Palstra, T. T. M., Kortan, A. R., Zahurak, S. M. and Makhija, A. V., *Phys. Rev. Lett.*, 1991, **66**, 2830.
5. The carbon sp^2 hybridization easily leads to a local two-dimensional (planar) character in organic molecules.
6. McGlynn, S. P. *et al., Molecular Spectroscopy of the Triplet State*, Prentice Hall, New Jersey, 1969.
7. Silinsh, E. A., *Organic Molecular Crystals*, Springer Series in Solid State Science, No. 16, Springer, New York, 1980.
8. Edward, C. Lim, V. (ed.), *Excited States*, Academic Press, 1982, Vol. 6, First article.
9. Weaver, J. H., José Luiś Martins, Komeda, T., Chen, Y., Ohno, T. R., Kroll, G. H., Troullier, N., Haufler, R. E. and Smalley, R. E., *Phys. Rev. Lett.*, 1991, **66**, 1741; Benning, P. J. *et al.*, preprint, April 1991.
10. Haddon, R. C., private communication.
11. Little, W. A., *Phys. Rev.*, 1984, **A134**, 1416; Ginzburg, V. L., *Sov. Phys. JETP*, (*Engl. Transl.*) 1965, **20**, 1549.
12. Haymet, A. D. J., *Chem. Phys. Lett.*, 1985, **122**, 421; Haddon, R. C., *Chem. Phys. Lett.*, 1986, **125**, 459; Disch, R. L., Schulman, J. M., *Chem. Phys. Lett.*, 1986, **125**, 465; Fowler, P. W., Woolrich, J., *Chem. Phys. Lett.*, 1986, **127**, 78; Ozaki, M. and Takahashi, A., *Chem. Phys. Lett.*, 1986, **127**, 242; Satpathy, S., *Chem. Phys. Lett.*, 1986, **130**, 545.
13. Baskaran, G. and Tosatti, E., to be published
14. Bassani, F. and Pastori Parravicini, G., *Electronic Structure and Optical Transitions in Solids*, Pergamon Press, New York, p. 139, and references therein; Saito, S. and Oshiyama, A., *Phys. Rev. Lett.*, 1991, **66**, 2665.
15. Pauling, L., *The Nature of the Chemical Bond*, Oxford University Press, London, 1963.
16. Coulson, C. A., *Valence*, Oxford University Press, London, 1965.
17. Yu Lu, *Solitons and Polarons in Conducting Polymers*, World Scientific, Singapore, 1988, and many of the papers reprinted there, especially those dealing with the effect of Coulomb interactions.
18. Baskaran, G., to be published.
19. Leib, E. and Mattis, D., *Mathematical Physics in One Dimension*, Academic Press, New York.
20. Kivelson, S., Rokhsar, D. and Sethna, J., *Phys. Rev.*, 1987, **B35**, 8865.
21. Anderson, P. W., Baskaran, G., Zou, Z. and Hsu, T., *Phys. Rev. Lett.*, 1987, **58**, 2790.
22. Ovchinnikov, A. A., Ukrainskii, I. I., Kventsel, G. V., *Sov. Phys. Usp.*, 1973, **15**, 575.
23. Inkson, J. C. and Anderson, P. W., *Phys. Rev.*, 1973, **B8**, 4429; Allender, D., Bray, J. and Bardeen, J., *Phys. Rev.*, 1973, **B8**, 4433.
24. A note about the dielectric constant. We have used a dielectric constant of $\varepsilon = 5$, which is estimated using the plasma frequency of the π-electron system as well as the overall gap from the optical absorption experiment. This value is also very close to the value in graphite, which is very similar to C_{60} as far as local electronic character is concerned. As the potassium concentration increases the polarizability of the potassium will also contribute and we expect it to increase, Academic Press, New York, 1966.
25. Micnas, R., Ranninger, J. and Robaszkiewiscz, S., *Rev. Mod. Phys.*, 1990, **62**, 113.
26. Anderson, P. W., *Phys. Rev. Lett.*, 1975, **34**, 953.
27. Chakravarti, B. K., *J. Phys. Lett.*, 1979, **B40**, L99.
28. Anderson, P. W., *Phys. Rev. Lett.*, 1990, **64**, 1839; **65**, 2306.
29. Varma, C. M., Littlewood, P. B., Schmitt-Rink, S., Abrahams, E. and Ruckenstein, A. E., *Phys. Rev. Lett.*, 1989, **63**, 1996.
30. Johnson, K. H. *et al.*, preprint.
31. Su, W. P., Schrieffer, J. R. and Heeger, A. J., *Phys. Rev.*, 1980, **B22**, 2099.
32. Anderson, P. W., *Science*, 1987, **235**, 1196.
33. Arbogast, J. W. *et al.*, *J. Phys. Chem.*, 1991, **95**, 11.

