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Structures of the Antileprosy Phenazine Derivatives Clofazimine–*N*,*N*-Dimethylformamide, $C_{27}H_{22}Cl_2N_4.C_3H_7NO$, and B1912, $C_{30}H_{27}ClN_4$

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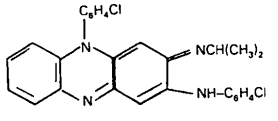
Abstract. $C_{27}H_{22}Cl_2N_4.C_3H_7NO$ [3-(*p*-chloroanilino)-10-(*p*-chlorophenyl)-2,10-dihydro-2-(isopropylimino)-phenazine–DMF]: $M_r = 546{\cdot}50$, triclinic, $P\bar{1}$, $a = 12{\cdot}435$ (4), $b = 12{\cdot}807$ (5), $c = 10{\cdot}424$ (4) Å, $\alpha = 111{\cdot}74$ (3), $\beta = 112{\cdot}37$ (3), $\gamma = 90{\cdot}90$ (3)°, $V = 1403$ (4) Å^3, $D_m = 1{\cdot}29$ (2) (flotation in aqueous KI), $Z = 2$, $D_x = 1{\cdot}293$ Mg m^{-3}, Mo $K\alpha$, $\lambda K\alpha_1 = 0{\cdot}70926$, $\lambda K\alpha_2 = 0{\cdot}71354$ Å, $\mu = 0{\cdot}27$ mm^{-1}, $F(000) = 572$, $T = 293$ K, $R = 0{\cdot}082$ for 2939 unique data. $C_{30}H_{27}ClN_4$ [3-anilino-7-chloro-2-(cyclohexylimino)-2,10-dihydro-10-phenylphenazine]: $M_r = 479{\cdot}2$, triclinic, $P\bar{1}$, $a = 10{\cdot}986$ (3), $b = 24{\cdot}369$ (8), $c = 10{\cdot}145$ (5) Å, $\alpha = 101{\cdot}88$ (44), $\beta = 96{\cdot}84$ (4), $\gamma = 88{\cdot}53$ (3)°, $V = 2639$ (4) Å^3, $D_m = 1{\cdot}19$ (3), $Z = 4$, $D_x = 1{\cdot}203$ Mg m^{-3}, Mo $K\alpha$, $\mu = 0{\cdot}17$ mm^{-1}, $F(000) = 1008$, $T = 293$ K, $R = 0{\cdot}077$ for 3359 unique data. The structures of the three crystallographically independent species (clofazimine and two independent B1912 molecules) are all very similar, approach to the potential active sites being unhindered in all cases.

Introduction. While the substituted iminophenazine clofazimine (I) has been used in the treatment of leprosy patients for twenty years (Browne & Hogerzeil, 1962) and is in many ways the best antileprosy drug currently available (Jacobson, 1981; Browne, Harman, Waudby & McDougall, 1981), relatively little is known about the mode of action of this and related phenazine derivatives at the molecular level. Morrison and co-workers (Morrison & Marley, 1976, 1977, 1978; Tsutsumi & Morrison, 1979) have demonstrated that both clofazimine and B1912 interact with the G:C regions of DNA and act as minor-groove-binding drugs, but the precise nature of this interaction remains unclear.



(I)

Consequently, no working hypothesis has emerged to explain the marked difference in effectiveness between these two active drugs and their relatively less active analogues. Levy (1981) has suggested that the presence of the two *p*-chloro substituents in clofazimine is of importance, but the absence of such substituents in B1912 demonstrates that they are not essential. Morrison & Marley (1977) have also noted the possible significance of the chloro substituent at the 7-position of B1912, and the observation (Conalty, 1982) that the 7-chloro analogue of clofazimine (B1509) is active both *in vitro* and *in vivo* supports this view. No chemical, physical, or biological reason for this observation has been demonstrated, however.

We have, therefore, recently begun to examine the structural and electronic properties of these phenazine derivatives with the aim of establishing the essential structural and/or electronic features for antileprosy activity in this important class of molecules. We hope that this will allow the rational design of active drugs which contain these crucial parameters. We here report the crystal and molecular structures of the active molecules clofazimine and B1912, and compare their structural features.

