# Crystal and Molecular Structure of Isopropamide Iodide [4-Di-isopropylamino-2,2-diphenylbutyramide Methiodide]

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The structure of the title compound (I) has been determined by single-crystal *X*-ray diffraction. Crystals are orthorhombic in a unit cell of dimensions $a$ = 17.624(6), $b$ = 14.589(5), $c$ = 9.012(4) Å, space group $P2_12_12_1$, $Z$ = 4. The structure was solved by Patterson and Fourier methods and refined by least squares to $R$ 0.055 for 1 241 observed diffractometer data. All hydrogen atoms were located. The angle between the two phenyl groups is 82°. The amide group is planar and makes angles of 84 and 89° with the two phenyl groups.

ISOPROPAMIDE is an anticholinergic drug [1] and its iodide (I), $[H_2N\cdot C(:O)\cdot CPh_2\cdot[CH_2]_2\cdot\overset{+}{N}(CHMe_2)_2Me]I$, was chosen for structure determination as a part of systematic studies of drugs affecting the cholinergic nervous system.

## EXPERIMENTAL

Crystals of (I) grown from ethanol are elongated along $c$ with the following form: pinacoids {100}, {010}, and prisms {110}, {011}, and {101}. Crystals were examined under a polarizing microscope. A section normal to the acute bisectrix was examined in plane polarised convergent light and the sign of the crystal was determined to be positive.

*Crystal Data.*—$C_{23}H_{33}IN_2O$, $M$ = 480.42. Orthorhombic, $a$ = 17.624(6), $b$ = 14.589(5), $c$ = 9.012(4), $U$ = 2 317(1) Å$^3$, $D_m$ = 1.39(1) g cm$^{-3}$ (by flotation), $Z$ = 4, $D_c$ = 1.38 g cm$^{-3}$. Space group $P2_12_12_1$ ($D_2^4$) from systematic absences. Mo-$K_\alpha$ radiation, $\lambda$ = 0.710 7 Å, $\mu$(Mo-$K_\alpha$) = 16.1 cm$^{-1}$.

Space group and preliminary cell parameters were determined from oscillation and precession photographs. Refined cell-parameters and standard deviations were determined by use of the cell refinement program described in ref. 2.

*Intensity Measurement.*—Three-dimensional *X*-ray diffraction data from a single crystal (0.18 × 0.10 × 0.30 mm) of the title compound were collected on a computer-controlled [2] Stoe four-circle diffractometer by use of Mo-$K_\alpha$ radiation [graphite monochromator (002)]. A coupled $\theta$—$2\theta$ step scan with $\Delta 2\theta$ 0.04°, a counting time of 6 s per step, and a peak width of 1.4° were used. In the range $2\theta$ 5—60°, 3 268 observations covering one octant of reciprocal space were collected of which 1 241 were considered observed, having $I \geqslant 3\sigma(I)$, and were corrected for Lorentz and polarisation effects. No corrections for absorption were made.

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[1] The Merck Index 589, 8th edn., 1968.

[2] W. R. Busing, R. D. Ellison, H. A. Levy, S. P. King, and R. T. Rosebery, U.S. Atomic Energy Commission, Report ORNL 143, 1968.

*Structure Solution and Refinement*.—The position of the iodide ion was found from an unsharpened Patterson synthesis. A Fourier synthesis using observed data phased on the iodide ion produced a satisfactory trial structure. After successive cycles of full-matrix least-squares refinement of positional and anisotropic thermal parameters, a difference electron-density synthesis revealed all the hydrogen atom positions. The hydrogen-atom contribution to the calculated structure factors was included but not refined and non-hydrogen atoms refined until all parameter shifts were $<0.1\sigma$. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$ with $w = 4I/S^2$ where $S = \sigma(I) + 0.05I$. The term $0.05I$, added to the statistical standard deviation, was included because of long-term fluctuation in intensity measurement of the standard reflection, measured every 25 reflections. Atomic scattering factors for neutral carbon, nitrogen, oxygen, and for the iodide ion were taken from ref. 3 and for hydrogen from ref. 4. Final cycles of refinement were carried out on the two possible mirror-images of the molecule taking anomalous dispersion into account. The final values of *R* are 0.058 and 0.054. Atomic parameters (Tables 1 and 2) are derived from the refinement which gave a lower *R*.