ACKNOWLEDGEMENTS. We thank P. W. Anderson, P. Fazekas, S. Mazumdar and S. Ramasesha who have told us the importance of electron correlations in carbon $p\pi$-bonded system in the past. We also thank W. Andreoni and especially M. Parrinello for sharing with us their ideas and unpublished results. We also thank R. C. Haddon for sharing the unpublished results. ET wishes to acknowledge support from the Istituto Nationale di Struttura della Materia, IBM Italy, and the European Research Office, US Army.

Received 26 June 1991; accepted 28 June 1991

Note added in proof: After submission of this paper J. Bhattacharjee gave us a copy of a recent preprint by S. Chakravarty and S. Kivelson (UCLA preprint) where correlation-induced stability of evenly charged C_{60} molecule is discussed.

Steric and rotational constraints in the X-ray structure of the antimalarial drug amodiaquine

Hemant P. Yennawar and M. A. Viswamitra*

Department of Physics and *Jawaharlal Nehru Centre for Advanced Research, Indian Institute of Science, Bangalore 560 012, India

In the crystal structure of the antimalarial drug amodiaquine, the bonds linking the quinoline and the phenyl groups show partial double-bond character. The partial double-bond character of the two exocyclic bonds, together with stereochemical constraints, reduce flexibility of the two ring systems of the molecule. The dihedral angle between the two ring planes is lowest compared to those in the antileukaemic drug amsacrine and its derivatives. CPK-modelling studies suggest the way amodiaquine can bind to DNA. Stacking interaction between the quinoline and phenyl groups of independent molecules and the hydrogen-bond network stabilize the crystal structure.

AMODIAQUINE, 4-[(7-chloro-4-quinolinyl)amino]-2-[(diethylamino)methyl]phenol, an analogue of the widely used antimalarial drug chloroquine, is also used for treating malaria. It has some structural resemblance with the antileukaemic drug amsacrine (AMSA), where

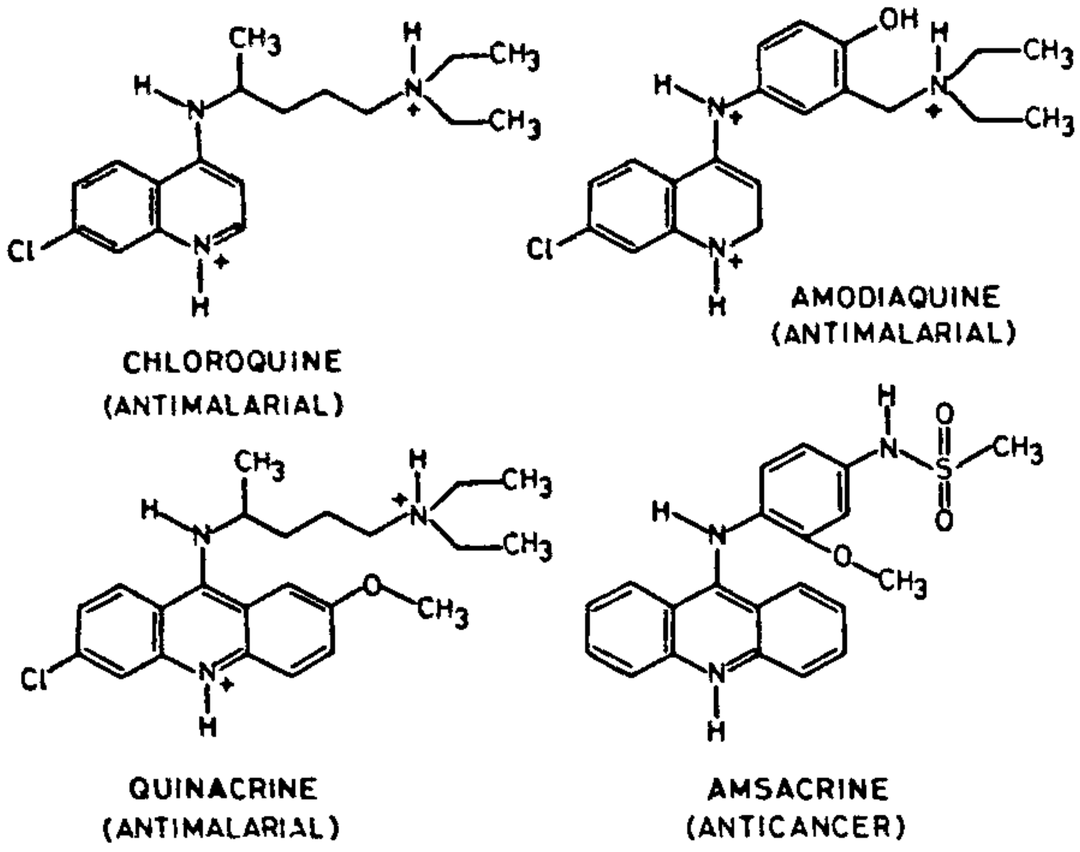

Figure 1. Chemical structures of amodiaquine and related drugs, where the chromophore is connected by a nitrogen to the rest of the molecule.