Table 1. *Experimental parameters*

	Clofazimine–DMF	B1912
Crystal size and shape	Red prisms (2) 0·85 × 0·85 × 0·65 mm 0·75 × 0·75 × 0·060 mm	Red needle 0·80 × 0·40 × 0·40 mm
No. of reflections and θ range for lattice parameters	25 reflections $14 \le \theta(\text{Mo}) \le 16°$	25 reflections $5 < \theta < 20°$
Max. $(\sin\theta)/\lambda$	0·651 Å^{-1}	0·596 Å^{-1}
Range of h, k, l	$-16 \le h \le 16$ $-16 \le k \le 16$ $0 \le l \le 13$	$-13 \le h \le 13$ $0 \le k \le 28$ $-12 \le l \le 12$
Standard reflections and max. deviation in F	$61\bar{5}$ (12%) $7\bar{1}5$ (10%) $22\bar{2}$ (5%)	$21\bar{2}$ (3%) $\bar{1}7\bar{1}$ (3%) $\bar{1}53$ (4%)
No. unique reflections measured	4902	6612
No. unobserved reflections [$I < 3\sigma(I)$]	1963	3253
H atoms	Calculated, fixed	Calculated, fixed
Parameters refined (refinement on F)	2 scale factors, 38 anisotropic atoms (344 variables)	scale factor, 70 anisotropic atoms in two equal blocks (631 variables)
R	0·082	0·077
wR	0·081	0·070
S	5·3	2·6
Max. Δ/σ	0·67	0·71
Max. height in difference Fourier	0·09 e Å^{-3}	0·27 e Å^{-3}

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Table 2. *Positional parameters and equivalent isotropic thermal parameters*

$$U_{eq} = \frac{1}{6\pi^2} \sum_i \sum_j \beta_{ij} \mathbf{a}_i . \mathbf{a}_j .$$

