hughess' (1941) weighting scheme with $|F_{\min}| = 0.75$ and unobserved reflections weighted as $\sqrt{3}|F_{\min}|$. Final positional and anisotropic thermal parameters for non-hydrogen atoms are given in Table 1. A difference Fourier synthesis showed all sixteen hydrogen atoms lying close to the positions expected theoretically. The theoretical positions, listed in Table 2, were incorporated into the final F_c calculations with scattering factors from *International Tables for X-ray Crystallography* (1962) and anisotropic thermal parameters the same as those of the atoms to which the hydrogen atoms are attached.

Table 2. Fractional coordinates of hydrogen atoms of the hydrochloride obtained theoretically, using C-H, 1.07 Å

| Hydrogen atom | Attached to | <i>x</i> | <i>y</i> | <i>z</i> |
|---------------|-------------|----------|----------|----------|
| 1 | N | -0.026 | 0.401 | 0.225 |
| 2 | N | -0.029 | 0.248 | 0.239 |
| 3 | C(2) | -0.373 | 0.138 | 0.210 |
| 4 | C(3) | -0.519 | 0.137 | 0.359 |
| 5 | C(4) | -0.538 | 0.317 | 0.467 |
| 6 | C(5) | -0.407 | 0.498 | 0.431 |
| 7 | C(6) | -0.258 | 0.499 | 0.284 |
| 8 | C(7) | -0.252 | 0.243 | 0.091 |
| 9 | C(7) | -0.251 | 0.397 | 0.091 |
| 10 | C(8) | -0.004 | 0.381 | 0.034 |
| 11 | C(9) | 0.212 | 0.267 | 0.216 |
| 12 | C(11) | -0.051 | 0.128 | 0.072 |
| 13 | C(11) | -0.098 | 0.210 | -0.049 |
| 14 | C(12) | 0.257 | 0.449 | 0.043 |
| 15 | C(12) | 0.237 | 0.475 | 0.184 |
| 16 | C(12) | 0.390 | 0.396 | 0.158 |

The final F_o , F_c listing is given in Table 3, the conventional *R* index for observed reflections being 0.099, and that for all reflections, 0.121.

Description of the structure

Bond lengths and interbond angles derived from Table 1, together with estimated standard deviations, are illustrated in Fig. 1(a) and (b). As stated earlier, the methyl group at C(9) is *trans* with respect to C(8)-N as postulated by Lukeš & Linhartová (1960). This can

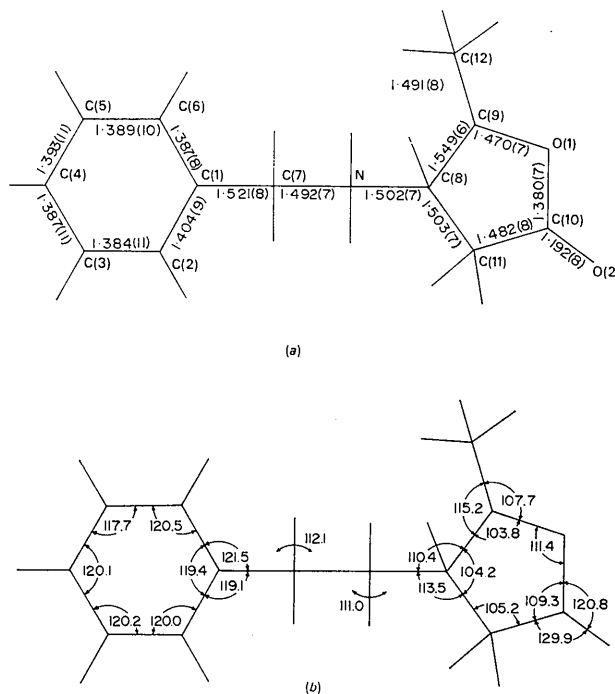


Fig. 1. Molecular geometry of the hydrochloride (schematic): (a) bond lengths, (b) interbond angles (e.s.d. ca. 1° in each case).

Table 3. F_o and F_c values for the hydrochloride

Asterisks refer to unobserved reflections with intensity assigned $\frac{1}{3}$ of the locally observed minimum (Hamilton, 1955).

