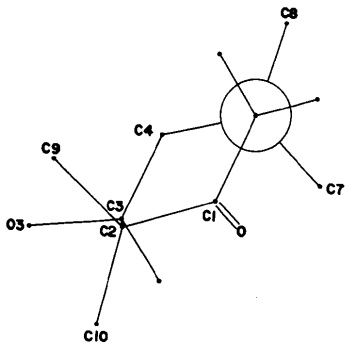

Fig. 2. A Newmann projection of the molecule, down C(5)–C(6).

relationship between C(3)–O(3) and C(4)–C(5) bonds is antiperiplanar. Therefore, the stereoelectronic requirements are met and the fragmentation reaction should occur with a relatively low activation energy.

This work has received partial support from CNPq, FAPESP and FINEP, which is hereby gratefully acknowledged. One of us (JZ-S) thanks CNPq for the award of a research grant (Proc. 405301/85). We thank Professor Cookson for providing experimental details for the preparation of 3-hydroxy-2,2,5,5-tetramethylcyclohexanone.

References

BROCKSOM, U., LASCALA TEIXEIRA, H., KANAWAGA, A. M. & BROCKSOM, T. J. (1987). In preparation.
COOKSON, R. C., EDWARDS, A. G., HUDEC, J. & KINGSLAND, M. (1965). *Chem. Commun.* pp. 98–99.
CREMER, D. & POPLE, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1344–1358.
CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
GAONI, Y. & WENKERT, E. (1966). *J. Org. Chem.* **31**, 3809–3814.
HAMILTON, W. C. (1959). *Acta Cryst.* **12**, 609–610.
JOHNSON, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
MARSHALL, J. A. (1969). *Rec. Chem. Prog.* **1**, 3–21.
SHELDRICK, G. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.
SIMONSEN, J. L. & OWEN, L. N. (1953). In *The Terpenes*, 2nd ed., Vol. 1, pp. 105–106. Cambridge Univ. Press.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1987). C**43**, 1992–1995

Nucleic Acid Binding Drugs. XVII. Structures of 4-Substituted Analogues of the Antitumour Drug Amsacrine

BY ZELDA H. L. ABRAHAM AND STEPHEN NEIDLE*

Cancer Research Campaign Biomolecular Structure Unit, Institute of Cancer Research, Sutton, Surrey SM2 5PX, England

AND R. MORRIN ACHESON

Department of Biochemistry, University of Oxford, South Parks Road, Oxford, England

(*Received* 20 *August* 1986; *accepted* 27 *May* 1987)

Abstract. 4′-(9-Oxo-4-acridinyl)methanesulfonanilide monohydrate (I), $C_{20}H_{16}N_2O_3S.H_2O$, $M_r = 382$, monoclinic, $P2_1/c$, $a = 7{\cdot}373$ (1), $b = 11{\cdot}266$ (4), $c = 20{\cdot}925$ (3) Å, $\beta = 94{\cdot}59$ (2)°, $V = 1732{\cdot}5$ Å^3, $Z = 4$, $D_x = 1{\cdot}466$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 18{\cdot}76$ cm^{-1}, $F(000) = 800$, $T = 293$ K, $R = 0{\cdot}078$ for 1238 observed reflections. 4′-(9-Amino-4-acridinyl)-methanesulfonanilide hydrochloride (II), $C_{20}H_{18}N_3O_2S^+.Cl^-$, $M_r = 399{\cdot}4$, monoclinic, $P2_1/c$, $a = 10{\cdot}437$ (2), $b = 16{\cdot}092$ (3), $c = 10{\cdot}866$ (1) Å, $\beta = 91{\cdot}28$ (2)°, $V = 1824{\cdot}5$ Å^3, $Z = 4$, $D_x = 1{\cdot}456$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 30{\cdot}99$ cm^{-1}, $F(000) = 832$, $T = 293$ K, $R = 0{\cdot}047$ for 1501 observed reflections. The acridone and acridine rings in (I) and (II) are highly planar. The methanesulfonanilide substituent groups are oriented in a similar manner in both structures, although the methanesulfonanide groups adopt different orientations with respect to the phenyl ring.