	x	y	z	U_{eq}(Å²)
(*a*) Clofazimine–DMF				
Cl(18)	0·4826 (1)	−0·0786 (2)	0·6898 (2)	0·096 (1)
Cl(24)	−0·2149 (2)	−0·4277 (2)	−1·0661 (2)	0·127 (1)
N(2)	0·2714 (4)	−0·2989 (4)	−0·1737 (5)	0·064 (1)
N(3)	0·0849 (4)	−0·3324 (4)	−0·4227 (4)	0·059 (1)
N(5)	−0·1286 (3)	−0·1508 (4)	−0·1299 (5)	0·054 (1)
N(10)	0·0631 (3)	−0·1262 (4)	0·1383 (5)	0·048 (1)
C(1)	0·1726 (4)	−0·2115 (5)	−0·0071 (6)	0·049 (1)
C(2)	0·1803 (4)	−0·2636 (5)	−0·1510 (6)	0·053 (2)
C(3)	0·0718 (5)	−0·2791 (4)	−0·2915 (6)	0·050 (2)
C(4)	−0·0271 (4)	−0·2434 (5)	−0·2782 (6)	0·051 (2)
C(6)	−0·2344 (4)	−0·0568 (5)	0·0182 (7)	0·060 (2)
C(7)	−0·2432 (5)	−0·0045 (5)	0·1536 (8)	0·069 (2)
C(8)	−0·1492 (5)	0·0085 (5)	0·2893 (6)	0·063 (2)
C(9)	−0·0465 (5)	−0·0311 (5)	0·2864 (6)	0·052 (2)
C(11)	−0·0379 (4)	−0·0836 (4)	0·1494 (6)	0·047 (2)
C(12)	−0·1323 (4)	−0·0984 (4)	0·0099 (6)	0·048 (2)
C(13)	−0·0327 (4)	−0·1883 (4)	−0·1348 (6)	0·047 (2)
C(14)	0·0731 (4)	−0·1764 (4)	0·0012 (6)	0·047 (2)
C(15)	0·1647 (4)	−0·1138 (5)	0·2771 (6)	0·045 (2)
C(16)	0·2437 (4)	−0·0119 (5)	0·3592 (6)	0·058 (2)
C(17)	0·3430 (5)	−0·0014 (5)	0·4895 (6)	0·064 (2)
C(18)	0·3587 (4)	−0·0919 (6)	0·5284 (6)	0·060 (2)
C(19)	0·2796 (5)	−0·1946 (5)	0·4472 (7)	0·063 (2)
C(20)	0·1800 (4)	−0·2046 (5)	0·3168 (6)	0·055 (2)
C(21)	0·0063 (5)	−0·3540 (5)	−0·5726 (6)	0·053 (2)
C(22)	−0·0695 (5)	−0·2805 (5)	−0·6107 (6)	0·061 (2)
C(23)	−0·1391 (5)	−0·3055 (5)	−0·7634 (7)	0·065 (2)
C(24)	−0·1332 (6)	−0·4009 (6)	−0·8752 (7)	0·076 (2)
C(25)	−0·0584 (6)	−0·4737 (5)	−0·8394 (7)	0·076 (2)
C(26)	0·0096 (5)	−0·4519 (5)	−0·6901 (7)	0·064 (2)
C(27)	0·3821 (6)	−0·2802 (8)	−0·0400 (7)	0·094 (2)
C(28)	0·3993 (9)	−0·3761 (11)	−0·0169 (18)	0·316 (10)
C(29)	0·4795 (8)	−0·2447 (12)	−0·0630 (13)	0·215 (6)
O(DMF)	0·2832 (5)	0·5457 (5)	0·4736 (7)	0·126 (2)
N(DMF)	0·3627 (5)	0·3952 (5)	0·5045 (8)	0·100 (3)
C(1)(DMF)	0·3026 (7)	0·4795 (8)	0·5334 (10)	0·106 (4)
C(2)(DMF)	0·3989 (7)	0·3681 (7)	0·3844 (10)	0·126 (4)
C(3)(DMF)	0·3859 (10)	0·3223 (9)	0·5796 (13)	0·180 (6)
(*b*) B1912, molecule *A*				
Cl	0·9040 (2)	0·2105 (1)	−0·3621 (2)	0·070 (1)
N(2)	0·3491 (5)	−0·1051 (2)	−0·2497 (6)	0·077 (2)
N(3)	0·5319 (5)	−0·1511 (3)	−0·3738 (6)	0·057 (2)
N(5)	0·6825 (5)	0·0285 (2)	−0·3894 (6)	0·047 (2)
N(10)	0·4930 (5)	0·0824 (2)	−0·2492 (5)	0·040 (1)
C(1)	0·4099 (5)	−0·0094 (3)	−0·2523 (7)	0·042 (2)
C(2)	0·4216 (6)	−0·0688 (3)	−0·2794 (7)	0·042 (2)
C(3)	0·5261 (7)	−0·0937 (3)	−0·3486 (7)	0·046 (2)
C(4)	0·6083 (6)	−0·0603 (3)	−0·3846 (7)	0·050 (2)
C(6)	0·7737 (6)	0·1171 (3)	−0·3792 (7)	0·049 (2)
C(7)	0·7784 (6)	0·1741 (3)	−0·3340 (8)	0·046 (2)
C(8)	0·6890 (7)	0·2016 (3)	−0·2626 (8)	0·051 (2)
C(9)	0·5926 (7)	0·1719 (3)	−0·2354 (7)	0·052 (2)
C(11)	0·5862 (6)	0·1147 (3)	−0·2782 (7)	0·041 (2)
C(12)	0·6777 (6)	0·0864 (3)	−0·3507 (7)	0·042 (2)
C(13)	0·5983 (6)	−0·0009 (3)	−0·3541 (7)	0·045 (2)
C(14)	0·4967 (6)	0·0244 (3)	−0·2820 (7)	0·038 (2)
C(15)	0·3950 (7)	0·1096 (3)	−0·1822 (8)	0·042 (2)
C(16)	0·3881 (7)	0·1087 (3)	−0·0482 (9)	0·059 (2)
C(17)	0·2898 (10)	0·1350 (4)	0·0148 (9)	0·075 (2)
C(18)	0·2027 (8)	0·1628 (3)	−0·0531 (13)	0·067 (2)
C(19)	0·2113 (7)	0·1632 (3)	−0·1867 (12)	0·071 (2)
C(20)	0·3063 (7)	0·1377 (3)	−0·2502 (8)	0·056 (2)
C(21)	0·6206 (7)	−0·1888 (3)	−0·4261 (8)	0·045 (2)
C(22)	0·7459 (7)	−0·1769 (3)	−0·3977 (7)	0·054 (2)
C(23)	0·8283 (7)	−0·2169 (4)	−0·4462 (9)	0·063 (2)
C(24)	0·7903 (10)	−0·2680 (4)	−0·5227 (10)	0·078 (2)
C(25)	0·6698 (10)	−0·2788 (3)	−0·5502 (10)	0·085 (2)
C(26)	0·5817 (7)	−0·2399 (3)	−0·5035 (9)	0·066 (2)
C(27)	0·2426 (7)	−0·0861 (3)	−0·1816 (8)	0·4049 (2)
C(28)	0·2749 (6)	−0·0644 (3)	−0·0304 (9)	0·054 (2)
C(29)	0·1601 (7)	−0·0479 (3)	0·0402 (8)	0·066 (2)
C(30)	0·0718 (8)	−0·0957 (4)	0·0160 (10)	0·074 (2)
C(31)	0·0381 (7)	−0·1186 (4)	−0·1349 (10)	0·073 (2)
C(32)	0·1519 (7)	−0·1348 (3)	−0·2068 (8)	0·064 (2)

