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# γ-(Aminocarbonyl)-*N*-methyl-*N*,*N*-bis-(1-methylethyl)-γ-phenylbenzenepropanamine Iodide (Isopropamide Iodide)

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**Abstract.** $(C_{23}H_{33}N_2O)^+I^-$, F.W. 479·9; orthorhombic, $P2_12_12_1$; $a=17\cdot548$ (5), $b=14\cdot564$ (4), $c=8\cdot993$ (3) Å; $Z=4$.

**Introduction.** Cooling of a saturated solution in boiling water yielded transparent colourless crystals of this potent anticholinergic agent. The space group was determined from rotation and Weissenberg photographs. The final cell dimensions and intensities were measured on a Hilger and Watts computer-controlled four-circle diffractometer. The experimental conditions are given in Table 1. No corrections were applied for absorption. The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). The most probable set of phases gave the position of the $I^-$ ion and the remaining atoms were located on a subsequent Fourier map. Isotropic and anisotropic full-matrix least-squares refinement gave a final $R$ of 0·05 for all observed reflexions. The scattering factors used are those given in *International Tables for X-ray Crystallography* (1962). The final coordinates and thermal parameters are given in Table 2.*

Table 1. *Experimental conditions*

Crystal dimensions: 0·08 × 0·1 × 0·5 mm
Source: Mo $K\alpha$, $\lambda=0\cdot7114$ Å; $\omega$–$2\theta$ step scan
$\theta_{\max}=58°$
Confidence level: 3·0
Total number of independent reflexions: 2316
Total observed: 2055

Table 2. *Final positional and thermal parameters* (× $10^4$) *with standard deviations in parentheses*

$$T=\exp\left[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)\right].$$

| | $x$ | $y$ | $z$ | $B_{11}$ | $B_{22}$ | $B_{33}$ | $B_{12}$ | $B_{13}$ | $B_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| I | 1238 (0) | 989 (0) | 8571 (1) | 38 | 46 | 174 | −3 | −8 | 0 |
| O | 4188 (4) | 2173 (4) | 6007 (7) | 54 | 43 | 124 | 0 | −27 | 16 |
| N(1) | 3587 (5) | 1473 (4) | 4127 (9) | 53 | 33 | 142 | −5 | −6 | −10 |
| N(2) | 5001 (4) | 4872 (4) | 6360 (8) | 29 | 35 | 94 | −4 | −9 | −11 |
| C(1) | 3637 (4) | 3173 (5) | 4166 (8) | 25 | 31 | 74 | −4 | 1 | −5 |
| C(2) | 3539 (4) | 3064 (5) | 2448 (9) | 31 | 20 | 92 | 0 | −4 | −3 |
| C(3) | 4187 (6) | 3143 (6) | 1512 (10) | 61 | 34 | 81 | 9 | 23 | 8 |
| C(4) | 4091 (5) | 2966 (6) | −29 (9) | 40 | 34 | 85 | 6 | 6 | −7 |
| C(5) | 3378 (6) | 2710 (6) | −600 (10) | 53 | 30 | 109 | 9 | −5 | −16 |
| C(6) | 2759 (6) | 2647 (7) | 311 (11) | 43 | 44 | 124 | −2 | −24 | −21 |
| C(7) | 2818 (5) | 2840 (5) | 1835 (9) | 34 | 41 | 114 | −5 | −13 | −9 |
| C(8) | 2887 (4) | 3532 (5) | 4811 (9) | 25 | 31 | 85 | 0 | −5 | −9 |
| C(9) | 2431 (5) | 3010 (6) | 5781 (9) | 29 | 49 | 100 | −4 | −3 | −3 |
| C(10) | 1739 (5) | 3390 (7) | 6288 (11) | 44 | 62 | 98 | −8 | 18 | −8 |
| C(11) | 1518 (5) | 4261 (7) | 5904 (11) | 37 | 65 | 115 | 3 | 3 | −9 |
| C(12) | 1966 (5) | 4791 (6) | 4937 (11) | 36 | 49 | 133 | 10 | −7 | −10 |
| C(13) | 2652 (5) | 4414 (5) | 4414 (11) | 36 | 26 | 149 | 0 | −9 | −6 |
| C(14) | 3839 (5) | 2227 (5) | 4837 (9) | 29 | 34 | 113 | 2 | −2 | 8 |
| C(15) | 4316 (4) | 3846 (5) | 4438 (9) | 27 | 36 | 96 | −10 | −10 | −6 |
| C(16) | 4342 (4) | 4206 (5) | 6064 (8) | 28 | 38 | 93 | −9 | 0 | −7 |
| C(17) | 5006 (6) | 4993 (7) | 8084 (9) | 48 | 65 | 64 | −7 | −14 | −17 |
| C(18) | 5756 (5) | 4485 (6) | 5806 (13) | 30 | 40 | 213 | −1 | −6 | −7 |
| C(19) | 5902 (6) | 3517 (6) | 6537 (15) | 49 | 46 | 221 | 3 | −13 | −5 |
| C(20) | 6444 (4) | 5098 (8) | 6261 (16) | 17 | 88 | 320 | −19 | −9 | −38 |
| C(21) | 4877 (5) | 5853 (5) | 5712 (11) | 44 | 21 | 156 | −4 | −8 | 7 |
| C(22) | 5007 (8) | 5884 (7) | 3975 (10) | 95 | 51 | 107 | −19 | −31 | 42 |
| C(23) | 4104 (6) | 6223 (7) | 6138 (20) | 34 | 56 | 463 | 28 | 6 | 17 |