TABLE 1

Fractional co-ordinates ($\times 10^4$) derived from least-squares refinement, with estimated standard deviations in parentheses

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| I(1) | 8 764(1) | 9 010(1) | 8 581(2) |
| N(1) | 5 002(7) | 5 124(7) | 6 388(14) |
| C(1) | 4 999(12) | 5 013(14) | 7 998(20) |
| C(2) | 5 144(10) | 4 148(12) | 5 786(20) |
| C(3) | 4 250(10) | 5 539(12) | 5 910(24) |
| C(4) | 5 642(9) | 5 812(10) | 6 061(16) |
| C(5) | 5 685(8) | 6 177(8) | 4 482(16) |
| C(6) | 6 368(9) | 6 806(9) | 4 175(17) |
| C(7) | 6 479(9) | 6 918(10) | 2 468(17) |
| C(8) | 5 855(9) | 6 847(9) | 1 497(20) |
| C(9) | 5 912(11) | 7 048(12) | −0 032(18) |
| C(10) | 6 608(12) | 7 268(12) | −0 594(19) |
| C(11) | 7 268(11) | 7 344(12) | 0 353(23) |
| C(12) | 7 190(9) | 7 135(13) | 1 839(16) |
| C(13) | 7 108(8) | 6 482(10) | 4 834(17) |
| C(14) | 7 566(9) | 6 972(11) | 5 751(19) |
| C(15) | 8 240(11) | 6 636(14) | 6 288(22) |
| C(16) | 8 485(11) | 5 739(15) | 5 845(25) |
| C(17) | 8 038(10) | 5 239(12) | 4 973(24) |
| C(18) | 7 381(10) | 5 592(11) | 4 424(23) |
| C(19) | 6 145(9) | 7 799(10) | 4 887(20) |
| O(1) | 5 806(7) | 7 833(8) | 6 011(12) |
| N(2) | 6 414(9) | 8 515(7) | 4 161(16) |
| C(20) | 4 093(11) | 6 498(12) | 6 493(30) |
| C(21) | 3 562(11) | 4 975(17) | 6 302(31) |
| C(22) | 5 081(17) | 4 096(14) | 4 199(37) |
| C(23) | 5 874(14) | 3 736(16) | 6 294(43) |

TABLE 2

Fractional co-ordinates ($\times 10^3$) for hydrogen atoms derived from difference-Fourier synthesis

| Atom | *x* | *y* | *z* | Atom | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| H(1,1) | 448 | 489 | 835 | H(17) | 819 | 459 | 460 |
| H(1,2) | 531 | 445 | 825 | H(18) | 701 | 526 | 369 |
| H(1,3) | 520 | 550 | 835 | H(20,1) | 417 | 698 | 580 |
| H(2) | 472 | 380 | 623 | H(20,2) | 449 | 666 | 737 |
| H(3) | 427 | 557 | 475 | H(20,3) | 370 | 650 | 660 |
| H(4,1) | 563 | 629 | 678 | H(21,1) | 332 | 468 | 547 |
| H(4,2) | 615 | 546 | 626 | H(21,2) | 316 | 533 | 687 |
| H(5,1) | 519 | 653 | 421 | H(21,3) | 380 | 450 | 703 |
| H(5,2) | 569 | 567 | 368 | H(22,1) | 561 | 399 | 381 |
| H(8) | 533 | 667 | 191 | H(22,2) | 470 | 367 | 390 |
| H(9) | 547 | 702 | 68 | H(22,3) | 489 | 474 | 382 |
| H(10) | 667 | 745 | 883 | H(23,1) | 603 | 402 | 563 |
| H(11) | 775 | 752 | 2 | H(23,2) | 583 | 309 | 657 |
| H(12) | 763 | 718 | 263 | H(23,3) | 598 | 403 | 744 |
| H(14) | 744 | 760 | 611 | H(N2,1) | 632 | 916 | 460 |
| H(15) | 861 | 693 | 702 | H(N2,2) | 672 | 846 | 317 |
| H(16) | 896 | 540 | 621 | | | | |