the chromophore is linked to the phenyl ring through a nitrogen atom (Figure 1). These drug molecules are known to intercalate in DNA to varying degrees, but it is not clear to what extent this provides an explanation for their pharmacological activity. In this connection there is considerable interest in structural and related features such as charge separation, the degree of planarity, and the orientations of the ring systems of these compounds. While there are several reports related to the structures of chloroquine[1-6] and AMSA[7-11] we have little information on amodiaquine. Here we report the crystal structure of amodiaquine.

Experimental

Amodiaquine hydrochloride (trade name Camoquin, Parke Davis) was bought as tablets. Crystals were grown from concentrated solution in distilled ethanol kept at −4°C in a sealed testtube. Deep yellow prismatic crystals appeared in about two weeks.

Intensities for the compound were recorded on an Enraf–Nonius CAD4 diffractometer with Cu K_α ($\lambda = 1.5418$ Å) radiation using $\omega/2\theta$ scan up to a Bragg angle of 75°. Cell constants for the crystal were determined by least-squares refinement on diffractometer angles for 25 automatically centred reflections (Table 1). Index range for unique data is $-19 \leqslant h \leqslant 19$, $0 \leqslant k \leqslant 9$, $0 \leqslant l \leqslant 12$. After data correction for Lorentz and polarization effects the reflections with the criteria $I > 3\sigma(I)$ were taken as observed. Empirical absorption correction was applied[12]; the minimum and maximum corrections were 0.758 and 0.992. MULTAN 11/82 program (ref. 13) and Fourier techniques revealed the complete structure. The hydrogens attached to nitrogen and oxygen atoms were located from difference-Fourier maps. Those attached to carbons were placed in idealized positions. Full-matrix least-squares refinement with non-hydrogens anisotropic and hydrogens isotropic converged to an R value of 0.057. All the calculations were done using the Enraf–Nonius structure determination package[14] on a PDP 11/44 computer.

Table 1. Crystal and relevant X-ray data.

Formula	$C_{20}H_{24}Cl_1N_3O^{3+}\cdot 2Cl^-\cdot OH^-$
Molecular weight	446.5
Crystal symmetry	Monoclinic
Space group	$P2_1/c$
Crystal size	0.65 mm × 0 34 mm × 0.27 mm
a	16.379 (6) Å
b	7.714 (5) Å
c	17.583 (6) Å
β	107.54 (4)°
V	2119.3 Å^3
Z	4
D_c	1.233 g cm^{-3}
μ(Cu Kα)	2.9 mm^{-1}
R_{obs}	0.057
R_w	0.059
ρ	0.23 (3) e Å^{-3}

Intramolecular features

The positional parameters of the non-hydrogen atoms of the molecule are given in Table 2. The stereographic projection of the molecule is seen in Figure 2. The three N atoms in the molecule are found protonated. The H

Table 2. Positional parameters of non-hydrogens and their estimated standard deviations.

Atom	x/a	y/b	z/c	B (Å^2)
Cl1	0 14122(7)	−0.0382(2)	0.49328(8)	4.90(3)
N1	0.4467(2)	0.1659(6)	0.5373(2)	3.58(8)
C2	0.5272(2)	0.1875(7)	0.5827(2)	3.41(9)
C3	0.5561(2)	0.1487(6)	0.6616(2)	3.16(9)
C4	0.4972(2)	0.0851(6)	0.7000(2)	2.58(7)
C5	0.4104(2)	0.0567(5)	0.6511(2)	2.55(7)
C6	0.3472(2)	−0.0190(6)	0.682?2)	2.85(8)
C7	0.2662(2)	−0.0445(6)	0 6331(2)	3.04(8)
C8	0.2455(2)	−0 0023(7)	0 5541(3)	3.41(9)
C9	0.3035(3)	0 0671(6)	0.5194(3)	3.21(9)
C10	0.3859(2)	0 0943(6)	0.5704(2)	2.83(8)
N11	0.5190(2)	0 0579(5)	0.7786(2)	3.05(7)
C12	0.3994(2)	−0 4578(6)	0.6660(2)	2 62(8)
C13	0 3304(2)	−0 5361(6)	0.6847(2)	2.66(8)
C14	0.2538(2)	−0.5609(6)	0.6260(2)	2.69(8)
C15	0.2441(2)	−0.5187(6)	0 5475(2)	2.96(8)
C16	0.3133(2)	−0.4388(7)	0.5290(2)	3.15(9)
C17	0.3884(2)	−0.4119(7)	0.5875(2)	3.27(9)
C18	0 8186(2)	−0.1524(6)	0 8522(2)	2.88(8)
N19	0 8768(2)	−0 0232(5)	0.8267(2)	2 64(6)
C20	0.9372(2)	−0.1238(7)	0 7916(2)	3.63(9)
C21	1 0004(3)	−0 2332(8)	0 8514(3)	5.0(1)
C22	0.9206(3)	0 0963(7)	0 8928(2)	3.38(9)
C23	0.9717(3)	0 2363(8)	0.8655(3)	4 7(1)
O1	0 8300(2)	−0.0543(5)	1 0088(2)	3.72(7)
Cl2	0 38213(6)	0.1788(2)	0 86917(6)	4 07(2)
Cl3	0 77638(7)	0 1904(2)	0 68664(7)	5 27(3)
OW1	0.8125(2)	−0 0715(6)	1.1564(2)	4.71(8)