Table 2 (*cont.*)

	x	y	z	U_{eq}(Å²)
(*c*) B1912, molecule *B*				
Cl	0·0753 (2)	−0·2704 (1)	−0·0154 (2)	0·077 (1)
N(2)	0·0020 (5)	−0·6336 (2)	0·3369 (6)	0·048 (2)
N(3)	0·2173 (6)	−0·6363 (2)	0·2524 (6)	0·054 (2)
N(5)	0·1352 (5)	−0·4601 (3)	0·1182 (6)	0·044 (1)
N(10)	−0·1001 (5)	−0·4565 (2)	0·2035 (6)	0·042 (1)
C(1)	−0·0563 (6)	−0·5457 (3)	0·2682 (7)	0·040 (2)
C(2)	0·0245 (7)	−0·5909 (3)	0·2849 (7)	0·045 (2)
C(3)	0·1487 (7)	−0·5895 (3)	0·2396 (7)	0·044 (2)
C(4)	0·1792 (6)	−0·5462 (3)	0·1849 (7)	0·043 (2)
C(6)	0·0980 (7)	−0·3706 (3)	0·0584 (8)	0·052 (2)
C(7)	0·0230 (8)	−0·3254 (3)	0·0501 (8)	0·050 (2)
C(8)	−0·0901 (8)	−0·3225 (3)	0·0920 (8)	0·057 (2)
C(9)	−0·1330 (7)	−0·3656 (3)	0·1425 (8)	0·052 (2)
C(11)	−0·0617 (7)	−0·4115 (3)	0·1527 (7)	0·041 (2)
C(12)	0·0576 (7)	−0·4152 (3)	0·1109 (7)	0·045 (2)
C(13)	0·0978 (6)	−0·4999 (3)	0·1713 (7)	0·039 (2)
C(14)	−0·0231 (6)	−0·5019 (3)	0·2178 (7)	0·039 (2)
C(15)	−0·2207 (7)	−0·4570 (3)	0·2426 (9)	0·044 (2)
C(16)	−0·2390 (8)	−0·4351 (3)	0·3780 (9)	0·062 (2)
C(17)	−0·3540 (10)	−0·4375 (4)	0·4151 (10)	0·074 (2)
C(18)	−0·4492 (9)	−0·4599 (4)	0·3275 (14)	0·082 (3)
C(19)	−0·4305 (8)	−0·4812 (4)	0·1938 (13)	0·086 (3)
C(20)	−0·3143 (8)	−0·4802 (4)	0·1506 (9)	0·068 (2)
C(21)	0·3270 (8)	−0·6544 (4)	0·2017 (8)	0·056 (2)
C(22)	0·4210 (10)	−0·6187 (4)	0·1925 (12)	0·096 (3)
C(23)	0·5258 (10)	−0·6404 (6)	0·1375 (15)	0·119 (4)
C(24)	0·5394 (11)	−0·6971 (7)	0·0959 (11)	0·104 (3)
C(25)	0·4544 (12)	−0·7318 (4)	0·1174 (12)	0·099 (3)
C(26)	0·3503 (8)	−0·7109 (4)	0·1699 (10)	0·075 (3)
C(27)	−0·1207 (7)	−0·6383 (3)	0·3773 (8)	0·045 (2)
C(28)	−0·1347 (7)	−0·6000 (3)	0·5149 (9)	0·056 (2)
C(29)	−0·2600 (7)	−0·6060 (3)	0·5553 (8)	0·058 (2)
C(30)	−0·2871 (7)	−0·6654 (4)	0·5627 (10)	0·069 (2)
C(31)	−0·2694 (7)	−0·7055 (3)	0·4282 (9)	0·064 (2)
C(32)	−0·1439 (7)	−0·6988 (3)	0·3882 (8)	0·057 (2)