| h | k | l | F_o | F_c | h | k | l | F_o | F_c | h | k | l | F_o | F_c | h | k | l | F_o | F_c | |
|-----|-----|-----|-------|-------|-----|-----|-----|-------|-------|-----|-----|-----|-------|-------|-----|-----|-----|-------|-------|-----|
| 1 | 0 | 0 | 100 | 100 | 1 | 0 | 0 | 100 | 100 | 1 | 0 | 0 | 100 | 100 | 1 | 0 | 0 | 100 | 100 | |
| 1 | 1 | 0 | 100 | 100 | 1 | 1 | 0 | 100 | 100 | 1 | 1 | 0 | 100 | 100 | 1 | 1 | 0 | 100 | 100 | 100 |
| 1 | 2 | 0 | 100 | 100 | 1 | 2 | 0 | 100 | 100 | 1 | 2 | 0 | 100 | 100 | 1 | 2 | 0 | 100 | 100 | 100 |
| 1 | 3 | 0 | 100 | 100 | 1 | 3 | 0 | 100 | 100 | 1 | 3 | 0 | 100 | 100 | 1 | 3 | 0 | 100 | 100 | 100 |
| 1 | 4 | 0 | 100 | 100 | 1 | 4 | 0 | 100 | 100 | 1 | 4 | 0 | 100 | 100 | 1 | 4 | 0 | 100 | 100 | 100 |
| 1 | 5 | 0 | 100 | 100 | 1 | 5 | 0 | 100 | 100 | 1 | 5 | 0 | 100 | 100 | 1 | 5 | 0 | 100 | 100 | 100 |
| 1 | 6 | 0 | 100 | 100 | 1 | 6 | 0 | 100 | 100 | 1 | 6 | 0 | 100 | 100 | 1 | 6 | 0 | 100 | 100 | 100 |
| 1 | 7 | 0 | 100 | 100 | 1 | 7 | 0 | 100 | 100 | 1 | 7 | 0 | 100 | 100 | 1 | 7 | 0 | 100 | 100 | 100 |
| 1 | 8 | 0 | 100 | 100 | 1 | 8 | 0 | 100 | 100 | 1 | 8 | 0 | 100 | 100 | 1 | 8 | 0 | 100 | 100 | 100 |
| 1 | 9 | 0 | 100 | 100 | 1 | 9 | 0 | 100 | 100 | 1 | 9 | 0 | 100 | 100 | 1 | 9 | 0 | 100 | 100 | 100 |
| 1 | 10 | 0 | 100 | 100 | 1 | 10 | 0 | 100 | 100 | 1 | 10 | 0 | 100 | 100 | 1 | 10 | 0 | 100 | 100 | 100 |
| 1 | 11 | 0 | 100 | 100 | 1 | 11 | 0 | 100 | 100 | 1 | 11 | 0 | 100 | 100 | 1 | 11 | 0 | 100 | 100 | 100 |
| 1 | 12 | 0 | 100 | 100 | 1 | 12 | 0 | 100 | 100 | 1 | 12 | 0 | 100 | 100 | 1 | 12 | 0 | 100 | 100 | 100 |
| 1 | 13 | 0 | 100 | 100 | 1 | 13 | 0 | 100 | 100 | 1 | 13 | 0 | 100 | 100 | 1 | 13 | 0 | 100 | 100 | 100 |
| 1 | 14 | 0 | 100 | 100 | 1 | 14 | 0 | 100 | 100 | 1 | 14 | 0 | 100 | 100 | 1 | 14 | 0 | 100 | 100 | 100 |
| 1 | 15 | 0 | 100 | 100 | 1 | 15 | 0 | 100 | 100 | 1 | 15 | 0 | 100 | 100 | 1 | 15 | 0 | 100 | 100 | 100 |
| 1 | 16 | 0 | 100 | 100 | 1 | 16 | 0 | 100 | 100 | 1 | 16 | 0 | 100 | 100 | 1 | 16 | 0 | 100 | 100 | 100 |
| 1 | 17 | 0 | 100 | 100 | 1 | 17 | 0 | 100 | 100 | 1 | 17 | 0 | 100 | 100 | 1 | 17 | 0 | 100 | 100 | 100 |
| 1 | 18 | 0 | 100 | 100 | 1 | 18 | 0 | 100 | 100 | 1 | 18 | 0 | 100 | 100 | 1 | 18 | 0 | 100 | 100 | 100 |
| 1 | 19 | 0 | 100 | 100 | 1 | 19 | 0 | 100 | 100 | 1 | 19 | 0 | 100 | 100 | 1 | 19 | 0 | 100 | 100 | 100 |
| 1 | 20 | 0 | 100 | 100 | 1 | 20 | 0 | 100 | 100 | 1 | 20 | 0 | 100 | 100 | 1 | 20 | 0 | 100 | 100 | 100 |
| 1 | 21 | 0 | 100 | 100 | 1 | 21 | 0 | 100 | 100 | 1 | 21 | 0 | 100 | 100 | 1 | 21 | 0 | 100 | 100 | 100 |
| 1 | 22 | 0 | 100 | 100 | 1 | 22 | 0 | 100 | 100 | 1 | 22 | 0 | 100 | 100 | 1 | 22 | 0 | 100 | 100 | 100 |
| 1 | 23 | 0 | 100 | 100 | 1 | 23 | 0 | 100 | 100 | 1 | 23 | 0 | 100 | 100 | 1 | 23 | 0 | 100 | 100 | 100 |
| 1 | 24 | 0 | 100 | 100 | 1 | 24 | 0 | 100 | 100 | 1 | 24 | 0 | 100 | 100 | 1 | 24 | 0 | 100 | 100 | 100 |
| 1 | 25 | 0 | 100 | 100 | 1 | 25 | 0 | 100 | 100 | 1 | 25 | 0 | 100 | 100 | 1 | 25 | 0 | 100 | 100 | 100 |
| 1 | 26 | 0 | 100 | 100 | 1 | 26 | 0 | 100 | 100 | 1 | 26 | 0 | 100 | 100 | 1 | 26 | 0 | 100 | 100 | 100 |
| 1 | 27 | 0 | 100 | 100 | 1 | 27 | 0 | 100 | 100 | 1 | 27 | 0 | 100 | 100 | 1 | 27 | 0 | 100 | 100 | 100 |
| 1 | 28 | 0 | 100 | 100 | 1 | 28 | 0 | 100 | 100 | 1 | 28 | 0 | 100 | 100 | 1 | 28 | 0 | 100 | 100 | 100 |
| 1 | 29 | 0 | 100 | 100 | 1 | 29 | 0 | 100 | 100 | 1 | 29 | 0 | 100 | 100 | 1 | 29 | 0 | 100 | 100 | 100 |
| 1 | 30 | 0 | 100 | 100 | 1 | 30 | 0 | 100 | 100 | 1 | 30 | 0 | 100 | 100 | 1 | 30 | 0 | 100 | 100 | 100 |
| 1 | 31 | 0 | 100 | 100 | 1 | 31 | 0 | 100 | 100 | 1 | 31 | 0 | 100 | 100 | 1 | 31 | 0 | 100 | 100 | 100 |
| 1 | 32 | 0 | 100 | 100 | 1 | 32 | 0 | 100 | 100 | 1 | 32 | 0 | 100 | 100 | 1 | 32 | 0 | 100 | 100 | 100 |