Introduction. A large number of acridines substituted at the 9 position have been synthesized and evaluated for antitumour activity (Baguley, Denny, Atwell & Cain, 1981; Denny, Cain, Atwell, Hansch, Panthananickal & Leo, 1982). The compound 4′-(9-acridinylamino)-3′-methoxymethanesulfonanilide (ansacrine) has outstanding experimental *in vivo* activity in the series, and is

* Address correspondence to this author.

0108-2701/87/101992-04$01.50

currently being examined for clinical efficacy. The present publication reports aspects of the effect of systematic variation of the position of the aromatic-group substitution; synthetic, biological-activity, DNA-binding and computer-modelling (Abraham, Cutbush, Kuroda, Neidle, Acheson & Taylor, 1985) studies are being reported elsewhere.

Experimental. (I) Crystallized from dioxane:methoxyethanol as pale-yellow prisms. Crystal 0·05 × 0·15 × 0·10 mm mounted on a glass fibre. Cell dimensions from 25θ values measured on a CAD-4 diffractometer. Ni-filtered Cu $K\alpha$ radiation. Intensity data collected with ω–2θ scan technique and max. scan time of 90 s per reflection, $1{\cdot}5 < \theta < 65{\cdot}0°$; $0 \le h \le 7$, $0 \le k \le 11$, $-22 \le l \le 22$. Three reflections monitored every 250 measured reflections; no significant decay. Absorption ignored. 2166 unique reflections: 1238 with $I > 2\sigma(I)$. Structure determined by direct methods (*MULTAN*82; Main *et al.*, 1982) and refined by full-matrix least squares on F. H atoms kept fixed during refinement. Final $R = 0{\cdot}078$, $wR = 0{\cdot}084$, $w = 1/[\sigma^2(F) + 0{\cdot}04(F^2)]$, max. $\Delta/\sigma = 0{\cdot}02$, $-0{\cdot}4 < \rho < 0{\cdot}5$ e Å^{-3}.

(II) Yellow prismatic crystals from ethanol solution. Crystal of dimensions 0·05 × 0·13 × 0·55 mm used. Experimental conditions as above. Data collection with 120 s max. time for scan, $1{\cdot}5 < \theta < 65{\cdot}0°$; $-12 \le h \le 12$, $0 \le k \le 18$, $0 \le l \le 12$. 3093 unique reflections with 1501 having $I > 2\sigma(I)$. $R = 0{\cdot}047$, $wR = 0{\cdot}049$, max. $\Delta/\sigma = 0{\cdot}01$, $-0{\cdot}4 < \rho < 0{\cdot}3$ e Å^{-3}. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Calculations performed with the *SDP* package (Frenz, 1980) on a VAX 11/750 computer.

Discussion. Atomic positions and equivalent isotropic thermal parameters for (I) and (II) are given in Table 1.* Their molecular structures are shown in Figs. 1 and 2, and bond geometry is given in Tables 2 and 3. These show that the overall conformations are very similar, except for the methanesulfonamide group, which is known to be able to adopt a wide range of conformations (Abraham *et al.*, 1985; Karle, Cysyk & Karle, 1980). Thus, the torsion angle C(16)–C(15)–N(15)–S(1) that specifies the orientation of this group with respect to the phenyl ring is −47·6 (6)° in (I) and 5·0 (3)° in (II). This flexibility has been noted previously in the crystal structures of amsacrine and its salts (Abraham *et al.*, 1985; Hall, Swann & Waters, 1974; Karle *et al.*, 1980). The conformations of the two molecules in terms of the relation between the phenyl ring and the acridone (in I) or acridine (in II) chromophore are very similar. The C(5A)–C(5)–C(12)–C(13) torsion angles differ by 9° (Table 4), which represents only a small energy difference in terms of the barrier to rotation about the C(5)–C(12) sp^2–sp^2 bond linking the two aromatic ring systems. The fact that in neither structure is the phenyl ring oriented precisely orthogonal to the acridine chromophore, suggests that the low-energy flexibility to the phenyl ring position would tend to increase further its effective van der Waals volume and thus diminish the nucleic acid intercalative ability of the acridine portion of these molecules.