Experimental. Purified samples of clofazimine (B663) and of B1912 generously provided by Dr A. Colin McDougall, Headington, England. Deep-red crystals of both compounds grown from *N,N*-dimethylformamide (DMF) solutions. Elemental analysis indicated that the clofazimine crystals contained one molecule of DMF per molecule of clofazimine. Enraf–Nonius CAD-4 diffractometer, Mo $K\alpha$ radiation, absorption corrections not applied; atomic scattering factors from *International Tables for X-ray Crystallography* (1974); weights as defined by Corfield, Doedens & Ibers (1967) with $p = 0{\cdot}01$; for clofazimine–DMF decomposition effects were so severe that two different crystals had to be used in order to obtain the data. Other experimental parameters listed in Table 1. Clofazimine–DMF solved by Patterson superposition using locally written program followed by tangent refinement in *P*1; B1912 solved by using relevant moiety of clofazimine as a fragment of known geometry as input to *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq, & Woolfson, 1978). Other programs from CAD-4/SDP.

Discussion. The atomic positional parameters, along with their standard deviations as estimated from the inverse matrix, are listed in Table 2.*

* Lists of structure amplitudes and anisotropic thermal parameters and a complete list of distances and angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38917 (50 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Clofazimine–DMF

A view of the clofazimine molecule in the crystals is shown in Fig. 1. Bond lengths and bond angles in the crystal are compared with those of B1912 (see below) in Tables 3 and 4, respectively. As expected for a dihydrophenazine, the phenazine moiety is asymmetric with the unsubstituted ring showing a normal aromatic distribution of bond lengths and angles while the substituted carbon ring shows four nominally single bonds [1·428 (7)–1·509 (7) Å] and two double bonds [1·345 (6) and 1·357 (7) Å]. This, of course, is in contrast to the observed structure of phenazine itself, which is symmetric and aromatic (Herbstein & Schmidt, 1955; Hirshfeld & Schmidt, 1957). The dihydrophenazine ring is approximately planar, with no atom deviating from the 14-atom least-squares plane by more than 0·06 Å. Of the four substituent atoms, only the imino nitrogen atom N(2) deviates substantially from the phenazine plane, lying 0·12 Å out of the plane. As can be seen in Fig. 1, the *p*-chlorophenyl ring at N(10) is almost perpendicular to the plane of the phenazine ring. The torsion angle around N(10)–C(15) [defined by C(14)–N(10)–C(15)–C(16)] is 83·3 (6)°, or only 6·7° from perpendicular. The phenyl ring of the anilino moiety, however, is inclined at only 34·4° to the phenazine ring.

There is evidently considerable thermal motion in the isopropyl group at N(2). No reasonable disordered model could be found, but the high apparent thermal motion of these atoms makes it impossible to rule out some form of disorder. Consequently, the metrical parameters associated with the isopropyl group are relatively unreliable.

The DMF solvent molecule forms a weak hydrogen bond to the anilino NH group with N···O and H···O distances of 3·251 and 2·35 Å, respectively, and associated N–H···O angle of 150°. Presumably, the presence of this relatively weak hydrogen bond to the only available donor stabilizes the crystal and explains the presence of the DMF in the crystals.

*B*1912

There are two crystallographically independent molecules of B1912 in the crystals (see Table 1) which for convenience are referred to as molecules *A* and *B*. Views of these two molecules are given in Figs. 2 and 3, respectively. In both molecules, the phenazine moiety is asymmetric as in clofazimine (see above), and the bond lengths and angles in the two independent molecules are entirely similar to each other and to those in clofazimine. The dihydrophenazine moieties are approximately planar, the maximum deviations from the 14-atom least-squares plane being 0·13 Å in molecule *A* and 0·05 Å in molecule *B*. The phenyl rings at N(10) are planar, with no atom deviating from the least-squares plane by more than 0·007 Å in molecule *A* and 0·005 Å in molecule *B*. The phenyl rings associated with the anilino groups are also planar, the maximum deviations being 0·005 and 0·05 Å in the *A* and *B* molecules, respectively.