| 1 | 33 | 0 | 100 | 100 | 1 | 33 | 0 | 100 | 100 | 1 | 33 | 0 | 100 | 100 | 1 | 33 | 0 | 100 | 100 | 100 |
| 1 | 34 | 0 | 100 | 100 | 1 | 34 | 0 | 100 | 100 | 1 | 34 | 0 | 100 | 100 | 1 | 34 | 0 | 100 | 100 | 100 |
| 1 | 35 | 0 | 100 | 100 | 1 | 35 | 0 | 100 | 100 | 1 | 35 | 0 | 100 | 100 | 1 | 35 | 0 | 100 | 100 | 100 |
| 1 | 36 | 0 | 100 | 100 | 1 | 36 | 0 | 100 | 100 | 1 | 36 | 0 | 100 | 100 | 1 | 36 | 0 | 100 | 100 | 100 |
| 1 | 37 | 0 | 100 | 100 | 1 | 37 | 0 | 100 | 100 | 1 | 37 | 0 | 100 | 100 | 1 | 37 | 0 | 100 | 100 | 100 |
| 1 | 38 | 0 | 100 | 100 | 1 | 38 | 0 | 100 | 100 | 1 | 38 | 0 | 100 | 100 | 1 | 38 | 0 | 100 | 100 | 100 |
| 1 | 39 | 0 | 100 | 100 | 1 | 39 | 0 | 100 | 100 | 1 | 39 | 0 | 100 | 100 | 1 | 39 | 0 | 100 | 100 | 100 |
| 1 | 40 | 0 | 100 | 100 | 1 | 40 | 0 | 100 | 100 | 1 | 40 | 0 | 100 | 100 | 1 | 40 | 0 | 100 | 100 | 100 |
| 1 | 41 | 0 | 100 | 100 | 1 | 41 | 0 | 100 | 100 | 1 | 41 | 0 | 100 | 100 | 1 | 41 | 0 | 100 | 100 | 100 |
| 1 | 42 | 0 | 100 | 100 | 1 | 42 | 0 | 100 | 100 | 1 | 42 | 0 | 100 | 100 | 1 | 42 | 0 | 100 | 100 | 100 |
| 1 | 43 | 0 | 100 | 100 | 1 | 43 | 0 | 100 | 100 | 1 | 43 | 0 | 100 | 100 | 1 | 43 | 0 | 100 | 100 | 100 |
| 1 | 44 | 0 | 100 | 100 | 1 | 44 | 0 | 100 | 100 | 1 | 44 | 0 | 100 | 100 | 1 | 44 | 0 | 100 | 100 | 100 |
| 1 | 45 | 0 | 100 | 100 | 1 | 45 | 0 | 100 | 100 | 1 | 45 | 0 | 100 | 100 | 1 | 45 | 0 | 100 | 100 | 100 |
| 1 | 46 | 0 | 100 | 100 | 1 | 46 | 0 | 100 | 100 | 1 | 46 | 0 | 100 | 100 | 1 | 46 | 0 | 100 | 100 | 100 |
| 1 | 47 | 0 | 100 | 100 | 1 | 47 | 0 | 100 | 100 | 1 | 47 | 0 | 100 | 100 | 1 | 47 | 0 | 100 | 100 | 100 |
| 1 | 48 | 0 | 100 | 100 | 1 | 48 | 0 | 100 | 100 | 1 | 48 | 0 | 100 | 100 | 1 | 48 | 0 | 100 | 100 | 100 |
| 1 | 49 | 0 | 100 | 100 | 1 | 49 | 0 | 100 | 100 | 1 | 49 | 0 | 100 | 100 | 1 | 49 | 0 | 100 | 100 | 100 |
| 1 | 50 | 0 | 100 | 100 | 1 | 50 | 0 | 100 | 100 | 1 | 50 | 0 | 100 | 100 | 1 | 50 | 0 | 100 | 100 | 100 |
| 1 | 51 | 0 | 100 | 100 | 1 | 51 | 0 | 100 | 100 | 1 | 51 | 0 | 100 | 100 | 1 | 51 | 0 | 100 | 100 | 100 |
| 1 | 52 | 0 | 100 | 100 | 1 | 52 | 0 | 100 | 100 | 1 | 52 | 0 | 100 | 100 | 1 | 52 | 0 | 100 | 100 | 100 |
| 1 | 53 | 0 | 100 | 100 | 1 | 53 | 0 | 100 | 100 | 1 | 53 | 0 | 100 | 100 | 1 | 53 | 0 | 100 | 100 | 100 |
| 1 | 54 | 0 | 100 | 100 | 1 | 54 | 0 | 100 | 100 | 1 | 54 | 0 | 100 | 100 | 1 | 54 | 0 | 100 | 100 | 100 |
| 1 | 55 | 0 | 100 | 100 | 1 | 55 | 0 | 100 | 100 | 1 | 55 | 0 | 100 | 100 | 1 | 55 | 0 | 100 | 100 | 100 |
| 1 | 56 | 0 | 100 | 100 | 1 | 56 | 0 | 100 | 100 | 1 | 56 | 0 | 100 | 100 | 1 | 56 | 0 | 100 | 100 | 100 |
| 1 | 57 | 0 | 100 | 100 | 1 | 57 | 0 | 100 | 100 | 1 | 57 | 0 | 100 | 100 | 1 | 57 | 0 | 100 | 100 | 100 |
| 1 | 58 | 0 | 100 | 100 | 1 | 58 | 0 | 100 | 100 | 1 | 58 | 0 | 100 | 100 | 1 | 58 | 0 | 100 | 100 | 100 |
| 1 | 59 | 0 | 100 | 100 | 1 | 59 | 0 | 100 | 100 | 1 | 59 | 0 | 100 | 100 | 1 | 59 | 0 | 100 | 100 | 100 |
| 1 | 60 | 0 | 100 | 100 | 1 | 60 | 0 | 100 | 100 | 1 | 60 | 0 | 100 | 100 | 1 | 60 | 0 | 100 | 100 | 100 |
| 1 | 61 | 0 | 100 | 100 | 1 | 61 | 0 | 100 | 100 | 1 | 61 | 0 | 100 | 100 | 1 | 61 | 0 | 100 | 100 | 100 |
| 1 | 62 | 0 | 100 | 100 | 1 | 62 | 0 | 100 | 100 | 1 | 62 | 0 | 100 | 100 | 1 | 62 | 0 | 100 | 100 | 100 |
| 1 | 63 | 0 | 100 | 100 | 1 | 63 | 0 | 100 | 100 | 1 | 63 | 0 | 100 | 100 | 1 | 63 | 0 | 100 | 100 | 100 |
| 1 | 64 | 0 | 100 | 100 | 1 | 64 | 0 | 100 | 100 | 1 | 64 | 0 | 100 | 100 | 1 | 64 | 0 | 100 | 100 | 100 |
| 1 | 65 | 0 | 100 | 100 | 1 | 65 | 0 | 100 | 100 | 1 | 65 | 0 | 100 | 100 | 1 | 65 | 0 | 100 | 100 | 100 |
| 1 | 66 | 0 | 100 | 100 | 1 | 66 | 0 | 100 | 100 | 1 | 66 | 0 | 100 | 100 | 1 | 66 | 0 | 100 | 100 | 100 |
| 1 | 67 | 0 | 100 | 100 | 1 | 67 | 0 | 100 | 100 | 1 | 67 | 0 | 100 | 100 | 1 | 67 | 0 | 100 | 100 | 1 |

