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Nucleic Acid Binding Drugs. IX. The Structures of 5-*n*-Butyl-11-demethylellipticine, $C_{19}H_{18}N_2$, and 9-Methoxyellipticine, $C_{18}H_{16}N_2O$

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Abstract. (I) $C_{19}H_{18}N_2$ (5-*n*-butyl-6*H*-pyrido[4,3-*b*]carbazole), $M_r = 274{\cdot}37$, $P2_1/c$, $a = 5{\cdot}023$ (3), $b = 17{\cdot}848$ (5), $c = 16{\cdot}454$ (5) Å, $\beta = 93{\cdot}67$ (2)°, $V = 1472{\cdot}1$ (11) Å^3, $Z = 4$, $D_m = 1{\cdot}24$, $D_x = 1{\cdot}238$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 0{\cdot}528$ mm^{-1}, $F(000) = 584$, $R = 0{\cdot}068$ for 815 unique significant reflections measured at 298 K. (II) $C_{18}H_{16}N_2O$ (5,11-dimethyl-9-methoxy-6*H*-pyrido[4,3-*b*]carbazole), $M_r = 276{\cdot}34$, $P2_1/c$, $a = 6{\cdot}508$ (1), $b = 24{\cdot}281$ (8), $c = 8{\cdot}938$ (2) Å, $\beta = 98{\cdot}46$ (2)°, $V = 1397{\cdot}0$ (10) Å^3, $Z = 4$, $D_m = 1{\cdot}33$, $D_x = 1{\cdot}314$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 0{\cdot}616$ mm^{-1}, $F(000) = 584$, $R = 0{\cdot}052$ for 1736 unique significant reflections measured at 298 K. The dimensions of the ring systems in the two compounds are similar to one another and to those found in ellipticine itself [Courseille, Busetta & Hospital (1974). *Acta Cryst.* B**30**, 2628–2631].

Introduction. Ellipticine is a plant alkaloid which shows pronounced anti-tumour activity. There is considerable evidence that this activity is related to the DNA-binding properties of this planar aromatic system (Gale, Cundliffe, Reynolds, Richmond & Waring, 1981; Neidle, 1979), and several studies of rational design of analogues with enhanced activity have been based on this postulate (Le Pecq, Xuong, Gosse & Paoletti, 1974; Paoletti, Cros, Xuong, Lecointe & Moisand, 1979). The crystal-structure analysis of an ellipticine–dinucleoside complex (Jain, Bhandary & Sobell, 1979) has demonstrated that the parent drug can indeed intercalate in between adjacent base pairs, at least in this model nucleic acid system.

One of us has recently developed efficient synthetic routes to various ellipticine derivatives, including the title compounds (Sainsbury, Weerasinghe & Dolman, 1982). The present study is the first in a series directed at describing the molecular characteristics of these analogues, with special reference to differences in interactions with DNA.

A preliminary report of an X-ray analysis of 9-methoxyellipticine has recently appeared (Bandyopadhyay & Basak, 1981), based on photographic intensity data. No details of structural parameters arising from this study have been published, so the present accurate analysis is the first to describe this structure fully.

Experimental. Crystals of both compounds were obtained from ethanol solution as light-yellow prisms; (I) could only be produced as very small crystals. Densities measured by flotation; X-ray photographs taken to determine crystal class; accurate cell dimensions obtained by least-squares analysis of 25 θ values measured on an Enraf–Nonius CAD-4 diffractometer; intensity data collected with graphite-monochromated Cu $K\alpha$ radiation, θ–2θ scan; $\theta_{max} = 55°$ ($-5 \le h \le 5$, $0 \le k \le 18$, $0 \le l \le 17$) for (I), and $\theta_{max} = 65°$ ($0 \le h \le 7$, $0 \le k \le 28$, $-10 \le l \le 10$) for (II). Crystal (I) was ~0·04 × 0·09 × 0·03 mm and (II), ~0·04 × 0·20 × 0·12 mm. The intensities of three standard reflections were monitored at intervals of 3600 s; in neither case was any crystal decomposition noted. 2012 unique reflections for (I); 815 with $I > 2\sigma(I)$ were used for the refinement. The high number of unobserved reflections reflects the small size of crystal used. 2645 unique reflections for (II), 1736 with $I > 2\sigma(I)$. Direct methods [*MULTAN*80 (Main *et al.*, 1980)], refinement on F by full-matrix least squares with anisotropic thermal parameters. Some H-atom positions for (I) were found from difference Fourier syntheses, and positions for the remainder were calculated from standard geometric considerations. All H-atom parameters for (I) were kept fixed during the course of the refinement. Final difference Fourier maps for (I) and (II) showed no peaks >0·15 e Å^{-3}. Unit weights for (I), final $R = 0{\cdot}068$, maximum shift/error 0·01. For (II) $w = 1/[\sigma(I)^2 + (0{\cdot}03I)^2]^{1/2}$, final $R = 0{\cdot}052$, $R_w = 0{\cdot}060$, maximum shift/error 0·07. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974); all calculations performed on a PDP

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11/34A computer using the *SDP* program system (Frenz, 1980).

