Acta Cryst. (1979). B35, 477–479

9-(3-Dimethylaminopropylamino)-2-nitroacridine

BY A. HEMPEL* AND S. E. HULL

Department of Physics, University of York, York YO1 5DD, England

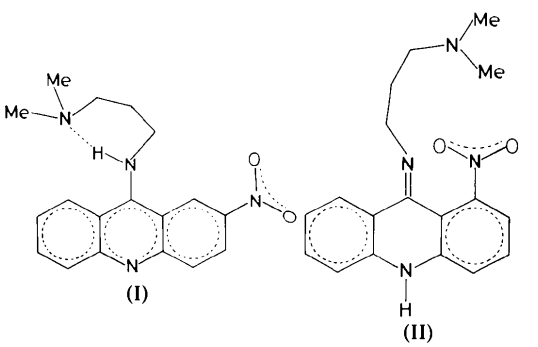
AND Z. DAUTER, M. BOGUCKA-LEDOCHOWSKA AND A. KONITZ

Department of Pharmaceutical Technology and Biochemistry, Technical University, 80-952 Gdańsk, Poland

(*Received* 31 *August* 1978; *accepted* 30 *October* 1978)

Abstract. $C_{18}H_{20}N_4O_2$, FW 324, triclinic, $P\bar{1}$, a = 8·56 (1), b = 12·70 (1), c = 8·58 (1) Å, α = 98·35 (5), β = 99·92 (5), γ = 113·27 (5)°, V = 820 Å^3, Z = 2, D_m = 1·29, D_c = 1·31 Mg m^{-3}, $F(000)$ = 344, μ = 0·63 mm^{-1}. The structure was solved by direct methods and refined by the full-matrix least-squares method to a final R = 0·069 for 1667 reflections measured with a Syntex $P2_1$ diffractometer using graphite-monochromatized Cu $K\alpha$ radiation. The acridine moiety is planar and the nitro group is coplanar with the acridine plane. There is an intramolecular hydrogen bond between N(18) and N(22).

Introduction. 9-(3-Dimethylaminopropylamino)-2-nitroacridine (I), designated as C-264 and hereafter referred to as such, is one member of a long series of synthetic acridine derivatives obtained in the Department of Pharmaceutical Technology and Biochemistry of the Technical University of Gdańsk, Poland, in the course of research into new antineoplastic agents. One of its successors, C-283 [9-(3-dimethylaminopropylimino)-1-nitro-9,10-dihydroacridine] (II), has been registered in Poland as an antitumour drug having been previously preclinically and later clinically investigated (Radzikowski, 1974). The only difference between the two compounds is the position of the nitro group on the acridine nucleus and this accounts for large differences in their conformations and electronic structures. The unique conformational features of C-283 (Dauter, Bogucka-Ledochowska, Hempel, Ledochowski & Kosturkiewicz, 1976) are responsible for the biological activity of the compound. Recently an acridine derivative similar to C-283, 9-[3-(dimethyloxyamino)propylimino]-1-nitro-9,10-dihydroacridine (designated C-684), has shown promising antineoplastic properties and has been found to have a similar conformation in the solid state to that of C-283 (Hempel, Hull, Bogucka-Ledochowska & Dauter, 1979). C-264 is biologically inactive and this is due to a conformation which is completely different from those of C-283 and C-684.



(I) (II)

Crystals of C-264 were grown from methanol, in an atmosphere of diethyl ether, as thick yellow hexagonal plates. Precession photographs taken with Cu $K\alpha$