Atoms C(1), C(7), N and C(8) have closely similar y coordinates (Table 1) and hence are closely coplanar with the plane of Fig. 2. Thus the twist of the benzene ring with respect to this plane can be clearly seen. It is in fact 73.4° , reminiscent of the 70.5° in dibenzyl (Jeffrey, 1947). In the hydrobromide it is much nearer to the perpendicular value, 84.2° , as it is in the two other compounds discussed above,* namely in the benzylammonium ligands (86.7 and 87.4°) and in benzylazetidinium bromide, 89.7° . These results illustrate the flexibility of the benzyl system.

The molecular packing is shown in Fig. 3. The extended direction of the molecules lies normal to the y axis and close to the (102) plane. The molecules are so stacked that a Cl^- ion is closely associated with an NH_2^+ group (they overlap in y projection) either due to weak hydrogen bonding or ionic attraction, or both. The screw axes operate so as to make this into a spiral (Fig. 4). Centrosymmetrically related (as opposed to screw related) pairs of molecules have their lactone rings fairly close together and these are thus required

*Angles not given by the authors cited but calculated from their published data.

to be close to $y = \frac{1}{4}$ and $\frac{3}{4}$ (the actual mean of the lactone atom fractional y coordinates is 0.235).

Apart from possible hydrogen bonding between the nitrogen atom and Cl^- there are no non-bonded interactions of note. The $\text{Cl}^- \cdots \text{O}$ distances are all in excess of 3.74 \AA and $\text{N} \cdots \text{O}(2)$ at 3.265 \AA is too long for a hydrogen bond.

The packing resembles that of the hydrobromide which crystallizes in the $P2_1$ space group.

CRYSTAL STRUCTURE OF THE HYDROBROMIDE

Introduction

The collection of X-ray data for the hydrobromide actually preceded that for the corresponding hydrochloride but because the assigned space group seemed unlikely on chemical grounds, X-ray analysis was delayed until we could be certain that this assignment was correct. Analysis was then followed through to see how the molecule differed, if at all, from that of the corresponding hydrochloride.

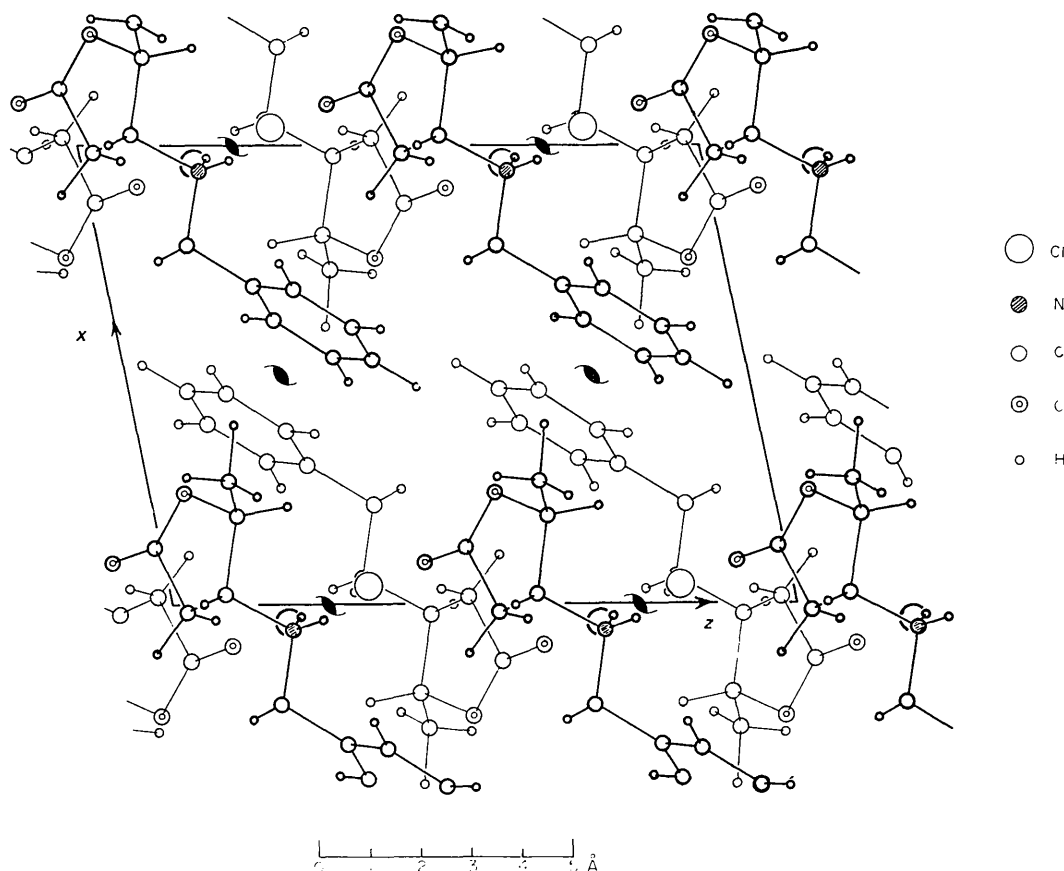


Fig. 3. Molecular packing of the hydrochloride in y projection.