As is apparent from Figs. 2 and 3, the phenyl substituents at N(10) are approximately perpendicular to the phenazine rings, the torsion angle C(14)–N(10)–C(15)–C(16) being 106·4 (7)° in molecule *A* and 92·4 (8)° in molecule *B*. The phenyl rings of the anilino groups are inclined at 35·9 and 29·0° relative to the phenazine rings in the *A* and *B* molecules, respectively. The cyclohexyl groups at N(2) adopt the classical chair conformation in both molecules. Thus, the four atoms C(28), C(29), C(31), and C(32) are coplanar (maximum deviations 0·005 and 0·001 Å in the *A* and *B* molecules, respectively) while C(27) sits above this plane by 0·66 Å in *A* and 0·71 Å in *B* and C(30) lies below it by 0·65 Å in both molecules.

Figs. 1, 2, and 3 have all been drawn from the same relative direction, so that the fundamental structural similarity of these three molecules is apparent. Of particular potential significance is the similarity of the torsion angle between the phenazine rings and the 10-phenyl [or 10-(*p*-chlorophenyl)] substituents. These three values of 83·3, 106·4, and 92·4° are all near 90° as might be expected; this orientation minimizes the steric interactions between the H atoms on the *ortho* C atoms of the phenyl rings [C(16) and C(20)] and those on phenazine atoms C(1) and C(9). Values in the range 99·3 to 115·4° have been observed for the related molecule *N*-(*p*-bromophenyl)phenothiazine (Chu & Yang, 1977), and a value of 91·1° was found in the more hindered compound *N*-(*o*-methoxyphenyl)-phenothiazine (Chu, Yang & van der Helm, 1976). Presumably, it is this structural feature which prevents clofazimine from intercalating in DNA (Morrison & Marley, 1976).

Similarly, the interplanar angle between the phenyl (or *p*-chlorophenyl) group at N(3) and the phenazine ring is substantially similar in the three molecules, with values of 34·4, 35·9, and 29·0°. The angles are small enough to allow considerable overlap between the π systems of the two rings and the p_z orbital on the trigonal N(3) atom (Camerman & Jensen, 1970). The presence of this interaction may be partially responsible for the intense coloration of the crystals.

While the active site(s) of these molecules are unknown, an examination of Figs. 1, 2, and 3 reveals that approach to the three most probable candidates [N(5), N(2), and N(3)] is remarkably unhindered. The ability of a DMF molecule to interact with N(3) in the solid state demonstrates that approach to this site is possible for small acceptor molecules, and examination of the figures suggests that small donor molecules could readily approach N(2) or N(5). In the absence of structural information on inactive clofazimine analogues it is impossible to assess the significance of this structural feature, but it is entirely possible that

crystallographic examination of inactive analogues will reveal a more hindered approach to one or more of these sites. We expect to obtain information in the near future, from examination of inactive analogues and of molecular complexes of active molecules with biologically significant donors and acceptors, which will enhance our understanding of this issue.

Table 3. *Principal bond distances* (Å) *in clofazimine and B*1912, *with e.s.d.'s in parentheses*

	Clofazimine	B1912, molecule *A*	B1912, molecule *B*
C(1)–C(2)	1·440 (7)	1·423 (9)	1·422 (10)
C(1)–C(14)	1·345 (6)	1·376 (8)	1·351 (9)
C(2)–C(3)	1·509 (7)	1·469 (10)	1·494 (10)
C(2)–N(2)	1·297 (6)	1·307 (7)	1·301 (8)
C(3)–C(4)	1·357 (7)	1·360 (9)	1·356 (9)
C(3)–N(3)	1·358 (6)	1·372 (8)	1·370 (9)
C(4)–C(13)	1·428 (7)	1·421 (9)	1·440 (10)
N(5)–C(13)	1·304 (6)	1·310 (7)	1·299 (8)
N(5)–C(12)	1·380 (6)	1·386 (8)	1·380 (9)
C(6)–C(12)	1·405 (7)	1·398 (9)	1·407 (9)
C(6)–C(7)	1·368 (7)	1·370 (9)	1·370 (11)
C(7)–C(8)	1·399 (7)	1·369 (9)	1·355 (11)
C(7)–Cl	—	1·742 (7)	1·750 (7)
C(8)–C(9)	1·389 (7)	1·383 (9)	1·376 (10)
C(9)–C(11)	1·381 (7)	1·372 (9)	1·364 (10)
N(10)–C(11)	1·405 (6)	1·402 (8)	1·396 (8)
N(10)–C(14)	1·388 (6)	1·383 (8)	1·396 (8)
N(10)–C(15)	1·466 (6)	1·420 (9)	1·430 (9)
C(11)–C(12)	1·421 (7)	1·400 (9)	1·420 (10)
C(13)–C(14)	1·476 (6)	1·461 (9)	1·466 (9)
C(18)–Cl(18)	1·744 (5)	—	—
C(24)–Cl(24)	1·748 (6)	—	—
C(27)–N(2)	1·475 (7)	1·447 (9)	1·469 (9)
N(3)–C(21)	1·408 (6)	1·397 (9)	1·392 (9)