Isotropic equivalent displacement parameter defined as: (4/3) [a2 B (1, 1) + b2 B(2, 2) + c2 B(3, 3) + ab(cos γ) B(1, 2) + ac(cos β) B(1, 3) + bc (cos α) B(2, 3)].

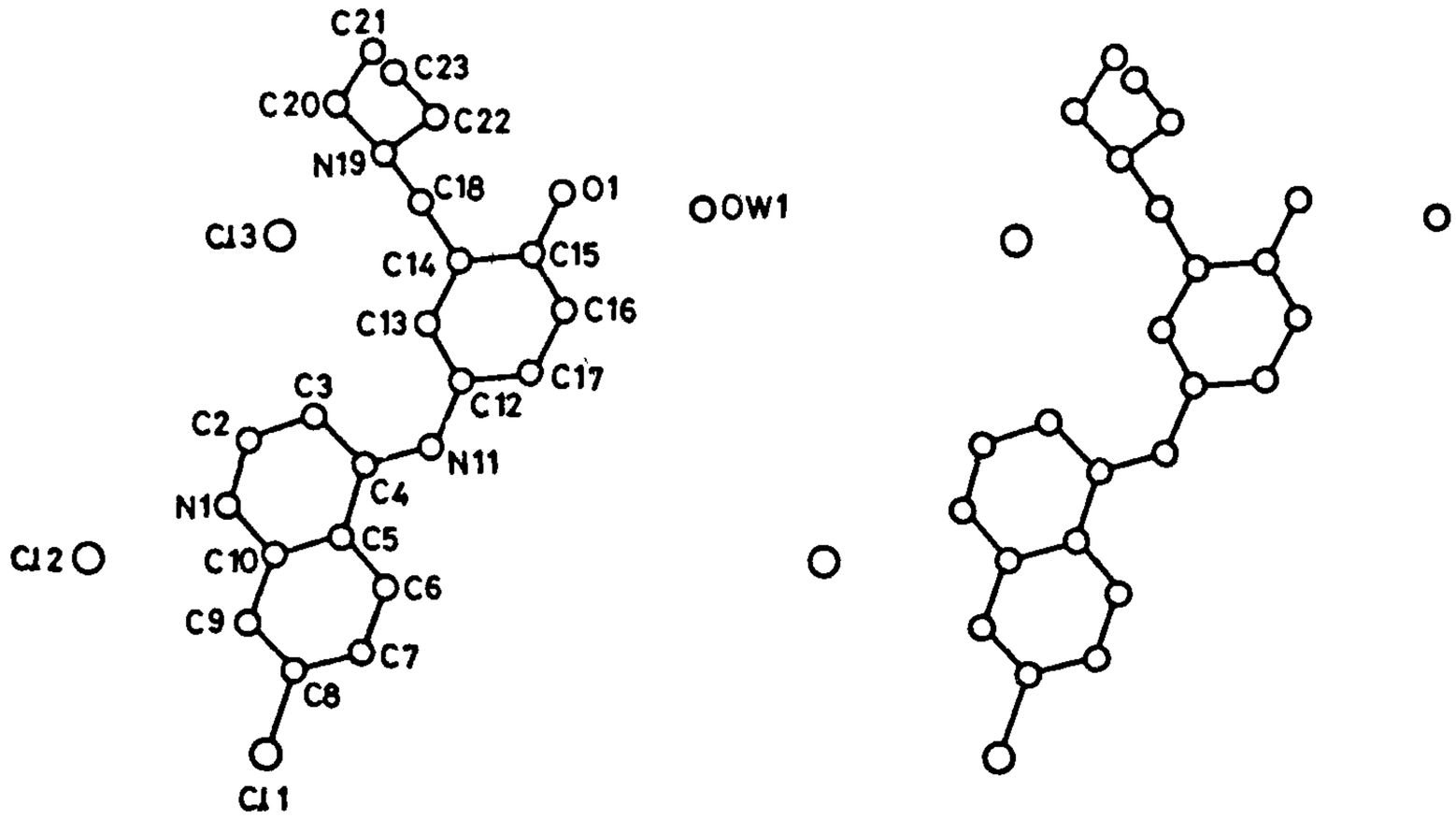

Figure 2. Stereo diagram of amodiaquine molecular structure.