Discussion. Final atomic parameters are in Table 1.*

Figs. 1 and 2 show views of the molecular structures of (I) and (II), and Table 2 details the bond lengths and angles in these structures. Comparison of the observed bond lengths in the two compounds with each other, and with those found in a structure analysis of ellipticine itself (Courseille, Busetta & Hospital, 1974) (Table 2), reveals virtually no significant differences in

* Lists of structure factors, anisotropic thermal parameters for the heavier atoms, and H-atom coordinates and isotropic temperature factors have been deposited with the Britsh Library Lending Division as Supplementary Publication No. SUP 38340 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Positional and equivalent isotropic thermal parameters* (Å^2) *with e.s.d.'s in parentheses*

$B_{eq} = \frac{1}{3}(B_{11} + B_{22} + B_{33})$.

Compound (I)

	x	*y*	*z*	B_{eq}
N(2)	0·502 (1)	0·3185 (3)	1·0083 (3)	5·2 (2)
N(6)	0·360 (1)	0·1399 (3)	0·6716 (3)	3·9 (1)
C(1)	0·356 (1)	0·2613 (5)	0·9794 (4)	4·5 (3)
C(3)	0·677 (2)	0·3477 (4)	0·9577 (5)	5·0 (2)
C(4)	0·705 (1)	0·3215 (4)	0·8797 (4)	4·3 (2)
C(5)	0·563 (1)	0·2334 (4)	0·7679 (4)	3·6 (2)
C(7)	0·071 (2)	0·0362 (4)	0·6145 (4)	4·6 (2)
C(8)	−0·128 (2)	−0·0132 (4)	0·6324 (5)	5·2 (2)
C(9)	−0·228 (2)	−0·0141 (5)	0·7103 (5)	5·5 (2)
C(10)	−0·131 (2)	0·0342 (4)	0·7706 (5)	4·9 (2)
C(11)	0·198 (1)	0·1698 (4)	0·8766 (4)	4·0 (2)
C(12)	0·362 (1)	0·2301 (4)	0·8999 (4)	3·8 (2)
C(13)	0·549 (1)	0·2616 (4)	0·8474 (4)	3·9 (2)
C(14)	0·394 (1)	0·1767 (4)	0·7456 (4)	3·4 (2)
C(15)	0·213 (1)	0·1424 (4)	0·7991 (4)	3·2 (2)
C(16)	0·067 (1)	0·0849 (4)	0·7536 (4)	3·8 (2)
C(17)	0·165 (1)	0·0846 (4)	0·6748 (4)	3·7 (2)
C(18)	0·754 (1)	0·2654 (4)	0·7088 (4)	3·7 (2)
C(19)	0·640 (1)	0·3352 (4)	0·6658 (4)	4·2 (2)
C(20)	0·815 (1)	0·3643 (5)	0·6002 (4)	4·7 (2)
C(21)	0·695 (2)	0·4331 (5)	0·5563 (5)	6·3 (2)

Compound (II)

	x	*y*	*z*	B_{eq}
O(20)	0·4381 (3)	1·05157 (7)	0·7513 (2)	6·47 (5)
N(2)	0·0323 (3)	0·70140 (9)	1·0582 (2)	4·47 (5)
N(6)	0·6807 (3)	0·83531 (9)	0·7234 (2)	3·89 (4)
C(1)	0·0713 (4)	0·7532 (1)	1·0358 (3)	4·12 (6)
C(3)	0·1557 (4)	0·6644 (1)	0·9984 (3)	4·46 (6)
C(4)	0·3108 (4)	0·6787 (1)	0·9191 (3)	3·99 (6)
C(5)	0·5179 (4)	0·7517 (1)	0·8157 (2)	3·46 (5)
C(7)	0·7386 (4)	0·9340 (1)	0·6611 (3)	5·02 (6)
C(8)	0·6666 (5)	0·9865 (1)	0·6728 (3)	5·44 (7)
C(9)	0·4973 (4)	0·9972 (1)	0·7495 (3)	4·73 (6)
C(10)	0·4012 (4)	0·9551 (1)	0·8150 (3)	4·30 (6)
C(11)	0·2545 (4)	0·8314 (1)	0·9365 (2)	3·58 (5)
C(12)	0·2273 (4)	0·7745 (1)	0·9558 (2)	3·55 (5)
C(13)	0·3549 (4)	0·7347 (1)	0·8953 (2)	3·45 (5)
C(14)	0·5392 (4)	0·8076 (1)	0·7975 (2)	3·36 (5)
C(15)	0·4086 (4)	0·8480 (1)	0·8539 (2)	3·38 (5)
C(16)	0·4734 (4)	0·9012 (1)	0·8040 (3)	3·65 (5)
C(17)	0·6407 (4)	0·8911 (1)	0·7247 (3)	3·85 (5)
C(18)	0·1246 (4)	0·8740 (1)	1·0042 (3)	4·96 (6)
C(19)	0·6552 (4)	0·7119 (1)	0·7509 (3)	4·56 (6)
C(21)	0·2468 (5)	1·0627 (1)	0·8073 (4)	7·24 (9)