Experimental

Colorless crystals were obtained from ethanol solution. Smaller specimens tended to be platy, larger crystals were prismatic. Two sets of intensity data were collected with Cu $K\alpha$ radiation, one by the multi-film photographic technique and the other by automated four-circle diffractometer in the ω - 2θ scan mode.

The calculated linear absorption coefficient for Cu $K\alpha$ radiation is 49.08 cm^{-1} . For both sets of data the crystal was a prismatic needle about $0.1 \times 0.1 \text{ mm}$ in cross section and about 0.75 mm long. No absorption corrections were applied to either set of intensities.

Cell dimensions were obtained by Al-wire calibration of the photographs as for the hydrochloride. The dimensions were later checked from diffractometer settings and found to match exactly. Accordingly no refinement of cell parameters from diffractometer settings was carried out.

Crystal data are:

$\text{C}_{12}\text{H}_{16}\text{BrNO}_2$, M.W. 287.1

Monoclinic (space group, see text)

$a = 6.612 (1)$, $b = 10.824 (3)$, $c = 9.054 (2) \text{ \AA}$.

$\beta = 98.4 (3)^\circ$ $V = 641.04 \text{ \AA}^3$

$\rho = 1.50 \text{ g.cm}^{-3}$ (chloroform-carbon tetrachloride),
calculated for $Z = 2$ molecules per cell, 1.499 g.cm^{-3} .

Systematic absences were only $0k0$ for k odd, implying either space group $P2_1$ or $P2_1/m$. However the latter would require the molecule to have either m symmetry, which would be highly improbable on stereochemical grounds, or $\bar{1}$ symmetry which is impossible. However $P2_1$ requires the crystal to be composed of molecules of one hand only, whereas the chemical preparation would generate both enantiomers in equal amounts. The case for $P2_1$ was however strengthened by $N(z)$ tests (Howells, Phillips & Rogers, 1950; Hargreaves & Gogoi, 1966) indicating a centric $h0l$ zone and acentric $0kl$ zone. Spontaneous resolution on crystallization from the racemic solution seemed to be the only likely explanation. We were able to confirm

this as follows. Methanol solutions of the compound were allowed to evaporate slowly over several weeks and from the crystalline deposit eight of the largest crystals, several mm in overall dimensions, were picked out. Although we could not be sure that each was a

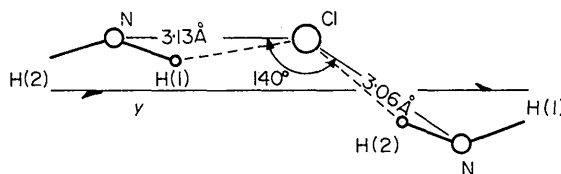


Fig. 4. The $\text{NH}_2^+ \cdots \text{Cl}^- \cdots \text{NH}_2^+$ spiral along y .

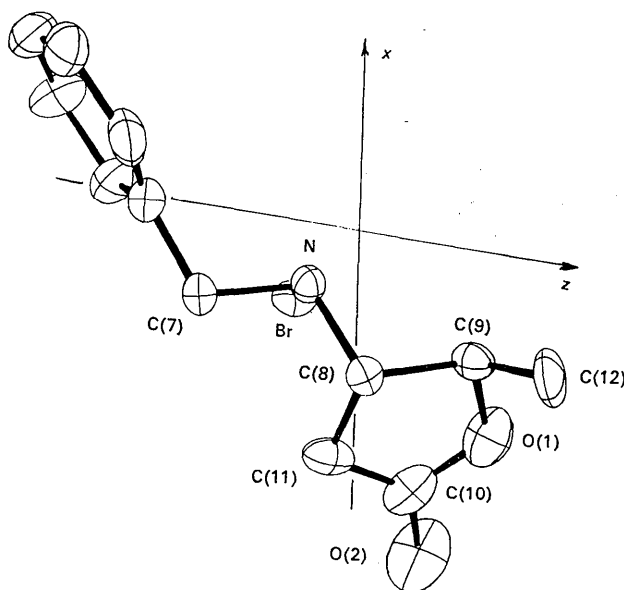


Fig. 5. Molecule of hydrobromide in y projection viewed from about 20 \AA with 40% probability thermal ellipsoids (Johnson, 1965).

Table 5. Fractional coordinates and anisotropic thermal parameters of non-hydrogen atoms of the hydrobromide

Temperature factor in form: $10^{-4} \exp [-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