atoms attached to them were clearly identified from difference-Fourier maps. The positive charge on N atoms is balanced by two chloride and one hydroxyl anions in the structure. The phenyl ring is planar as expected, within experimental errors. However, the quinoline moiety is slightly but significantly nonplanar, its two fused rings showing a propeller-like twist about the common bond C5–C10 (Table 3). This is unlike in the structure of chloroquine sulphate[2], where the quinoline moiety is perfectly planar. In the structure of chloroquine bis (dihydrogenphosphate) dihydrate[1] the two rings of the moiety are individually planar but make a small angle (3.7°) between them.

The bond lengths and bond angles are shown in Figure 3. N11–C4, one of the two exocyclic bonds between quinoline and phenyl rings, is 1.341(5) Å, almost that for a double bond. The low rotation observed about the bond (C3–C4–N11–C12 = −17.2(7)°) can be attributed to its double-bond nature. N11–C12, the second exocyclic bond, is also a partial double bond though considerably longer (1.397(6) Å), allowing greater rotational freedom (C4–N11–C12–C13 = −34.7(7)°). From the van der Waals distance

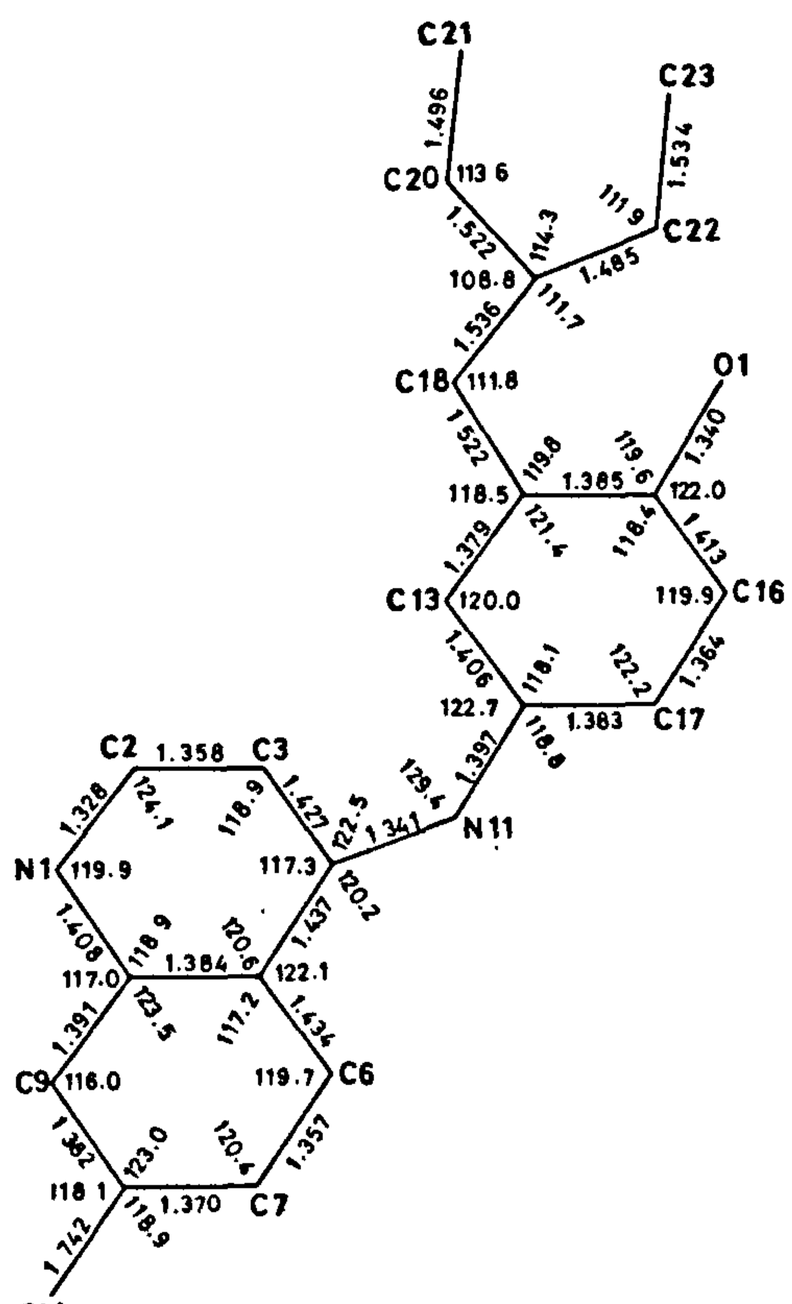

Figure 3. Bond distances and bond angles for amodiaquine. The e.s.d.'s are 0.005 Å and 0.4° respectively.