Table 1. *Fractional coordinates and average thermal parameters*

E.s.d.'s are in parentheses.

	x	y	z	B^*(Å^2)
(I)				
S(1)	−0·0585 (4)	−0·1658 (2)	1·2723 (1)	2·99 (5)
O(1)	−0·013 (1)	−0·1749 (7)	1·3390 (3)	3·8 (2)
O*W*(1)	0·620	0·458	0·237	5·7
O(2)	0·073 (1)	−0·1981 (7)	1·2284 (4)	4·3 (2)
O(9)	−0·355 (1)	0·5011 (7)	0·8643 (3)	4·2 (2)
N(10)	−0·238 (1)	0·3734 (7)	1·0449 (4)	2·3 (2)
N(15)	−0·116 (1)	−0·0261 (7)	1·2585 (4)	3·0 (2)
C(1)	−0·249 (1)	0·666 (1)	0·9649 (5)	3·7 (3)
C(2)	−0·193 (2)	0·736 (1)	1·0153 (6)	3·8 (3)
C(3)	−0·149 (2)	0·688 (1)	1·0750 (5)	3·7 (3)
C(4A)	−0·224 (1)	0·4945 (9)	1·0346 (5)	2·5 (2)
C(4)	−0·164 (1)	0·569 (1)	1·0862 (5)	3·1 (2)
C(5)	−0·296 (1)	0·1718 (9)	1·0107 (4)	2·1 (2)
C(5A)	−0·290 (1)	0·2949 (9)	0·9962 (4)	2·1 (2)
C(6)	−0·344 (1)	0·0962 (9)	0·9602 (5)	2·9 (2)
C(7)	−0·384 (2)	0·136 (1)	0·8973 (5)	3·4 (3)
C(8)	−0·379 (2)	0·255 (1)	0·8841 (5)	3·5 (3)
C(8A)	−0·332 (1)	0·337 (1)	0·88345 (4)	2·4 (2)
C(9A)	−0·267 (1)	0·542 (1)	0·9734 (5)	2·6 (2)
C(9)	−0·320 (1)	0·464 (1)	0·9197 (4)	2·9 (2)
C(12)	−0·250 (1)	0·1227 (8)	1·0758 (4)	2·3 (2)
C(13)	−0·351 (1)	0·1452 (9)	1·1273 (5)	3·1 (2)
C(14)	−0·309 (1)	0·0931 (9)	1·1867 (5)	2·8 (2)
C(15)	−0·157 (1)	0·203 (8)	1·967 (4)	2·2 (2)
C(16)	−0·054 (1)	0·001 (1)	1·1469 (5)	3·1 (2)
C(17)	−0·096 (1)	0·0506 (9)	1·0881 (4)	2·9 (2)
C(18)	−0·251 (2)	−0·251 (1)	1·2532 (7)	5·3 (3)
(II)				
Cl	0·5099 (1)	0·60295 (9)	0·7107 (1)	4·20 (3)
S(1)	0·6107 (1)	0·14461 (9)	0·2520 (1)	2·39 (2)
O(1)	0·6478 (3)	0·2075 (2)	0·3387 (3)	3·37 (8)
O(2)	0·7099 (3)	0·0942 (3)	0·1988 (3)	3·67 (8)
N(9)	−0·2095 (4)	0·1340 (3)	0·9441 (4)	3·1 (1)
N(10)	0·1486 (3)	0·1041 (3)	0·7972 (3)	2·32 (8)
N(15)	0·5167 (4)	0·0797 (3)	0·3172 (4)	2·43 (9)
C(1)	0·0094 (5)	0·1046 (3)	1·1060 (4)	2·8 (1)
C(2)	0·1138 (5)	0·0822 (4)	1·1765 (5)	3·2 (1)
C(3)	0·2296 (5)	0·0656 (4)	1·1195 (5)	3·2 (1)
C(4A)	0·1346 (4)	0·0954 (3)	0·9218 (4)	2·0 (1)
C(4)	0·2418 (4)	0·0721 (3)	0·9957 (5)	2·5 (1)
C(5A)	0·0478 (4)	0·1267 (3)	0·7206 (4)	2·1 (1)
C(5)	0·694 (5)	0·1373 (3)	0·5935 (4)	2·2 (1)
C(6)	−0·0349 (5)	0·1615 (3)	0·5195 (4)	3·0 (1)
C(7)	−0·1575 (5)	0·1712 (3)	0·5671 (5)	3·0 (1)
C(8)	−0·1780 (4)	0·1590 (3)	0·6881 (4)	2·6 (1)
C(8A)	−0·0750 (4)	0·1378 (3)	0·7678 (4)	2·09 (9)
C(9A)	0·0162 (4)	0·1276 (3)	0·9763 (4)	2·2 (1)
C(9)	−0·0838 (4)	0·1276 (3)	0·8973 (4)	2·1 (1)
C(12)	0·1963 (4)	0·1240 (3)	0·5343 (4)	2·3 (1)
C(13)	0·2417 (5)	0·0446 (3)	0·5151 (5)	2·6 (1)
C(14)	0·3492 (4)	0·0315 (3)	0·4447 (4)	2·1 (1)
C(15)	0·4125 (4)	0·0984 (3)	0·3931 (4)	2·0 (1)
C(16)	0·3705 (5)	0·1784 (3)	0·4150 (5)	2·4 (1)
C(17)	0·2624 (5)	0·1907 (3)	0·4841 (5)	2·5 (1)
C(18)	0·5239 (5)	0·1925 (4)	0·1312 (5)	3·2 (1)