All hydrogen atoms have *U* 0.063 Å$^2$, the mean isotropic thermal parameter of all non-hydrogen atoms.

TABLE 3

Interatomic distances (Å) and angles (°) for non-hydrogen atoms, with estimated standard deviations in parentheses

(*a*) Distances

| | | | |
|---|---|---|---|
| N(1)–C(1) | 1.46(2) | C(7)–C(12) | 1.41(2) |
| N(1)–C(2) | 1.54(2) | C(8)–C(9) | 1.41(2) |
| N(1)–C(3) | 1.52(2) | C(9)–C(10) | 1.37(3) |
| N(1)–C(4) | 1.54(4) | C(10)–C(11) | 1.45(3) |
| C(2)–C(22) | 1.44(3) | C(11)–C(12) | 1.38(3) |
| C(2)–C(23) | 1.49(3) | C(13)–C(14) | 1.36(2) |
| C(3)–C(20) | 1.52(3) | C(13)–C(18) | 1.43(2) |
| C(3)–C(21) | 1.51(3) | C(14)–C(15) | 1.37(3) |
| C(4)–C(5) | 1.52(4) | C(15)–C(16) | 1.44(3) |
| C(5)–C(6) | 1.54(2) | C(16)–C(17) | 1.33(3) |
| C(6)–C(7) | 1.56(2) | C(17)–C(18) | 1.36(3) |
| C(6)–C(13) | 1.51(2) | C(19)–O(1) | 1.18(2) |
| C(6)–C(19) | 1.63(2) | C(19)–N(2) | 1.32(2) |
| C(7)–C(8) | 1.41(2) | | |

(*b*) Angles

| | | | |
|---|---|---|---|
| C(1)–N(1)–C(2) | 104(2) | C(6)–C(7)–C(8) | 120(2) |
| C(1)–N(1)–C(3) | 109(2) | C(6)–C(7)–C(12) | 122(2) |
| C(1)–N(1)–C(4) | 106(2) | C(8)–C(7)–C(12) | 117(2) |
| C(2)–N(1)–C(3) | 114(2) | C(7)–C(8)–C(9) | 122(2) |
| C(2)–N(1)–C(4) | 115(2) | C(8)–C(9)–C(10) | 118(2) |
| C(3)–N(1)–C(4) | 109(2) | C(9)–C(10)–C(11) | 121(2) |
| N(1)–C(2)–C(22) | 113(2) | C(10)–C(11)–C(12) | 118(2) |
| N(1)–C(2)–C(23) | 114(2) | C(11)–C(12)–C(7) | 122(2) |
| C(22)–C(2)–C(23) | 111(2) | C(6)–C(13)–C(14) | 126(2) |
| N(1)–C(3)–C(20) | 115(2) | C(6)–C(13)–C(18) | 118(2) |
| N(1)–C(3)–C(21) | 115(2) | C(14)–C(13)–C(18) | 116(2) |
| C(20)–C(3)–C(21) | 106(2) | C(13)–C(14)–C(15) | 123(2) |
| N(1)–C(4)–C(5) | 116(3) | C(14)–C(15)–C(16) | 119(2) |
| C(4)–C(5)–C(6) | 115(2) | C(15)–C(16)–C(17) | 119(2) |
| C(5)–C(6)–C(7) | 110(1) | C(16)–C(17)–C(18) | 121(2) |
| C(5)–C(6)–C(13) | 115(1) | C(17)–C(18)–C(13) | 122(2) |
| C(5)–C(6)–C(19) | 106(1) | O(1)–C(19)–C(6) | 120(2) |
| C(7)–C(6)–C(13) | 108(1) | N(2)–C(19)–C(6) | 115(2) |
| C(7)–C(6)–C(19) | 109(2) | O(1)–C(19)–N(2) | 125(2) |
| C(13)–C(6)–C(19) | 109(2) | | |