Table 3. Equations of least-squares planes in the form of $Ax+By+Cz+D=0$, where x, y and z are orthogonalized coordinates. Displacement (Å) of atoms from the planes are listed. Atoms excluded from a plane calculation are indicated by an asterisk.

Plane 1. Chloroquinoline plane, N1–C10

$0.3262x-0.9225y-0.2062z-1.5561=0$

N1 −0.025(4), C2 0.017(5), C3 0.038(5), C4 −0.024(4), C5 −0.032(4), C6 0.008(5), C7 0 012(5), C8 0.011(5), C9 0.007(5), C10 −0.012(4), Cl1* 0.024(2), N11* −0.121(4)

Plane 2. Phenyl plane, C12–C17

$0.3918x+0.9039y-0.1718z+0.0141=0$

C12 0 000(4), C13 −0 010(4), C14 0.018(4), C15 −0.016(5), C16 0.006(5), C17 0.002(5), N11* −0.139(4), O1* −0 066(4), C18* −0.048(4)

criteria it appears that any attempt to reduce the torsions about these bonds will result in unfavourable contacts between H atoms attached to C3 and C13 carbons and also those attached to C6 and N11. The present interatomic distances are 2.281 Å between the hydrogens HC3 and HC13 and 2.080 Å between the hydrogens HC6 and HN11. The conformation of the molecule observed in the crystal structure thus seems to

Table 4. The bonds and torsions involving the nitrogen bridge between chromophore and phenyl ring in amodiaquine and AMSA drugs.

	Bond length N11–C4 (Å)	Torsion about N11–C4 (deg)	Bond length N11–Cl2 (Å)	Torsion about N11–C12 (deg)	Dihedral angle between rings (deg)
Amodiaquine	1.335	−17	1.398	−35	48
AMSA[10]	1.353	31	1.430	47	77
m-AMSA HCl[11]	1.359	21	1.431	48	54
2MeO-AMSA[11]	1.338	28	1.415	55	68
m-AMSA base[12]	1.395	129	1.406	19	66
m-AMSA[13]	1.387	54	1.409	−163	69
Mesyl-*m*-AMSA[13]	1.408	70	1.387	178	66
1-Me-AMSA HCl[14]	1.318	2	1.443	−127	*

*The acridine chromophore in 1-Me-AMSA HCl[14] is significantly non-planar with a butterfly conformation.

have been uniquely determined by intramolecular steric effects and rotational constraint about the two exocyclic bonds.

As seen in Figure 1, the two exocyclic bonds described above also exist in AMSA compounds. However, in all AMSA structures reported so far, these bonds are longer than in amodiaquine (Table 4), resulting in higher values for the torsion angles about these bonds[8] (*m*-AMSA·HCl 21 and 48°, AMSA 31 and 47° and 2MeO·AMSA 28 and 55°).

The dihedral angle between the quinoline and the phenyl rings of amodiaquine is 48°, lowest compared to that in AMSA compounds, where it ranges from 54 to 77° as listed in Table 4.

Intermolecular interactions

The hydrogen-bond parameters are described in Figure 4 and Table 5. The two chloride ions, namely Cl2 and Cl3, give rise to three hydrogen bonds. Cl2 is hydrogen-bonded to N1 of the quinoline ring (N1–H···Cl2 = 3.067 Å) and also to the exocyclic nitrogen N11 (N11–H···Cl2 = 3.253 Å). The second chloride ion, Cl3, acts as a proton acceptor for the hydrogen bond with N19 of the diethylamino group (N19–H···Cl3 = 3.008 Å).