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

* Tables of anisotropic thermal parameters, H-atom positions, and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44095 (28 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å) *and angles* (°) *for non*-H *atoms in* (I)

E.s.d.'s are in parentheses.

S(1)–O(1)	1·414 (4)	C(5A)–C(8A)	1·388 (8)
S(1)–O(2)	1·435 (5)	C(5A)–N(10)	1·382 (7)
S(1)–N(15)	1·649 (5)	C(6)–C(7)	1·400 (9)
S(1)–C(18)	1·736 (8)	C(7)–C(8)	1·368 (10)
C(1)–C(2)	1·354 (10)	C(8)–C(8A)	1·424 (9)
C(1)–C(9A)	1·423 (10)	C(8A)–C(9)	1·461 (9)
C(2)–C(3)	1·375 (10)	C(9)–O(9)	1·241 (7)
C(3)–C(4)	1·369 (10)	C(9)–C(9A)	1·457 (9)
C(4)–C(4A)	1·412 (9)	C(12)–C(13)	1·385 (9)
C(4A)–C(9A)	1·400 (8)	C(12)–C(17)	1·402 (9)
C(4A)–N(10)	1·386 (8)	C(13)–C(14)	1·387 (9)
C(5)–C(5A)	1·420 (9)	C(14)–C(15)	1·387 (9)
C(5)–C(6)	1·382 (9)	C(15)–C(16)	1·357 (9)
C(5)–C(12)	1·483 (8)	C(16)–C(17)	1·367 (9)
C(5A)–C(5)	1·414		