| | x | y | z | β_{11} | β_{22} | β_{33} | β_{12} | β_{13} | β_{23} |
|-------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Br | 0.1962 (1) | 0.2500 (1) | 0.0962 (1) | 273 (2) | 69 (1) | 228 (1) | -19 (2) | 58 (1) | -18 (1) |
| N | -0.1420 (1) | 0.0549 (6) | -0.0646 (8) | 244 (17) | 65 (6) | 161 (10) | -21 (8) | 36 (10) | -7 (6) |
| O(1) | -0.4169 (16) | -0.0369 (7) | 0.2200 (9) | 662 (34) | 96 (7) | 233 (13) | -13 (13) | 162 (18) | 48 (8) |
| O(2) | -0.7174 (20) | -0.1076 (11) | 0.1128 (14) | 691 (40) | 177 (14) | 564 (34) | -229 (23) | 294 (29) | -96 (17) |
| C(1) | -0.0149 (14) | 0.0830 (8) | -0.3073 (9) | 336 (25) | 92 (8) | 126 (10) | -7 (11) | 44 (13) | 5 (8) |
| C(2) | 0.0227 (19) | -0.0254 (10) | -0.3732 (12) | 461 (35) | 107 (10) | 191 (15) | -12 (15) | 99 (18) | -5 (10) |
| C(3) | 0.1809 (20) | -0.0345 (12) | -0.4602 (15) | 509 (43) | 138 (14) | 252 (19) | 19 (19) | 143 (24) | -24 (14) |
| C(4) | 0.2973 (19) | 0.0670 (15) | -0.4815 (12) | 420 (35) | 207 (18) | 172 (15) | -27 (21) | 79 (19) | 13 (14) |
| C(5) | 0.2630 (20) | 0.1747 (14) | -0.4124 (12) | 397 (32) | 168 (16) | 199 (17) | -64 (19) | 51 (19) | 42 (13) |
| C(6) | 0.1075 (18) | 0.1859 (10) | -0.3245 (11) | 469 (34) | 117 (10) | 145 (13) | -27 (16) | 27 (17) | 12 (9) |
| C(7) | -0.1907 (16) | 0.0973 (11) | -0.2244 (10) | 358 (28) | 150 (13) | 131 (12) | 50 (15) | 56 (14) | 24 (10) |
| C(8) | -0.3116 (13) | 0.0833 (8) | 0.0240 (10) | 279 (22) | 69 (7) | 159 (11) | 5 (10) | 55 (13) | -5 (8) |
| C(9) | -0.2530 (15) | 0.0466 (10) | 0.1880 (11) | 303 (25) | 121 (10) | 182 (14) | 48 (14) | 67 (15) | 40 (10) |
| C(10) | -0.5646 (22) | -0.0488 (10) | 0.0981 (17) | 540 (46) | 87 (10) | 302 (25) | 61 (17) | 163 (29) | -49 (13) |
| C(11) | -0.5090 (18) | 0.0101 (12) | -0.0325 (10) | 256 (21) | 105 (9) | 173 (18) | 18 (11) | 49 (18) | -2 (12) |
| C(12) | -0.2478 (17) | 0.1566 (13) | 0.2919 (12) | 417 (33) | 184 (16) | 159 (14) | -89 (20) | 42 (17) | -34 (12) |

single crystal, they were separately dissolved in the minimum of ethanol and the solution checked by plane polarized light. Four solutions gave +ve rotation, two -ve and the other two a rotation too small to be determined with certainty. Clearly spontaneous resolution had occurred, a phenomenon not as rare as sometimes suspected (Secor, 1963).

Structure analysis was carried out on the photographic intensity data, the diffractometer data were used for refinement and are those listed (Table 5).

A total of 1404 photographic intensities were collected and measured out of a possible 1493. A three-dimensional sharpened Patterson function was computed using $F^2 = F_o^2 / (\sum f_r) \exp(-2.5 \sin^2 \theta / \lambda^2)$, $\sum f_r$ being the sum of the scattering factors per unit cell. The Harker section $v = \frac{1}{2}$ yielded Br^- ion (x, z) coordinates of (0.197, 0.0965) and y was set arbitrarily to $\frac{1}{4}$. Electron density phased on Br^- positions had, of course, false symmetry $P2_1/m$ but it was easy to pick out at least 15 independent non-hydrogen atoms of one molecule by carefully checking against the Patterson map.

Refinement, although uneventful, was not completely satisfactory. A final conventional R of 0.097 was reached but there were a number of inexplicable photographic intensity discrepancies and the difference map calculated to determine hydrogen atom positions was poorly defined. Accordingly a complete new set of data was collected by diffractometer. A total of 1170 reflections were measured, only 7 of which were too weak to be considered observable. Refinement com-

menced with the atomic parameters found from the photographic data (hydrogen atoms excluded). We used the $XFLS$ variant of $ORFLS$ (Ellison, 1967) with scattering factors including anomalous dispersion taken from *International Tables for X-ray Crystallography* (1962).

When refinement had converged to a conventional R index of 0.058 a difference Fourier synthesis was carried out but there were no clearly resolved hydrogen peaks. Accordingly we calculated hypothetical positions for all hydrogen atoms except those of the methyl group. When these were included with the same anisotropic thermal parameters as the atoms to which these are attached, R fell to 0.052 (all reflections) and the non-hydrogen parameters changed slightly; their final values are given in Table 5. The 40% probability ellipsoids are plotted *via ORTEP* in Fig. 5. (Johnson, 1965). The hydrogen atom positions were again slightly adjusted but the new values were not included in the F_c calculation. These hydrogen atom positions are given in Table 6 and final F_c and F_o values in Table 7. The three hydrogen atoms attached to C(12) were excluded owing to uncertainty in their location.

Table 6. Fractional coordinates of hydrogen atoms of the hydrobromide obtained theoretically, using C-H, 1.07 Å

| Hydrogen atom | Attached to | x | y | z |
|---------------|-------------|--------|--------|--------|
| 1 | N | -0.138 | -0.044 | -0.073 |
| 2 | N | 0.039 | 0.088 | 0.035 |
| 3 | C(2) | -0.068 | -0.101 | -0.358 |
| 4 | C(3) | 0.212 | -0.117 | -0.509 |
| 5 | C(4) | 0.397 | 0.063 | -0.542 |
| 6 | C(5) | 0.356 | 0.250 | -0.426 |
| 7 | C(6) | 0.083 | 0.269 | -0.273 |
| 8 | C(7) | -0.362 | 0.056 | -0.324 |
| 9 | C(7) | -0.215 | 0.195 | -0.221 |
| 10 | C(8) | -0.350 | 0.180 | -0.005 |
| 11 | C(9) | -0.076 | 0.004 | 0.260 |
| 12 | C(11) | -0.494 | -0.065 | -0.102 |
| 13 | C(11) | -0.666 | 0.065 | -0.125 |