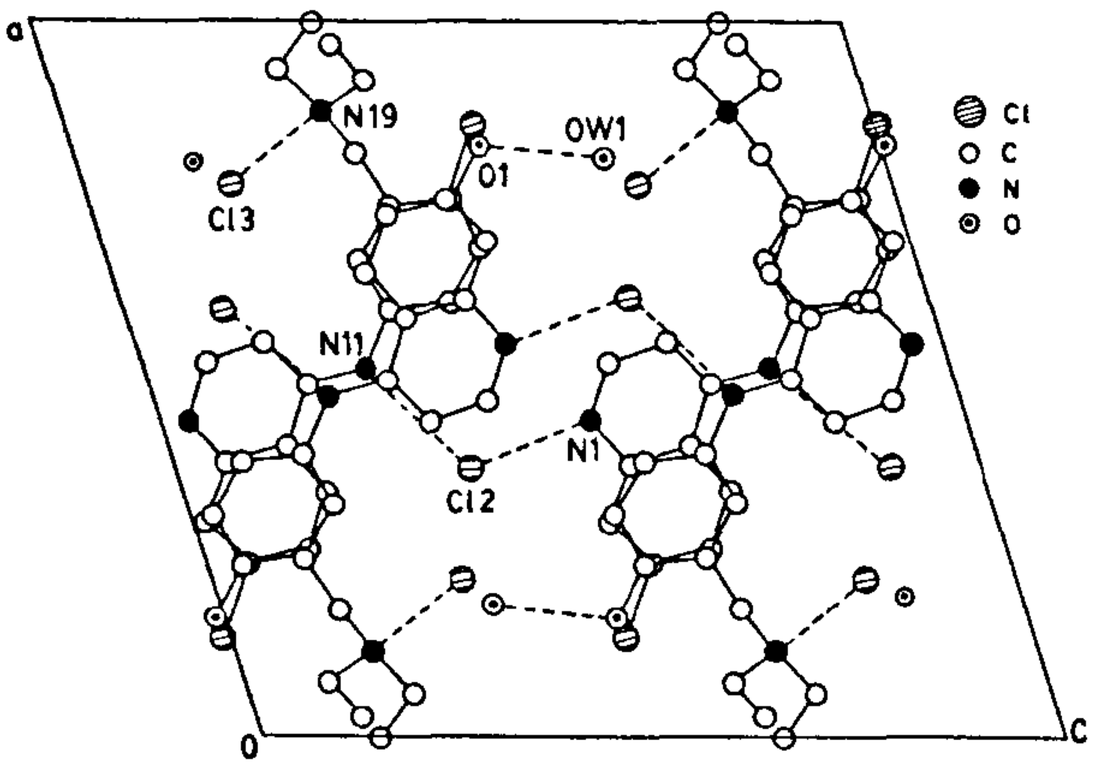

Figure 4. Packing diagram down *b* axis showing ring overlap. The hydrogen bonds and ionic interactions are indicated by dotted lines.

Table 5. Hydrogen-bond parameters.

X–H···Y	X–H (Å)	X–Y (Å)	X–H···Y (deg)
N1–H22···Cl 2[a]	1.076	3.067	171.9
O1–H22···OW1	1.048	2.700	163.7
N11–H24···Cl2	0.767	3.253	160.1
N19–H25···Cl3	1.068	3.008	179.4

[a]Symmetry code: $-x$, 1/2-y, 1/2+z.

The exocyclic nitrogen N11 is significantly displaced from the mean planes of the quinoline (0.121(4) Å) and the phenyl (0.139(4) Å) rings, towards the Cl2 ion to which it is hydrogen-bonded. The phenolic hydroxyl O1 is a proton donor for the hydrogen bond with hydroxyl ion $OW1^-$.

In addition to the hydrogen bonds, the molecules are also attracted by stacking forces between the neighbouring 2_1 screw-related molecules as shown by the overlapping of the phenyl and the quinoline rings (Figure 4). The ring planes are almost parallel and separated by a mean distance of 3.5 Å.

As mentioned earlier, chloroquine and some of its analogues containing the quinoline group have been implicated in binding to DNA by intercalation. Using CPK models and computer graphics we are trying to look at the possible ways in which amodiaquine can bind to DNA. CPK models show that the quinoline chromophore of an amodiaquine molecule with the geometry found in the crystal structure could partially intercalate between base pairs of the DNA double helix in both minor and major grooves, with the phenyl diethylamino group remaining in the groove. Further modelling and physicochemical studies are necessary before we can compare the DNA-binding properties of this drug with those of chloroquine and quinacrine, which lack a phenyl ring.

1. Karle, J. M. and Karle, I. L., *Acta Crystallogr.*, 1988, **B44**, 1605.
2. Leger, J. M. and Bideau, J. P., *C. R. Acad. Sci. Paris*, 1972, t. 275, 313.