O(1)–S(1)–O(2)	119·6 (3)	C(6)–C(7)–C(8)	119·8 (6)
O(1)–S(1)–N(15)	106·3 (3)	C(7)–C(8)–C(8A)	119·7 (6)
O(1)–S(1)–C(18)	108·2 (4)	C(5A)–C(8A)–C(8)	119·2 (6)
O(2)–S(1)–N(15)	108·0 (3)	C(5A)–C(8A)–C(9)	121·4 (6)
O(2)–S(1)–C(18)	107·2 (4)	C(8)–C(8A)–C(9)	119·4 (5)
N(15)–S(1)–C(18)	107·1 (4)	O(9)–C(9)–C(8A)	121·3 (6)
C(4A)–N(10)–C(5A)	122·4 (5)	O(9)–C(9)–C(9A)	122·6 (6)
S(1)–N(15)–C(15)	123·3 (4)	C(8A)–C(9)–C(9A)	116·2 (5)
C(2)–C(1)–C(9A)	120·1 (6)	C(1)–C(9A)–C(4A)	118·2 (6)
C(1)–C(2)–C(3)	121·0 (7)	C(1)–C(9A)–C(9)	121·4 (6)
C(2)–C(3)–C(4)	121·5 (7)	C(4A)–C(9A)–C(9)	120·3 (6)
N(10)–C(4A)–C(4)	119·4 (6)	C(5)–C(12)–C(13)	123·3 (6)
N(10)–C(4A)–C(9A)	120·1 (6)	C(5)–C(12)–C(17)	120·4 (6)
C(4)–C(4A)–C(9A)	120·5 (6)	C(13)–C(12)–C(17)	116·3 (6)
C(3)–C(4)–C(4A)	118·6 (7)	C(12)–C(13)–C(14)	121·5 (6)
C(5A)–C(5)–C(6)	116·6 (6)	C(13)–C(14)–C(15)	120·5 (6)
C(5A)–C(5)–C(12)	123·5 (5)	N(15)–C(15)–C(14)	118·1 (6)
C(6)–C(5)–C(12)	119·8 (6)	N(15)–C(15)–C(16)	123·7 (6)
C(5)–C(5A)–N(10)	118·6 (5)	C(14)–C(15)–C(16)	118·1 (6)
C(8A)–C(5A)–C(5)	121·8 (6)	C(15)–C(16)–C(17)	121·9 (6)
C(8A)–C(5A)–N(10)	119·6 (5)	C(12)–C(17)–C(16)	121·6 (6)
C(5)–C(6)–C(7)	122·8 (6)		

Table 3. *Bond lengths* (Å) *and angles* (°) *for non*-H *atoms in* (II)

E.s.d.'s are in parentheses.

S(1)–O(1)	1·430 (3)	C(5A)–C(8A)	1·403 (5)
S(1)–O(2)	1·445 (3)	C(5)–C(6)	1·394 (6)
S(1)–N(15)	1·608 (4)	C(5)–C(12)	1·491 (6)
S(1)–C(18)	1·757 (5)	C(6)–C(7)	1·400 (6)
N(9)–C(9)	1·325 (5)	C(7)–C(8)	1·351 (6)
N(10)–H(10)	1·3276 (5)	C(8)–C(8A)	1·407 (6)
N(15)–C(15)	1·411 (5)	C(8A)–C(9)	1·435 (6)
C(1)–C(2)	1·366 (7)	C(9A)–C(9)	1·446 (6)
C(1)–C(9A)	1·416 (6)	C(12)–C(13)	1·384 (6)
C(2)–C(3)	1·397 (7)	C(12)–C(17)	1·400 (6)
C(3)–C(4)	1·358 (6)	C(13)–C(14)	1·387 (6)
C(4A)–C(4)	1·413 (6)	C(14)–C(15)	1·389 (6)
C(4A)–C(9A)	1·401 (5)	C(15)–C(16)	1·382 (6)
C(5A)–C(5)	1·414 (6)	C(16)–C(17)	1·383 (6)