Description of the structure

Bond lengths and interbond angles obtained from the coordinates of Table 5 are given in Fig. 6(a) and (b). The methyl group at C(9) is *trans* with respect to C(8)-N as in the hydrochloride, but the lactone ring itself shows significant differences. Whereas in the latter C(8) is at the envelope 'flap', in the hydrobromide C(11) is at the flap, being 0.12 Å out of plane on the 'nitrogen side' of the ring (see Table 8). The differences in the lactone ring of the hydrochloride and the hydrobromide can be most easily recognized (Fig. 7) by use of a molecular least-squares fit on atoms C(4), C(1), C(7), N and C(8) of the two molecules (Nyburg, 1969). The conclusion that the lactone ring is flexible enough to respond to packing forces seems inescapable. There is some clue to this. If, in the hydrochloride, one lists all the non-bonded halide distances less than 4 Å then

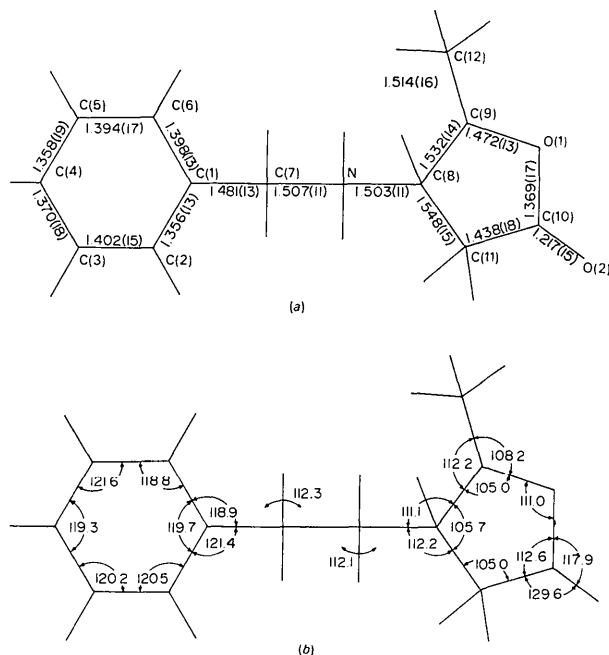


Fig. 6. (a) Bond lengths and (b) interbond angles of the hydrobromide (schematic).

3-BENZYLAMINO-4-HYDROXYBUT-2-ENOIC ACID LACTONE

Table 7. F₀ and F_C values for the hydrobromide

Second column 10F₀, third column 10F_C.

Table with multiple columns containing numerical data for various parameters (H=0, H=1, H=2, H=3, H=4, H=5, H=6, H=7, H=8, H=9, H=10) and their corresponding F0 and FC values. The table is organized into vertical columns for each H value, with sub-columns for F0 and FC. Some columns include additional labels like 'H=0', 'H=1', etc., and some rows include additional labels like 'H=0', 'H=1', etc.

C(8) appears three times in the list with C(8)-Cl⁻ distances 3.49, 3.56 and 3.67 Å, whereas other lactone ring atoms appear only once in the list. Conversely, in the hydrobromide, only C(11) appears twice, with C(11)-Br⁻ 3.55 and 3.59 Å; C(10) appears only once and the rest not at all. There seems to be a *prima facie* case therefore for concluding that the relatively large interatomic forces between halide ions and carbon atoms are responsible for the observed lactone ring variations.

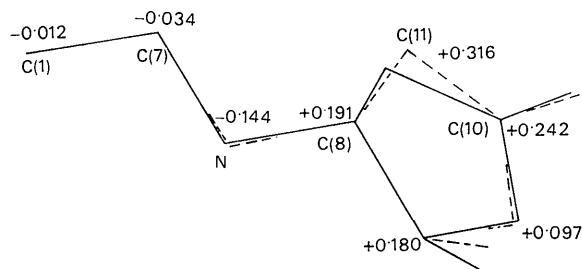


Fig. 7. Projection of the molecule of hydrochloride and hydrobromide (broken lines) compared by best least-squares fit of atoms C(4), C(1), C(7), N and C(8). Separation of corresponding atoms normal to the plane of the diagram is given in Å.

Table 8. Displacements, δ , of lactone atoms of the hydrobromide from the best least-squares plane through O(1), C(8), C(9) and C(10)

| | δ |
|-------|----------|
| O(1) | 0.010 Å |
| C(8) | 0.005 |
| C(9) | -0.009 |
| C(10) | -0.006 |
| C(11) | 0.123 |

The equation of the plane is $0.5319X - 0.7955Y - 0.2903Z = -1.876$ where X, Y, Z are real orthogonal coordinates with axes X along x and Z along z^* .

The remaining features of the hydrobromide molecule compare well with those of the hydrochloride except, as we noted in the previous paper (Jones *et al.*, 1968), the lengths of C(1)-C(7) and C(7)-N are reversed in order; in addition the plane C(1)-C(7)-N is more nearly perpendicular, 84.2° , to the plane of the benzene ring than in the hydrochloride, 73.4° .