Table 2. *Bond lengths* (Å) *and bond angles* (°) *for the non-hydrogen atoms, with e.s.d.'s in parentheses*

	(I)	(II)	Ellipticine*
C(1)–N(2)	1·327 (7)	1·305 (4)	1·313
C(1)–C(12)	1·424 (7)	1·422 (3)	1·424
N(2)–C(3)	1·356 (7)	1·365 (3)	1·361
C(3)–C(4)	1·380 (8)	1·361 (4)	1·362
C(4)–C(13)	1·408 (7)	1·412 (3)	1·415
C(5)–C(13)	1·407 (7)	1·423 (3)	1·414
C(5)–C(14)	1·356 (7)	1·375 (3)	1·373
C(5)–C(18)	1·523 (7)		1·509
C(5)–C(19)		1·490 (4)	
N(6)–C(14)	1·384 (6)	1·385 (3)	1·378
N(6)–C(17)	1·392 (7)	1·381 (3)	1·375
C(7)–C(8)	1·378 (8)	1·368 (4)	1·375
C(7)–C(17)	1·377 (8)	1·386 (4)	1·398
C(8)–C(9)	1·406 (8)	1·405 (4)	1·393
C(9)–C(10)	1·381 (8)	1·375 (4)	1·374
C(10)–C(16)	1·387 (8)	1·398 (4)	1·398
C(11)–C(12)	1·396 (8)	1·406 (4)	1·415
C(11)–C(15)	1·374 (7)	1·391 (3)	1·383
C(11)–C(19)		1·517 (4)	1·512
C(12)–C(13)	1·432 (7)	1·430 (3)	1·440
C(14)–C(15)	1·442 (7)	1·437 (3)	1·443
C(15)–C(16)	1·441 (7)	1·448 (3)	1·454
C(16)–C(17)	1·415 (7)	1·405 (3)	1·411
C(18)–C(19)	1·526 (8)		
C(19)–C(20)	1·529 (8)		
C(20)–C(21)	1·528 (8)		
C(9)–O(20)		1·376 (3)	
O(20)–C(21)		1·434 (3)	

	(I)	(II)
N(2)–C(1)–C(12)	125·9 (7)	126·6 (2)
C(1)–N(2)–C(3)	116·2 (6)	115·8 (2)
N(2)–C(3)–C(4)	123·3 (6)	124·0 (2)
C(3)–C(4)–C(13)	121·5 (6)	120·5 (2)
C(13)–C(5)–C(14)	116·9 (6)	116·2 (2)
C(13)–C(5)–C(19)		122·6 (2)
C(13)–C(5)–C(18)	122·0 (6)	
C(14)–C(5)–C(18)	121·1 (6)	
C(14)–C(5)–C(19)		121·2 (2)
C(14)–N(6)–C(17)	110·5 (5)	109·5 (2)
C(17)–C(7)–C(8)	117·8 (6)	119·0 (3)
C(7)–C(8)–C(9)	120·7 (6)	120·8 (3)
C(8)–C(9)–C(10)	121·1 (7)	120·6 (3)
C(8)–C(9)–O(20)		115·1 (2)
C(10)–C(9)–O(20)		124·3 (3)
C(9)–C(10)–C(16)	119·2 (6)	119·2 (2)
C(12)–C(11)–C(15)	117·5 (6)	117·7 (2)
C(12)–C(11)–C(18)		122·2 (2)
C(15)–C(11)–C(18)		120·1 (2)
C(1)–C(12)–C(11)	120·4 (7)	122·0 (2)
C(1)–C(12)–C(13)	117·1 (6)	116·2 (2)
C(11)–C(12)–C(13)	122·5 (6)	121·8 (2)
C(4)–C(13)–C(5)	124·4 (6)	122·6 (2)
C(4)–C(13)–C(12)	116·1 (6)	116·8 (2)
C(5)–C(13)–C(12)	119·5 (6)	120·6 (2)
C(5)–C(14)–N(6)	129·2 (6)	128·4 (2)
C(5)–C(14)–C(15)	124·1 (6)	123·9 (2)
N(6)–C(14)–C(15)	106·7 (5)	107·7 (2)
C(11)–C(15)–C(14)	119·4 (6)	119·8 (2)
C(11)–C(15)–C(16)	132·8 (6)	133·5 (2)
C(14)–C(15)–C(16)	107·7 (5)	106·7 (2)
C(10)–C(16)–C(15)	134·9 (7)	134·1 (2)
C(10)–C(16)–C(17)	118·6 (6)	119·4 (2)
C(15)–C(16)–C(17)	106·5 (6)	106·4 (2)
N(6)–C(17)–C(7)	128·9 (7)	129·4 (2)
N(6)–C(17)–C(16)	108·5 (6)	109·6 (2)
C(7)–C(17)–C(16)	122·6 (6)	120·9 (2)
C(5)–C(18)–C(19)	111·6 (5)	
C(18)–C(19)–C(20)	112·8 (5)	
C(19)–C(20)–C(21)	112·3 (5)	
C(9)–O(20)–C(21)		116·3 (2)