3. O'Brien, R. L., Allison, J. L. and Hahn, F. E., *Biochim. Biophys. Acta*, 1966, **129**, 622.
4. Waring, M., *J. Mol. Biol.*, 1970, **54**, 247.
5. Geary, T. G., Jenson, J. B. and Ginsburg, H., *Biochem. Pharmacol.*, 1986, **35**, 3805.
6. Krogstad, D. J. and Schlesinger, P. H., *Am. J. Trop. Med. Hyg.*, 1987, **36**, 213.
7. North, A. C. T., Phillips, D. C. and Mathews, F. S., *Acta Crystallogr.*, 1968, **A24**, 351.
8. Main, P. *et al.*, MULTAN 11/82, a system of computer programs for the automatic solution of crystal structures from X-ray diffraction data, Universities of York, England, and Louvain, Belgium, 1982.
9. Enraf–Nonius Structure determination package, Enraf–Nonius, Delft, The Netherlands, 1984.
10. Hall, D., Swann, D. A. and Waters, T. N., *J. Chem. Soc., Perkin Trans.*, 2, 1974, 1334.
11. Karle, J. M., Cysyk, R. L. and Karle, I. L., *Acta Crystallogr.*, 1980, **B36**, 3012.
12. Buckleton, J. S. and Waters, T. N., *Acta Crystallogr.*, 1984, **C40**, 1587.
13. Abraham, Z. H. L. *et al.*, *J. Chem. Soc., Perkin Trans.*, 2, 1985, 461.
14. Neidle, S., Webster, G. D., Baguley, B. C. and Denny, W. A., *Biochem. Pharmacol.*, 1986, **35**, 3915.

ACKNOWLEDGEMENTS. We thank the Department of Science and Technology, the Department of Biotechnology and the Indian Council of Medical Research, New Delhi, for financial support. MAV thanks Jawaharlal Nehru Memorial Fund for a fellowship.

Supplementary material relating to crystallographic calculations has been deposited with the journal.

Received 14 March 1991; accepted 15 March 1991

RESEARCH COMMUNICATIONS

The dependence of rotationally inelastic cross-sections on the parameters of the potential

P. M. Agrawal and Vinod Garg*
School of Studies in Physics, Vikram University, Ujjain 456 010, India
*Permanent address: Department of Physics, Govt. College, Ajmer 305 001, India

The dependence of cross-sections, $\sigma(0 \rightarrow j)$, on the parameters of the intermolecular potential for rotational transitions in a diatomic molecule due to collision with an atom has been investigated. It is found that a 300% increase in the potential leads to only about 33% increase in the cross-sections. It is explained on the basis of the importance of the torque at the classical turning point, range of the potential and the collision time.

THE study of rotational energy transfer (RET) is important to many areas[1], such as lasers, astrophysics, molecular-beam experiments, spin–lattice relaxation of NMR signals, ultrasonic absorption and dispersion, thermal conductivity and transpiration, shock-wave propagation, microwave broadening, and intermolecular interaction. In many situations, it is useful to have an estimate of a set of cross-sections from a few parameters that can be obtained from some known cross-sections. Scaling and fitting laws such as the power-gap law[2] and the exponential-gap law[3] serve such a purpose. Further, it would also be worthwhile to arrive at some semiempirical expressions that give the dependence of cross-sections on the parameters of the intermolecular potential. In this paper we present one such empirical relationship, obtained by investigating a set of computed cross-sections. We also discuss the physical explanation.

A system of a homonuclear diatomic molecule and an atom has been considered, and the following form of the intermolecular potential has been used:

$$V(r,\theta) = v(r)\left[1 + \sum_{l=2}^{10} a_l P_l(\cos\theta)\right] \quad (1)$$

with

$$v(r) = C\,e^{-\alpha r}, \quad (2)$$

where r is the distance between the centre of mass of the molecule and the atom, θ the angle between vector **r** and the bond, and P denotes the Legendre polynomial. Due to symmetry of the homonuclear molecule odd terms in the summation in eq. (1) would be zero. The masses of the molecule and atom are taken as 28.0 and 4.0 amu. The bond length of the molecule is chosen as 1.0 Å.

The computations have been performed at relative translational energy $E = 0.1$ eV by using the modified infinite-order sudden approximation (IOSAM) given by Agrawal and Raff[4]. IOSAM is a modification of the well-known infinite-order sudden approximation[5] (IOSA) to the solution of the Schrödinger equation.

Table 1 gives the variation of the cross-sections, $\sigma(0 \rightarrow j)$, with the parameter C of eq. (2). As the magnitude of the torque ($= \partial V/\partial\theta$) acting on the molecular is proportional to C, one may expect a strong dependence of cross-sections on C. However, only about 33%

Table 1. Computed cross-sections $\sigma(0 \rightarrow j)$ in Å^2 and r_0^2/σ values as a function of j and C in eV. ($a_2 = a_4 = a_6 = a_8 = a_{10} = 0.1$, and $\alpha = 3.0$ Å^{-1}).

	$\sigma(0 \rightarrow j)$ when C =			r_0^2/σ when C =		
j	200	400	800	200	400	800
2	0.949	1.109	1.281	6.76	6.89	7.00
4	0.510	0.596	0 684	12.59	12 82	13.12
6	0.358	0.417	0.481	17.93	18.33	18.65
8	0.248	0.288	0.332	25.88	26.53	27 03
10	0.140	0.163	0 187	45.85	46.89	47.99
12	0.126	0.150	0.176	50.94	50.95	50.99