TABLE 4

Interatomic distances (Å) involving hydrogen atoms

| | | | |
|---|---|---|---|
| H(1,1)–C(1) | 0.99 | H(17)–C(17) | 1.04 |
| H(1,2)–C(1) | 1.02 | H(18)–C(18) | 1.05 |
| H(1,3)–C(1) | 0.89 | H(20,1)–C(20) | 0.96 |
| H(2)–C(2) | 0.99 | H(20,2)–C(20) | 1.08 |
| H(3)–C(3) | 1.05 | H(20,3)–C(2) | 0.90 |
| H(4,1)–C(4) | 0.96 | H(21,1)–C(21) | 0.96 |
| H(4,2)–C(4) | 1.05 | H(21,2)–C(21) | 1.04 |
| H(5,1)–C(5) | 1.04 | H(21,3)–C(21) | 1.04 |
| H(5,2)–C(5) | 1.03 | H(22,1)–C(22) | 1.01 |
| H(8)–C(8) | 1.03 | H(22,2)–C(22) | 0.95 |
| H(9)–C(9) | 0.97 | H(22,3)–C(22) | 1.05 |
| H(10)–C(10) | 1.04 | H(23,3)–C(23) | 0.84 |
| H(11)–C(11) | 0.94 | H(23,2)–C(23) | 0.98 |
| H(12)–C(12) | 1.05 | H(23,3)–C(23) | 1.13 |
| H(14)–C(14) | 1.00 | H(N2,1)–N(2) | 1.04 |
| H(15)–C(15) | 1.03 | H(N2,2)–N(2) | 1.05 |
| H(16)–C(16) | 1.03 | | |

Positional parameters for non-hydrogen atoms are given in Table 1 and the hydrogen atom positions derived from

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[3] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

[4] 'International Tables for *X*-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

the difference Fourier synthesis in Table 2. Bond distances and angles are given in Tables 3 and 4. Observed and calculated structure factors and anisotropic thermal parameters are listed in Supplementary Publication No. SUP 21911 (7 pp., 1 microfiche).*

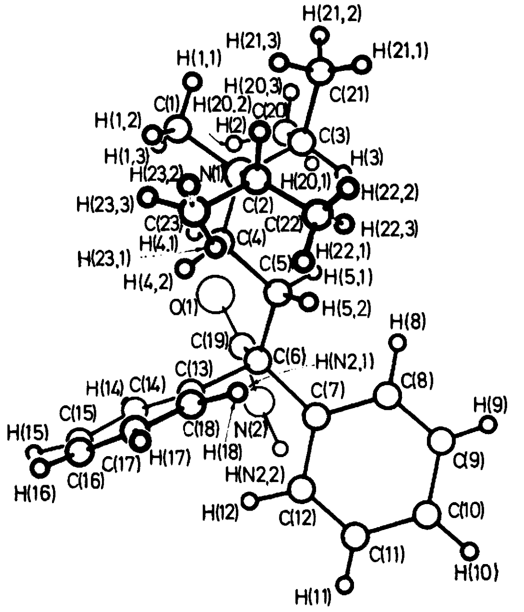

FIGURE 1 Perspective view of molecule showing the atom numbering system used in the analysis