Table 4. *Principal bond angles* (°) *in clofazimine and B*1912, *with e.s.d.'s in parentheses*

	Clofazimine	B1912, molecule *A*	B1912, molecule *B*
C(2)–C(1)–C(14)	121·1 (5)	121·6 (6)	122·5 (6)
C(1)–C(2)–C(3)	117·3 (5)	117·9 (6)	117·3 (7)
N(2)–C(2)–C(1)	127·0 (5)	127·4 (6)	126·7 (7)
N(2)–C(2)–C(3)	115·8 (5)	114·7 (6)	116·0 (7)
C(2)–C(3)–C(4)	119·7 (5)	120·3 (6)	119·5 (7)
C(2)–C(3)–N(3)	113·7 (5)	115·4 (6)	113·1 (6)
N(3)–C(3)–C(4)	126·6 (5)	124·2 (7)	127·3 (7)
C(3)–C(4)–C(13)	122·6 (5)	121·7 (6)	122·8 (7)
C(13)–N(5)–C(12)	118·4 (5)	118·1 (6)	117·5 (6)
C(12)–C(6)–C(7)	122·0 (5)	119·9 (7)	119·8 (7)
C(6)–C(7)–C(8)	120·2 (5)	120·7 (6)	121·2 (7)
C(6)–C(7)–Cl	—	120·5 (6)	119·0 (7)
Cl–C(7)–C(8)	—	118·7 (6)	119·8 (7)
C(7)–C(8)–C(9)	119·7 (5)	120·0 (6)	120·5 (7)
C(8)–C(9)–C(11)	119·9 (5)	120·5 (7)	120·4 (7)
C(11)–N(10)–C(14)	122·9 (4)	121·0 (5)	121·7 (6)
C(11)–N(10)–C(15)	119·1 (4)	119·6 (5)	120·3 (6)
C(14)–N(10)–C(15)	117·9 (4)	119·3 (5)	118·0 (6)
N(10)–C(11)–C(9)	122·8 (5)	122·9 (7)	123·1 (7)
N(10)–C(11)–C(12)	115·7 (5)	117·5 (6)	116·9 (7)
C(9)–C(11)–C(12)	121·5 (5)	119·6 (6)	120·1 (7)
C(11)–C(12)–C(6)	116·8 (5)	119·2 (7)	118·0 (7)
C(11)–C(12)–N(5)	123·8 (5)	123·1 (6)	123·5 (7)
N(5)–C(12)–C(6)	119·4 (5)	117·5 (7)	118·5 (7)
N(5)–C(13)–C(4)	119·4 (5)	118·2 (6)	118·5 (6)
N(5)–C(13)–C(14)	123·7 (5)	123·2 (6)	124·8 (7)
C(4)–C(13)–C(14)	116·9 (5)	118·5 (6)	116·7 (6)
C(13)–C(14)–C(1)	122·2 (5)	119·7 (6)	121·1 (7)
C(13)–C(14)–N(10)	115·4 (5)	116·8 (6)	115·5 (6)
C(1)–C(14)–N(10)	122·3 (5)	123·5 (6)	123·4 (6)
C(3)–N(3)–C(21)	129·3 (5)	132·0 (6)	129·7 (6)
C(2)–N(2)–C(27)	118·2 (5)	120·3 (6)	118·2 (6)