Table 1. *Fractional coordinates of the non-hydrogen atoms* (×10^4)

	x	y	z
C(1)	1586 (6)	−595 (4)	4800 (5)
C(2)	812 (6)	−1552 (4)	5403 (6)
C(3)	1629 (7)	−1664 (4)	6889 (6)
C(4)	3187 (7)	−815 (5)	7730 (6)
C(5)	8186 (7)	2773 (5)	8534 (6)
C(6)	9138 (6)	3764 (5)	8115 (6)
C(7)	8456 (7)	4015 (4)	6695 (7)
C(8)	6853 (7)	3260 (4)	5728 (6)
C(9)	4147 (6)	1343 (4)	5064 (5)
N(10)	5645 (5)	980 (4)	8099 (4)
C(11)	3251 (5)	316 (4)	5616 (5)
C(12)	4081 (6)	199 (4)	7147 (5)
C(13)	6487 (6)	1954 (4)	7563 (5)
C(14)	5814 (5)	2203 (4)	6104 (5)
N(15)	−894 (5)	−2476 (4)	4485 (6)
O(16)	−1508 (5)	−3361 (4)	5012 (5)
O(17)	−1649 (5)	−2341 (3)	3231 (5)
N(18)	3568 (5)	1556 (3)	3656 (4)
C(19)	2152 (6)	806 (4)	2217 (5)
C(20)	2433 (11)	1345 (6)	751 (7)
C(21)	2791 (12)	2530 (6)	898 (8)
N(22)	4471 (6)	3407 (4)	2005 (5)
C(23)	4293 (9)	4492 (6)	2519 (8)
C(24)	5913 (10)	3637 (7)	1278 (9)

* Present address: Department of Pharmaceutical Technology and Biochemistry, Technical University, 80-952 Gdańsk, Poland.

0567-7408/79/020477-03$01.00

radiation showed triclinic symmetry. The crystal selected had dimensions 0·4 × 0·3 × 0·5 mm. Data were collected on a Syntex $P2_1$ diffractometer ($\omega/2\theta$ scan, scan range 0·6°, θ_{max} 50°). The unit-cell dimensions were calculated by a least-squares fit of 15 high-angle reflexions. The intensity data were converted into structure amplitudes by application of the usual Lorentz and polarization corrections.

The structure was solved by direct methods using the *MULTAN* 78 package (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). The normalization of the structure amplitudes was carried out using a non-analytical K curve. The E map revealed the positions of 18 of the 24 nonhydrogen atoms of the molecule. The missing six atoms were subsequently found from a difference electron density map. All H atoms were also found from a difference electron density map. The structure was refined by *SHELX* 76 (Sheldrick, 1976). For the non-hydrogen atoms anisotropic thermal parameters were refined, and isotropic temperature factors were allowed for the H atoms. Throughout the refinement 1677 structure amplitudes were used with unit weights.* The function minimized was $\sum||F_o| - |F_c||^2$. The final difference electron density map showed no residual electron density higher than 0·40 e Å^{-3}. The final R index was 0·069 where $R = \sum||F_o| - |F_c||/\sum|F_o|$. The calculations were performed with the University of York DEC-10 computer. The positional parameters of the atoms are given in Tables 1 and 2.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34014 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *The hydrogen-atom coordinates* (×10⁴) *and isotropic temperature factors* (Å² × 10⁴)

	x	y	z	U
H(10)	1022 (42)	−563 (28)	3948 (39)	401 (97)
H(30)	1120 (38)	−2270 (25)	7188 (35)	303 (83)
H(40)	3748 (49)	−849 (33)	8633 (46)	709 (121)
H(50)	8585 (45)	2555 (31)	9356 (42)	572 (108)
H(60)	10282 (42)	4292 (28)	8763 (39)	473 (97)
H(70)	9067 (38)	4629 (25)	6391 (35)	376 (83)
H(80)	6454 (43)	3419 (29)	4903 (40)	472 (99)
H(180)	4005 (36)	2123 (25)	3499 (34)	231 (79)
H(191)	1063 (50)	792 (34)	2539 (46)	786 (123)
H(192)	2192 (53)	−0 (35)	1901 (49)	888 (133)
H(201)	1330 (36)	806 (24)	−278 (34)	876 (114)
H(202)	3606 (35)	1296 (23)	517 (34)	1190 (146)
H(211)	2735 (34)	2708 (22)	−299 (32)	1056 (114)
H(212)	1738 (35)	2626 (23)	1344 (32)	1536 (159)
H(231)	3876 (55)	4641 (36)	1507 (52)	1008 (135)
H(232)	3245 (68)	4281 (45)	2907 (63)	1338 (178)
H(233)	5426 (66)	5049 (42)	3196 (59)	1305 (166)
H(241)	5699 (73)	3959 (48)	371 (70)	1497 (201)
H(242)	6896 (48)	4163 (33)	1891 (46)	764 (111)
H(243)	6431 (81)	3064 (58)	1291 (76)	2029 (240)