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31537 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

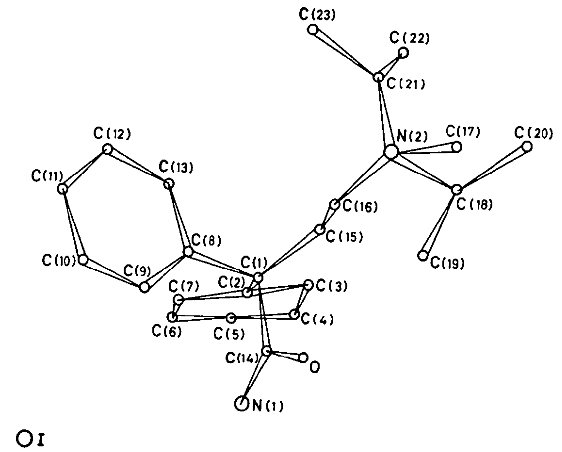

Fig. 1. Conformation and atomic numbering of $(C_{23}H_{33}N_2O)^+I^-$.

**Discussion.** The conformation of the molecule and the numbering scheme are shown in Fig. 1 and the bond distances and angles in Table 3. The torsion angles defining the conformation are given in Table 4.

Table 3. *Intramolecular bond distances* (Å) *and angles* (°)

(Standard deviations are 0·01 Å for distances and 0·6° for angles.)

| | | | |
|---|---|---|---|
| C(1)-C(2) | 1·56 | C(10)-C(11) | 1·37 |
| C(1)-C(8) | 1·53 | C(11)-C(12) | 1·40 |
| C(1)-C(14) | 1·54 | C(12)-C(13) | 1·40 |
| C(1)-C(15) | 1·56 | C(14)-N(1) | 1·34 |
| C(2)-C(3) | 1·42 | C(14)-O | 1·22 |
| C(3)-C(4) | 1·42 | C(15)-C(16) | 1·55 |
| C(4)-C(5) | 1·40 | C(16)-N(2) | 1·53 |
| C(5)-C(6) | 1·36 | N(2)—C(17) | 1·56 |
| C(6)-C(1) | 1·40 | N(2)—C(18) | 1·52 |
| C(7)-C(2) | 1·42 | N(2)—C(21) | 1·56 |
| C(8)-C(9) | 1·41 | C(18)-C(19) | 1·58 |
| C(8)-C(13) | 1·40 | C(18)-C(20) | 1·56 |
| C(9)-C(10) | 1·41 | C(21)-C(22) | 1·58 |
| | | C(21)-C(23) | 1·51 |