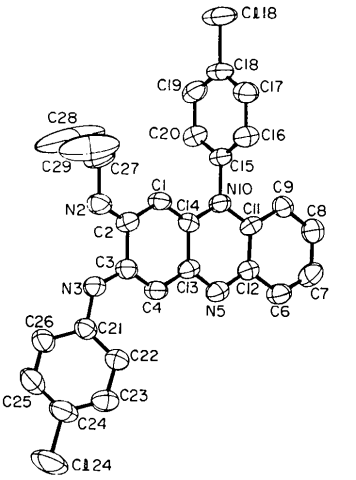

Fig. 1. View of the clofazimine molecule showing the atomic numbering scheme. Thermal ellipsoids are drawn at the 50% probability level, with H atoms omitted for clarity. The view direction in subsequent figures is the same as that in this figure.

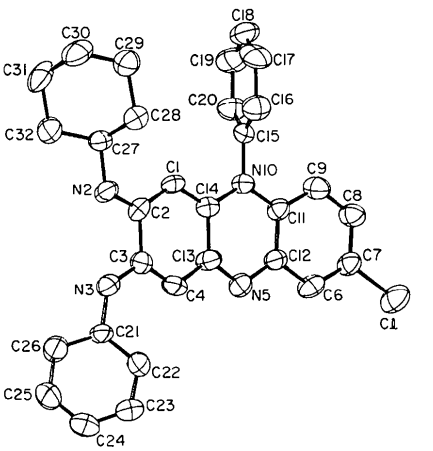

Fig. 2. View of B1912 molecule *A*, drawn as in Fig. 1.

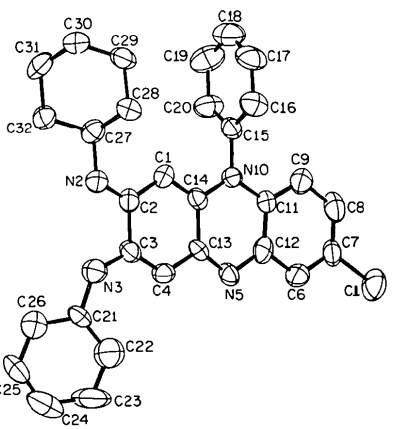

Fig. 3. View of B1912 molecule *B*, drawn as in Fig. 1.

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Azido-2 Désoxy-2 β-D-Galactopyrannoside Isopropylique, $C_9H_{17}N_3O_5$

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Abstract. $M_r = 247{\cdot}2$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}706$ (1), $b = 8{\cdot}275$ (1), $c = 18{\cdot}364$ (1) Å, $V = 1171{\cdot}0$ (3) Å^3, $Z = 4$, $D_x = 1{\cdot}402$, $D_m = 1{\cdot}40$ (5) Mg m^{-3}, λ(Mo $K\bar{\alpha}$) = 0·7107 Å, μ(Mo $K\alpha$) = 0·12 mm^{-1}, $T = 293$ K, $F(000) = 528$, final $R = 0{\cdot}036$ for 942 reflexions. The conformation of the hydroxyl group about the C(5)–C(6) bond is *trans–gauche*. The conformational angles φ, ψ and ψ' are 157·8, 81·9 and −156·2°, respectively.

Introduction. Ce travail s'inscrit dans le cadre d'un ensemble de recherches concernant l'étude des propriétés conformationnelles de glycosides complexes en solution aqueuse par résonance magnétique nucléaire du ^{13}C (Pavia & Lacombe, 1981) et à l'état solide par diffraction de rayons X (Oddon, Ferrari, Guy, Pavia, Reboul & Pèpe, 1983). L'objectif majeur de ce travail est une meilleure appréciation de l'importance de l'effet *exo*-anomère (Lemieux, Koto & Voisin, 1979) comme facteur déterminant de la conformation autour de la liaison glycosidique.

Partie expérimentale. Préparation par désacétylation de tri-*O*-acétyl-3,4,6 azido-2 désoxy-2 β-D-galactopyrannoside isopropylique. Recristallisation dans le dichlorométhane. Cristaux incolores, forme parallélipipédique irrégulière. Mesure de la masse volumique par flottaison du cristal dans un mélange hexane/CCl_4. Cristal taillé en forme de sphère de 0,16 mm. Paramètres affinés sur Nonius CAD-4 à

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