O(1)–S(1)–C(2)	118·4 (2)	C(6)–C(7)–C(8)	120·6 (5)
O(1)–S(1)–N(15)	109·1 (2)	C(7)–C(8)–C(8A)	120·0 (4)
O(1)–S(1)–C(18)	108·0 (3)	C(5A)–C(5A)–C(8)	119·8 (4)
O(2)–S(1)–N(15)	105·2 (2)	C(5A)–C(8A)–C(9)	119·3 (4)
O(2)–S(1)–C(18)	108·1 (3)	C(8)–C(8A)–C(9)	120·0 (4)
N(15)–S(1)–C(18)	107·7 (3)	C(1)–C(9A)–C(4A)	118·4 (4)
C(4A)–N(10)–C(5A)	121·8 (4)	C(1)–C(9A)–C(9)	123·1 (4)
S(1)–N(15)–C(15)	127·2 (4)	C(4A)–C(9A)–O(9)	118·5 (4)
C(2)–C(1)–C(9A)	121·1 (4)	N(9)–C(9)–C(8A)	120·8 (4)
C(1)–C(2)–C(3)	119·3 (5)	N(9)–C(9)–C(9A)	120·4 (4)
C(2)–C(3)–C(4)	121·7 (5)	C(8A)–O(9)–C(9A)	118·7 (4)
N(10)–C(4A)–C(4)	119·2 (4)	C(5)–C(12)–C(13)	120·8 (4)
N(10)–C(4A)–C(9A)	120·9 (4)	C(5)–C(12)–C(17)	120·8 (4)
C(4)–C(4A)–C(9A)	119·9 (4)	C(13)–C(12)–C(17)	118·0 (4)
C(3)–C(4)–C(4A)	119·6 (5)	C(12)–C(13)–C(14)	120·9 (5)
N(10)–C(5A)–C(5)	119·1 (4)	C(13)–C(14)–C(15)	120·1 (5)
N(10)–C(5A)–C(8A)	120·3 (4)	N(15)–C(15)–C(14)	116·8 (4)
C(5)–C(5A)–C(8A)	120·6 (4)	N(15)–C(15)–C(16)	123·4 (4)
C(5A)–C(5)–C(6)	117·2 (4)	C(14)–C(15)–C(16)	119·8 (4)
C(5A)–C(5)–C(12)	124·4 (4)	C(15)–C(16)–C(17)	119·6 (5)
C(6)–C(5)–C(12)	118·4 (4)	C(12)–C(17)–C(16)	121·5 (5)
C(5)–O(6)–C(7)	121·8 (4)		

The acridone and acridine ring systems in (I) and (II) are both highly coplanar, as has been observed in other acridine crystal structures, such as that of 9-aminoacridine (Talacki, Carrell & Glusker, 1974)

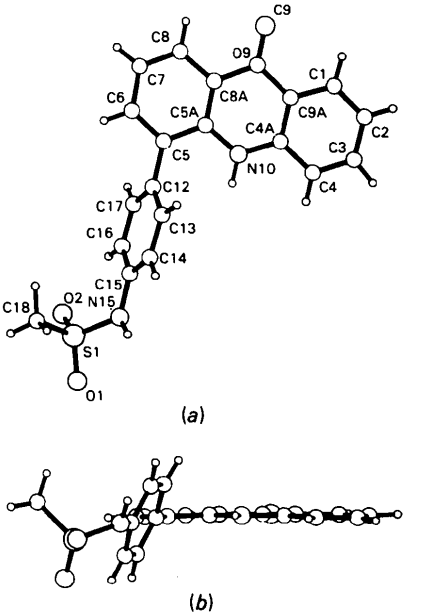

Fig. 1. Computer-drawn representations of the molecular structure of compound (I): (*a*) projected onto the mean plane of the chromophore, (*b*) shown at 90° to the view in (*a*).

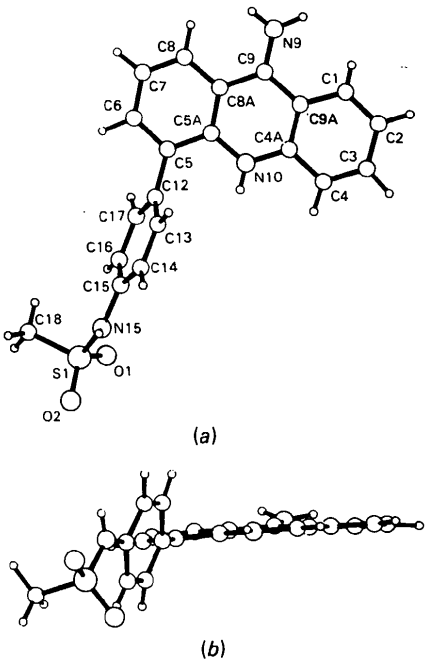

Fig. 2. Computer-drawn views of the cation in the structure of compound (II), with views as in Fig. 1.