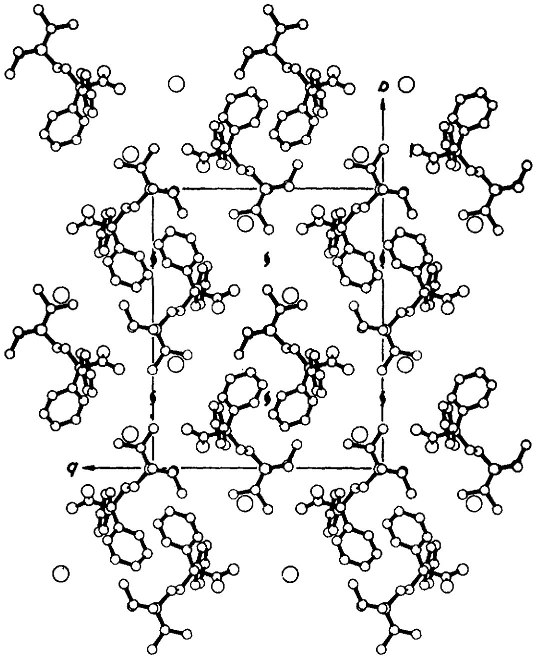

FIGURE 2 Molecular packing viewed along the *c* axis

All computational work was carried out on the University College London IBM 360 computer.

TABLE 5

Equations * of mean planes with displacements (Å) of relevant atoms in square brackets

Plane (1): C(7)—(12)

$$-0.198X + 0.965Y + 0.173Z = 15.528$$

[C(7) 0.02, C(8) −0.01, C(9) 0.01, C(10) −0.01, C(11) 0.02, C(12) −0.02]

Plane (2): C(13)—(18)

$$-0.477X + -0.385Y + 0.790Z = 17.084$$

[C(13) 0.01, C(14) 0.00, C(15) 0.00, C(16) −0.01, C(17) 0.02, C(18) −0.02]

Plane (3): C(6), C(19), O(1), N(2), H(N2,1), H(N2,2)

$$0.847X + -0.024Y + 0.531Z = 16.279$$

[C(6) 0.01, C(19) −0.02, O(1) 0.01, N(2) 0.01, H(N2,1) 0.05, H(N2,2) −0.01]

* Based on orthonormalized co-ordinates: *X* is parallel to crystallographic *a* axis, *Y* is perpendicuar to *X* in the plane *ab*, and *Z* is perpendicular to the plane *ab* and completes a right-handed set of axes, *X*, *Y*, *Z*.