Discussion. The molecule and the atom numbering scheme are shown in Fig. 1. The bond lengths and angles are given in Tables 3 and 4. The X-ray analysis shows that the acridine moiety is planar and the nitro group at C(2) is coplanar with it; in contrast, the acridine fragments of C-283 and C-684 are not planar, the molecules being bent by 21 and 19° respectively across the line C(9)···N(10), and the nitro groups are twisted with respect to the side ring of the acridine fragment by 65 and 64° respectively. The deviations of

Table 3. *Bond lengths* (Å)

E.s.d.'s 0·01 Å.

C(1)–C(2)	1·36	C(9)–N(18)	1·33
C(1)–C(11)	1·41	N(10)–C(12)	1·34
C(2)–C(3)	1·40	N(10)–C(13)	1·36
C(2)–N(15)	1·45	C(11)–C(12)	1·44
C(3)–C(4)	1·33	C(13)–C(14)	1·42
C(4)–C(12)	1·43	N(15)–O(16)	1·23
C(5)–C(6)	1·34	N(15)–O(17)	1·23
C(5)–C(13)	1·42	N(18)–C(19)	1·46
C(6)–C(7)	1·39	C(19)–C(20)	1·53
C(7)–C(8)	1·35	C(20)–C(21)	1·39
C(8)–C(14)	1·41	C(21)–N(22)	1·47
C(9)–C(11)	1·42	N(22)–C(23)	1·46
C(9)–C(14)	1·44	N(22)–C(24)	1·43

Table 4. *Bond angles* (°)

E.s.d.'s 1°.

C(2)–C(1)–C(11)	122	C(4)–C(12)–C(11)	119
C(1)–C(2)–C(3)	121	N(10)–C(12)–C(11)	125
C(1)–C(2)–N(15)	119	C(5)–C(13)–N(10)	117
C(3)–C(2)–N(15)	119	C(5)–C(13)–C(14)	118
C(2)–C(3)–C(4)	119	N(10)–C(13)–C(14)	125
C(3)–C(4)–C(12)	122	C(8)–C(14)–C(9)	124
C(6)–C(5)–C(13)	122	C(8)–C(14)–C(13)	118
C(5)–C(6)–C(7)	120	C(9)–C(14)–C(13)	118
C(6)–C(7)–C(8)	121	C(2)–N(15)–O(16)	118
C(7)–C(8)–C(14)	122	C(2)–N(15)–O(17)	119
C(11)–C(9)–C(14)	117	O(16)–N(15)–O(17)	123
C(11)–C(9)–N(18)	125	C(9)–N(18)–C(19)	132
C(14)–C(9)–N(18)	118	N(18)–C(19)–C(20)	110
C(12)–N(10)–C(13)	116	C(19)–C(20)–C(21)	119
C(1)–C(11)–C(9)	125	C(20)–C(21)–N(22)	117
C(1)–C(11)–C(12)	117	C(21)–N(22)–C(23)	108
C(9)–C(11)–C(12)	118	C(21)–N(22)–C(24)	113
C(4)–C(12)–N(10)	116	C(23)–N(22)–C(24)	110

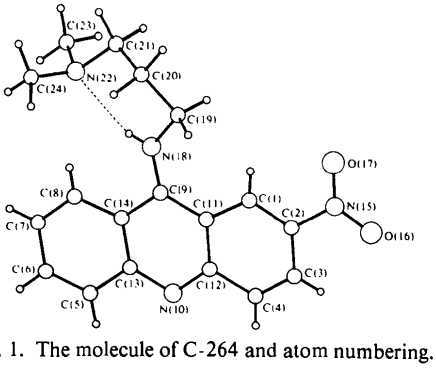


Fig. 1. The molecule of C-264 and atom numbering.

the atoms in C-264 from the least-squares plane are listed in Table 5.