| | | | |
|---|---|---|---|
| C(8)—C(1)—C(14) | 110·7 | C(11)-C(12)-C(13) | 118·2 |
| C(8)—C(1)—C(2) | 108·4 | C(12)-C(13)-C(8) | 121·8 |
| C(8)—C(1)—C(15) | 112·5 | C(1)—C(14)-O | 120·6 |
| C(14)-C(1)—C(2) | 108·7 | C(1)—C(14)-N(1) | 117·8 |
| C(14)-C(1)—C(15) | 108·9 | N(1)—C(14)-O | 121·5 |
| C(2)—C(1)—C(15) | 107·7 | C(1)—C(15)-C(16) | 112·5 |
| C(1)—C(2)—C(7) | 120·4 | C(15)-C(16)-N(2) | 113·5 |
| C(1)—C(2)—C(3) | 119·4 | N(2)—C(18)-C(19) | 109·6 |
| C(7)—C(2)—C(3) | 120·1 | N(2)—C(18)-C(20) | 112·1 |
| C(2)—C(3)—C(4) | 118·0 | C(19)-C(18)-C(20) | 106·1 |
| C(3)—C(4)—C(5) | 120·8 | N(2)—C(21)-C(22) | 112·1 |
| C(4)—C(5)—C(6) | 120·5 | N(2)—C(21)-C(23) | 111·0 |
| C(5)—C(6)—C(7) | 121·0 | C(22)-C(21)-C(23) | 111·8 |
| C(6)—C(7)—C(2) | 119·5 | C(16)-N(2)—C(17) | 104·4 |
| C(1)—C(8)—C(9) | 122·6 | C(16)-N(2)—C(18) | 111·4 |
| C(1)—C(8)—C(13) | 118·1 | C(16)-N(2)—C(21) | 114·2 |
| C(9)—C(8)—C(13) | 119·3 | C(17)-N(2)—C(18) | 111·2 |
| C(8)—C(9)—C(10) | 118·5 | C(17)-N(2)—C(21) | 105·5 |
| C(9)—C(10)-C(11) | 121·8 | C(18)-N(2)—C(21) | 109·8 |
| C(10)-C(11)-C(12) | 120·4 | | |

Table 4. *Torsional angles defining the conformation of the molecule*

| | |
|---|---|
| C(9)—C(8)—C(1)—C(15) | −127° |
| C(3)—C(2)—C(1)—C(15) | 30 |
| N(1)—C(14)-C(1)—C(15) | −145 |
| C(14)-C(1)—C(15)-C(16) | −77 |
| C(2)—C(1)—C(15)-C(16) | 165 |
| C(1)—C(15)-C(16)-N(2) | 180 |
| C(15)-C(16)-N(2)—C(17) | −170 |
| C(15)-C(16)-N(2)—C(21) | 75 |
| C(15)-C(16)-N(2)—C(18) | −50 |
| C(16)-N(2)—C(21)-C(22) | −76 |
| C(16)-N(2)—C(21)-C(23) | 49 |
| C(16)-N(2)—C(18)-C(19) | −56 |
| C(16)-N(2)—C(18)-C(20) | −173 |

Structurally isopropamide is related to benzetimide, another potent and persistent anticholinergic agent. In the latter it was shown that this rigid molecule fits into a footprint of the *trans* conformation of acetylcholine which has been associated with muscarinic activity (Spek, Peerdeman, van Wijngaarden & Soudijn, 1971). The structure of isopropamide can be superimposed on that of benzetimide after a rotation of 180° about C(1)-C(15). The distances between corresponding groups are given in Table 5. The numbering of the atoms in benzetimide refers to the original paper (Koch & Dideberg, 1973); *A* is the centre of the phenyl rings. The great similarity in the spatial structures of isopropamide and benzetimide suggests that both compounds interact with the same receptors.

Table 5. *Distances* (Å) *between corresponding groups in benzetimide* (*B*) *and isopropamide, in the crystal* (I*a*), *and after a rotation of* 180° *about* C(1)–C(15), (I*b*)

| *B* | | | (I*a*) | (I*b*) |
|---|---|---|---|---|
| N(2)-C(5) | 5·24 | N(2)-C(14) | 4·57 | 4·76 |
| N(2)-O(2) | 5·30 | N(2)-O | 4·19 | 4·91 |
| N(2)-N(1) | 6·41 | N(2)-N(1) | 5·89 | 5·74 |
| N(2)-*A* | 6·28 | N(2)-*A*[C(8)-C(13)] | 5·19 | 6·35 |
| N(2)-C(4) | 4·38 | N(2)-C(1) | 3·97 | 3·96 |
| O(2)-*A* | 4·24 | O——*A*[C(8)-C(13)] | 4·34 | 4·30 |
| N(1)-*A* | 4·31 | N(1)-*A*[C(8)-C(13)] | 4·43 | 4·38 |

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