Molecular packing

Fig. 8 shows the crystal structure in y projection. Although the space groups are different there is a very close relation between the packing in the hydrobromide

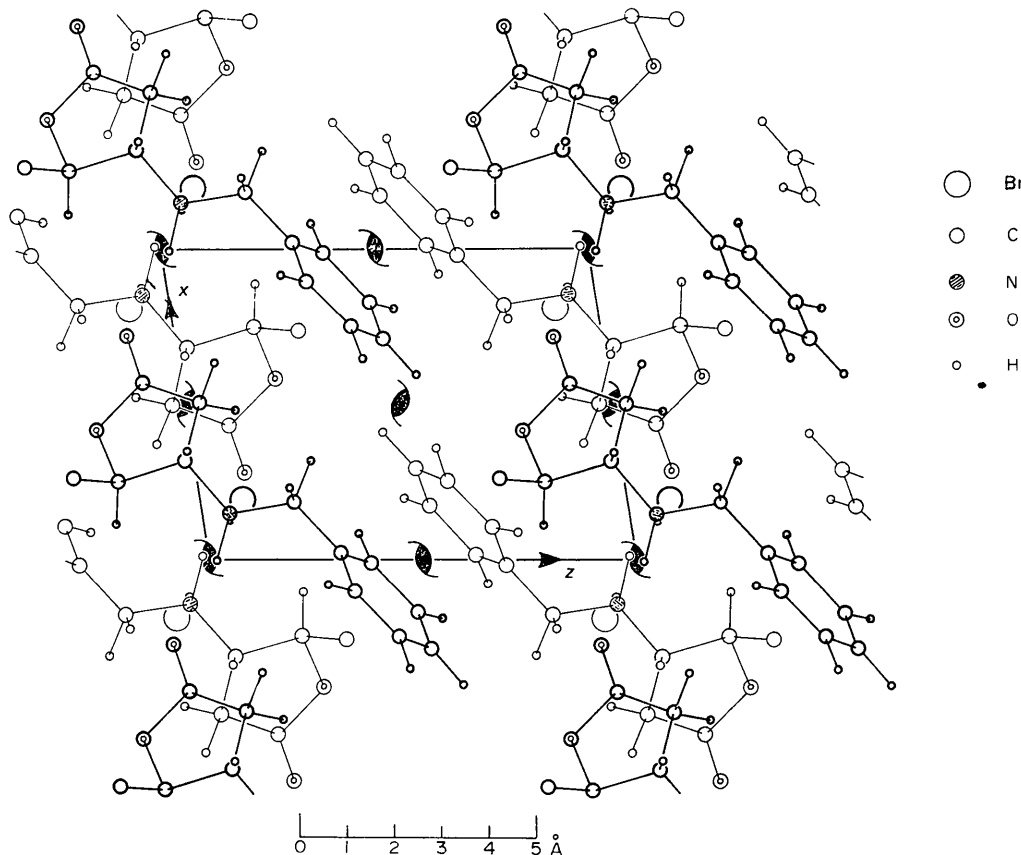


Fig. 8. Structure of the hydrobromide in y projection.

and that in the hydrochloride. This can be seen by a suitable comparison of the two projections (Fig. 9). In the hydrochloride the two enantiomorphously related molecules have been designated *L* and *R*, in the hydrobromide *R* has been arbitrarily assigned to all the molecules. The essential difference between the two modes of packing is that centers of symmetry relating *L* and *R* molecules in the hydrochloride are replaced by screw axes relating molecules of the same hand in the hydrobromide.

The Br^- ions are located adjacent to the NH_2^+ ion in a way similar to that for Cl^- in the hydrochloride. The actual dimensions are given in Fig. 10.

As in the hydrochloride, no non-bonded interactions call for special comment.

Computer programs used were local variants of *ORFLS* (Busing, Martin & Levy, 1962) and *ORFFE* (Busing, Martin & Levy, 1964).

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References

- BONAMICO, M. & DESSY, G. (1967). *Theor. Chim. Acta*, **7**, 367.
- BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). Report ORNL-TM-305, Oak Ridge National Laboratory, Tennessee.
- BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1964). Report ORNL-TM-306, Oak Ridge National Laboratory, Tennessee.
- DICKENS, F. & JONES, H. E. H. (1961). *Brit. J. Cancer*, **15**, 85.
- ELLISON, R. D. (1967). Private Communication.
- HAMILTON, W. C. (1955). *Acta Cryst.* **8**, 185.
- HARGREAVES, A. & GOGOI, B. N. (1966). *Acta Cryst.* **21**, 27.
- HOWELLS, E. R., PHILLIPS, D. C. & ROGERS, D. (1950). *Acta Cryst.* **3**, 210.
- HUGHES, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737.
- International Tables for X-ray Crystallography* (1962). Vol. III p. 202. Birmingham. Kynoch Press.
- JEFFREY, G. A. (1947). *Proc. Roy. Soc. A* **188**, 222.
- JOHNSON, C. K. (1965). Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee.
- JONES, J. B., KOO, C. H., MELLOR, I. P. NYBURG, S. C. & YOUNG, J. M. (1968). *Canad. J. Chem.* **46**, 813.
- LUKEŠ, R. & LINHARTOVÁ, Z. (1960). *Coll. Czech. Chem. Comm.* **25**, 502.
- MORET, C. L. & TREFONAS, L. M. (1968). *J. Hetero. Chem.* **5**, 149.
- NYBURG, S. C. (1969). *Best Molecular Fit* (local program).
- SECOR, R. M. (1963). *Chem. Rev.* **63**, 297.

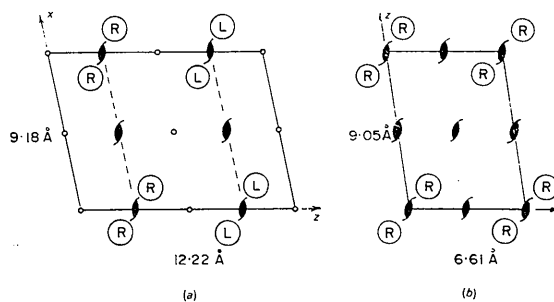


Fig. 9. Scale drawings comparing (a) the hydrochloride and (b) the hydrobromide. The region between broken lines in (a) should be compared with (b). The *R, L* designation is arbitrary and the symbols are located on the bonds C(7)-N, in both cases.

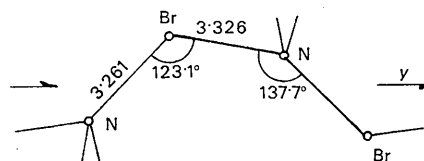


Fig. 10. The $\text{NH}_2^+\cdots\text{Br}^-\cdots\text{NH}_2$ spiral along *y*.