TABLE 6

Torsion angles (°), with estimated standard deviations in parentheses *

| | |
|---|---|
| N(1)–C(4)–C(5)–C(6) | −176(2) |
| C(1)–N(1)–C(2)–C(22) | 173(2) |
| C(1)–N(1)–C(2)–C(23) | −60(2) |
| C(1)–N(1)–C(3)–C(20) | 64(2) |
| C(1)–N(1)–C(3)–C(21) | −60(2) |
| C(1)–N(1)–C(4)–C(5) | −170(2) |
| C(2)–N(1)–C(3)–C(20) | 180(2) |
| C(2)–N(1)–C(3)–C(21) | 56(2) |
| C(2)–N(1)–C(4)–C(5) | 76(2) |
| C(3)–N(1)–C(2)–C(22) | 55(2) |
| C(3)–N(1)–C(2)–C(23) | −178(2) |
| C(3)–N(1)–C(4)–C(5) | −53(3) |
| C(4)–N(1)–C(2)–C(22) | −72(2) |
| C(4)–N(1)–C(2)–C(23) | 55(2) |
| C(4)–N(1)–C(3)–C(20) | −51(2) |
| C(4)–N(1)–C(3)–C(21) | −174(2) |
| C(4)–C(5)–C(6)–C(7) | 165(2) |
| C(4)–C(5)–C(6)–C(13) | 42(2) |
| C(4)–C(5)–C(6)–C(19) | −78(2) |
| C(5)–C(6)–C(7)–C(8) | 28(2) |
| C(5)–C(6)–C(7)–C(12) | −155(1) |
| C(5)–C(6)–C(13)–C(14) | −125(2) |
| C(5)–C(6)–C(13)–C(18) | 58(2) |
| C(5)–C(6)–C(19)–O(1) | 38(2) |
| C(5)–C(6)–C(19)–N(2) | −146(1) |
| C(6)–C(7)–C(8)–C(9) | 172(2) |
| C(6)–C(7)–C(12)–C(11) | −172(2) |
| C(6)–C(13)–C(14)–C(15) | −179(2) |
| C(6)–C(13)–C(18)–C(17) | −179(2) |
| C(7)–C(6)–C(13)–C(14) | 112(2) |
| C(7)–C(6)–C(13)–C(18) | −65(2) |
| C(7)–C(6)–C(19)–O(1) | 156(2) |
| C(7)–C(6)–C(19)–N(2) | −29(2) |
| C(7)–C(8)–C(9)–C(10) | 4(2) |
| C(7)–C(12)–C(11)–C(10) | −5(3) |
| C(8)–C(7)–C(6)–C(13) | 154(1) |
| C(8)–C(7)–C(6)–C(19) | −87(2) |
| C(8)–C(7)–C(12)–C(11) | 5(2) |
| C(8)–C(9)–C(10)–C(11) | −3(3) |
| C(9)–C(8)–C(7)–C(12) | −5(2) |
| C(9)–C(10)–C(11)–C(12) | 4(3) |
| C(12)–C(7)–C(6)–C(13) | −29(2) |
| C(12)–C(7)–C(6)–C(19) | 90(2) |
| C(13)–C(6)–C(19)–O(1) | −86(2) |
| C(13)–C(6)–C(19)–N(2) | 90(2) |
| C(13)–C(14)–C(15)–C(16) | 1(3) |
| C(13)–C(18)–C(17)–C(16) | −5(3) |
| C(14)–C(13)–C(6)–C(19) | −7(2) |
| C(14)–C(13)–C(18)–C(17) | 3(2) |
| C(14)–C(15)–C(16)–C(17) | −3(3) |

* The sign convention is that given in W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1976, Index issue.

## DISCUSSION

*Description of the Molecular Structure.*—The atomic numbering scheme used in this analysis and configuration of the molecule as observed in the crystal is shown in Figure 1. Observed torsion angles for non-hydrogen atoms and the mean plane equations for certain groups of atoms in the molecule are given in Tables 5 and 6, which show that the amide group [C(6), C(19), N(2) O(1), H(N2,1), and H(N2,2)] is planar, as are the two phenyl groups [C(7)—(12) and C(13)—(18)]. The angle between the planes of the phenyl groups is 82°, comparable to the values 84° which the mean plane of the cyclohexyl group makes with the phenyl group in hexapyrronium bromide[5] and 72° between the mean planes of the phenyl groups in benactyzine hydrochloride.[6] Both these compounds are antimuscarinic drugs. The interplanar angles between the amide group and the two phenyl groups C(7)—(12) and C(13)—(18) are 84 and 89° respectively.

There are only three intermolecular contacts $<3.5$ Å. These are O(1) $\cdots$ C(1) at $1 - x, \frac{1}{2} + y, 1 + \frac{1}{2} - z$ 3.59, O(1) $\cdots$ C(10) at $x, y, 1 - z$ 3.47, and C(9) $\cdots$ C(22) at $1 - x, 1 - \frac{1}{2} + y, \frac{1}{2} - z$ 3.54 Å.

Figure 2 shows the molecular packing viewed along the [001] axis. The diagram is produced by use of computer program PLUTO.[7]

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[5/2504 *Received*, 22*nd December*, 1975]

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[5] R. W. Baker, N. Datta, and P. J. Pauling, *J.C.S. Perkin II*, 1973, 1963.

[6] T. J. Petcher, *J.C.S. Perkin II*, 1974, 1151.

[7] S. Motherwell, 'PLUTO,' program for plotting molecular and crystal structures, University Chemical Laboratory, Cambridge.