Table 4. *Selected torsion angles* (°), *with e.s.d.'s in parentheses*

	(I)	(II)
C(5A)–C(5)–C(12)–C(13)	65·5 (9)	74·5 (6)
C(14)–C(15)–N(15)–S(1)	135·4 (7)	183·6 (4)
C(15)–N(15)–S(1)–C(18)	−69·5 (7)	−72·2 (4)

and 3,6-diaminoacridine (Jones & Neidle, 1975). The acridine bonding geometry in (I) is as expected, subtly different from that of a normal acridine, with differences in bond lengths being most apparent in the central ring. These differences, though not large, do indicate that the carbonyl group at C(9) has reduced the delocalization in the ring. The ring nitrogen atom N(10) is sp^2-hybridized as in normal acridines. Its low pK_a excludes it from being protonated, which would not in any case be feasible in structural terms as ring buckling would necessarily be produced. Thus, the single H atom attached to N(10) in (I) does not carry a positive charge, in contrast to that in (II), which exists as a salt.

References

ABRAHAM, Z. H. L., CUTBUSH, S. D., KURODA, R., NEIDLE, S., ACHESON, R. M. & TAYLOR, G. (1985). *J. Chem. Soc. Perkin Trans.* 2, pp. 461–465.

BAGULEY, B. C., DENNY, W. A., ATWELL, G. J. & CAIN, B. F. (1981). *J. Med. Chem.* **24**, 170–177.

DENNY, W. A., CAIN, B. F., ATWELL, G. J., HANSCH, C., PANTHANANICKAL, A. & LEO, A. (1982). *J. Med. Chem.* **25**, 276–315.

FRENZ, B. A. (1980). *Enraf–Nonius Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

HALL, D., SWANN, D. A. & WATERS, T. N. (1974). *J. Chem. Soc. Perkin Trans.* 2, pp. 1334–1337.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JONES, T. A. & NEIDLE, S. (1975). *Acta Cryst.* B**31**, 1324–1333.

KARLE, J. M., CYSYK, R. L. & KARLE, I. L. (1980). *Acta Cryst.* B**36**, 3012–3016.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN*82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

TALACKI, R., CARRELL, H. L. & GLUSKER, J. P. (1974). *Acta Cryst.* B**30**, 1044–1047.

Acta Cryst. (1987). C**43**, 1995–1998

Structure of Neoandrographolide Monohydrate

BY W. J. J. SMEETS, A. L. SPEK* AND A. J. M. DUISENBERG

Vakgroep Algemene Chemie, Afdeling Kristal- en Structuurchemie, University of Utrecht, Padualaan 8, 3584 *CH Utrecht, The Netherlands*

R. P. LABADIE

Department of Pharmacognosy, Pharmaceutical Laboratory, University of Utrecht, The Netherlands

AND K. T. D. DE SILVA AND S. RATNAYAKE

Department of Chemistry, University of Sri Jayewardenepura, Sri Lanka

(*Received* 5 *May* 1987; *accepted* 2 *June* 1987)

Abstract. [(1*R*)-(1α,4aβ,5α,8aα)]-3-(2-{5-[(β-D-Glucopyranosyloxy)methyl]decahydro-5,8a-dimethyl-2-methylene-1-naphthalenyl}ethyl)-2(5*H*)-furanone monohydrate, $C_{26}H_{40}O_8.H_2O$, M_r = 498·62, monoclinic, $P2_1$, a = 7·377 (3), b = 6·235 (9), c = 28·569 (8) Å, β = 95·73 (3)°, V = 1307 (2) Å^3, Z = 2, D_x = 1·266 g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, μ = 0·9 cm^{-1}, $F(000)$ = 540, T = 294 K, R = 0·0537 for 1697 observed reflections with $I > 2\sigma(I)$. The crystal structure consists of two-dimensional hydrogen-bonded layers, involving the β-D-glucopyranose moiety and the water molecule of crystallization, separated by layers consisting of a stacking of the neoandrographolide–aglucon moieties with no short intermolecular contacts.

Introduction. Within the framework of our immunopharmacognostic studies we isolated a sugar-bound diterpenoid from herb material of *Andrographis paniculata*. Since this constituent showed significant inhibitory action on both pathways of human complement *in vitro* it was decided to study its molecular structure. The compound was identified as neoandrographolide. Among other diterpenoids from *Andrographis paniculata* that are being used against bacillary dysentery in

* Author to whom correspondence should be addressed.

0108-2701/87/101995-04$01.50