The conformation of the aliphatic side chain is affected by an intramolecular hydrogen bond involving N(18)—H(180)···N(22). The distances involved are N(18)···N(22) 2·84, N(22)···H(180) 2·18, and N(18)—H(180) 0·71 Å. The side chain points in the opposite direction to the nitro group in contrast to the conformation of the side chains in C-283 and C-684. The unusually large C(9)—N(18)—C(19) angle (132°) is a result of the steric interaction between C(1) and C(19), the distance between them being 3·02 Å, and also the hydrogen bond mentioned above.

The bond lengths within the acridine nucleus of C-264 conform much more closely with those listed for other 9-aminoacridines by Dauter *et al.* (1976) than do those in C-283 and C-684. In particular, the involvement of the central ring of the nucleus in a delocalized system is made apparent by the shortness of the C(9)—C(11) [and C(9)—C(14)] and N(10)—C(12) [and N(10)—C(13)] bonds in comparison with those in C-283 and C-684.

The conformational and electronic differences between C-283 and C-684, and other 9-aminoacridine derivatives, arise because of the steric interaction between the 1-nitro group and the C(9) side chain, leading to migration of the proton at N(18) to N(10) and loss of planarity. It appears that lack of conjugation and planarity in the acridine nucleus is a requirement for biological activity in these compounds.

The packing is shown in Fig. 2. The molecules are stacked in a head-to-tail manner. The nearest molecules are 3·44 Å apart and are related by a centre of symmetry.

Table 5. *Least-squares plane through the listed atoms and atomic deviations* (Å) *expressed in orthogonal ångström space*

Equation: $-0{\cdot}7901X + 0{\cdot}3700Y + 0{\cdot}4887Z = -0{\cdot}577$

C(1)	0·001	C(7)	0·013	C(13)	−0·017
C(2)	−0·004	C(8)	−0·023	C(14)	−0·023
C(3)	−0·020	C(9)	0·023	N(15)	0·014
C(4)	−0·043	N(10)	−0·024	O(16)	0·088
C(5)	0·026	C(11)	0·013	O(17)	−0·051
C(6)	0·042	C(12)	−0·014		

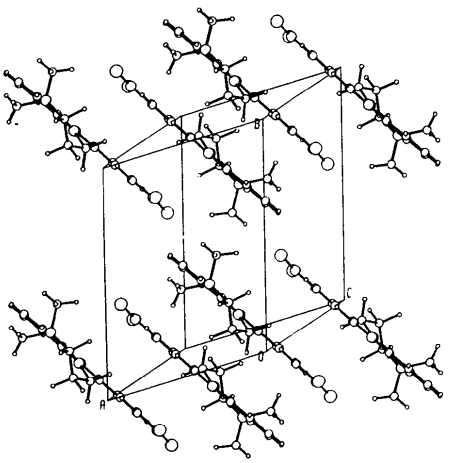


Fig. 2. The molecular arrangement in the crystal.

The authors thank Dr T. Głowiak from the Institute of Inorganic Chemistry, Wrocław, Poland, for measuring intensity data. We also thank the Science Research Council and the Polish Academy of Sciences for their financial support of this work.

References

DAUTER, Z., BOGUCKA-LEDOCHOWSKA, M., HEMPEL, A., LEDOCHOWSKI, A. & KOSTURKIEWICZ, Z. (1976). *Rocz. Chem.* **50**, 1573–1586.

HEMPEL, A., HULL, S. E., BOGUCKA-LEDOCHOWSKA, M. & DAUTER, Z. (1979). *Acta Cryst.* B**35**, 474–476.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J. P. & WOOLFSON, M. M. (1978). *MULTAN 78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univ. of York, England.

RADIZIKOWSKI, C. (1974). (Editor.) *Preparat* C-283: *Collective Work.* Univ. of Wrocław.

SHELDRICK, G. M. (1976). *SHELX* 76. Program for crystal structure determination. Univ. of Cambridge, England.