* Courseille, Busetta & Hospital (1974). Average e.s.d.'s are 0·004 Å.

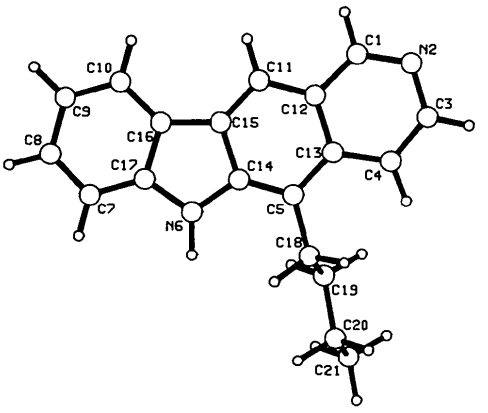

Fig. 1. The molecular structure of 5-*n*-butyl-11-demethylellipticine.

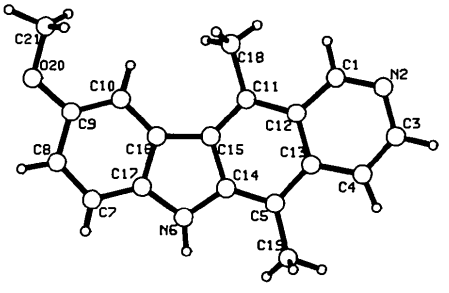

Fig. 2. The molecular structure of 9-methoxyellipticine.

these parameters. The largest difference between (I) and (II) occurs in the exocyclic bond to C(5), which is some 4σ longer in (I). The methoxy group attached at atom C(9) in (II) has produced no discernible effect on the bonding geometry of the ellipticine ring system, even though it may be presumed to have had some effect on its electronic properites. The exocyclic angles around C(9) in (II) are markedly asymmetric, angle C(8)–C(9)–O(20) being some 9° smaller than C(10)–C(9)–O(20); this is presumably due to steric repulsions from the proton on C(10). The dihedral angle C(10)–C(9)–O(20)–C(21) is 9·0 (3)°. The ellipticine ring system in both compounds is planar within experimental error, as is the parent ellipticine itself. The *n*-butyl side chain in (I) adopts a staggered conformation, with the dihedral angles around bonds C(18)–C(19) and C(19)–C(20) 174·5 (9) and 178·7 (9)°, respectively.

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Stereochemical Studies of Oligomers. III.* The Structure of 2,3-Butanediyl Dibenzoate, $C_{18}H_{18}O_4$

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Abstract. $M_r = 298{\cdot}3$, monoclinic, $P2_1/c$, $a = 11{\cdot}760\ (2)$, $b = 18{\cdot}104\ (2)$, $c = 7{\cdot}541\ (1)$ Å, $\beta = 106{\cdot}4\ (2)°$, $V = 1540{\cdot}2$ Å^3, $Z = 4$, $D_x = 1{\cdot}29$ Mg m^{-3}, Cu $K\alpha$ radiation, $\lambda = 1{\cdot}5418$ Å, $\mu = 7{\cdot}01$ cm^{-1}, $F(000) = 632$, $T = 298$ K, $R_w = 0{\cdot}038$ for 2281 independent measured reflections. The two aromatic rings

* Part II: Bocelli & Grenier-Loustalot (1982*b*).

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