Acta Cryst. (1969). B25, 2418

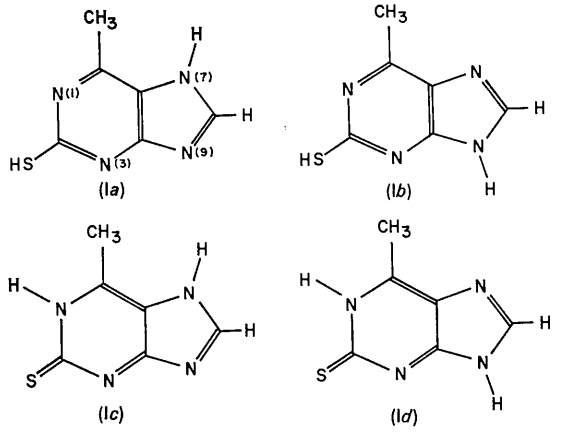
Hydrogen bonding in 2-mercapto-6-methylpurine monohydrate. Tautomerism in purine derivative.

By JERRY DONOHUE, *Department of Chemistry and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, Pa.* 19104, *U.S.A.*

(*Received* 30 *April* 1969)

Examination of the hydrogen bonding in the crystal structure of 2-mercapto-6-methylpurine monohydrate leads to the conclusion that the imidazole ring is protonated at N(7) rather than N(9). This result is compared with the protonation in other purine derivatives.

The results of a crystal structure determination of 2-mercapto-6-methylpurine (I) were recently reported by Srinivasan & Chandrasekharan (1968, hereinafter termed SC). They stated that their determination 'is not accurate enough to indicate which of the two atoms N(7) or N(9) is protonated or to draw definite conclusions regarding the hydrogen bonding system', further remarked that it seems likely that the SH group exists in the thione form, *i.e.* I(*c*) or I(*d*), and favored the structure in which N(9) was protonated instead of N(7), *i.e.* I(*d*).* The other possible tautomers of I were not mentioned, possibly because the structure indicates that either N(1) or S and N(7) or N(9) must be involved in the hydrogen bonding scheme.



The only interatomic distances given by SC are the four hydrogen bond distances N(9)H···O=2·81 Å, N(7)···HO=2·81 Å, S···HO=3·26 Å, and N(1)H···S=3·37 Å; no bond angles were given. The positional parameters were, however, tabulated by SC. These were used to calculate† the mean molecular plane, the deviations of the atoms from this plane, the angles associated with the hydrogen bonds, and the deviations of the hydrogen bonded ligands from the molecular plane. The results are shown in Fig. 1.

Discussion

The root-mean square deviation of the atoms from the molecular plane is 0·09 Å, or about that expected from the

* The numbering of the imidazole ring used by SC differs from that customarily used. The conventional numbering, shown in I*a*, is used in this paper.

† The lattice constant of $b = 21{\cdot}60$ Å as given on p. 1699 was used rather than the value 27·60 Å given in the abstract.

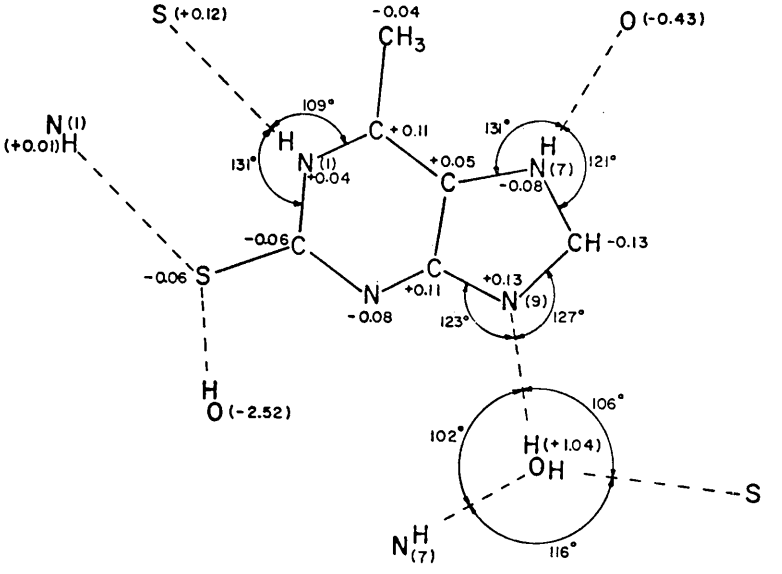
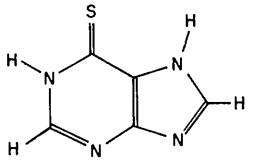


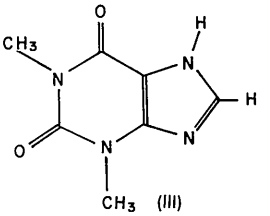
Fig. 1. One molecule of 2-mercapto-6-methylpurine and its hydrogen bonded ligands. Distances from the mean molecular plane, in Å, are shown. Atoms not used in the determination of this plane have these distances enclosed in parentheses.

standard deviations in the positional parameters given by SC. As far as the angles C–N···O are concerned, the hydrogen bonding scheme which includes N(9)H···O and N(7)···HO is just as satisfactory as the alternate possibility which includes N(9)···HO and N(7)H···O. The choice of which of these two schemes is correct, however, can be made on the basis of the distances of the two oxygen atoms from the molecular plane: the preference is clearly in favor of the hydrogen atom being covalently bonded to N(7) rather than N(9) because of the much greater deviation of the oxygen atom hydrogen bonded to the latter from the molecular plane. This conclusion follows from the tendency of N–H···O to be as linear as possible (Donohue, 1966) combined with the expectation that the hydrogen atom in question will lie close to the plane of this aromatic molecule. The correct tautomer is therefore I(*c*). (Because thiol forms such as I(*a*) and I(*b*), have never been observed in related compounds, these have been rejected).

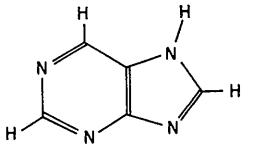
Localization of the hydrogen atom on N(7) has also been observed in 6-mercaptopurine, II (Brown, 1967; Sletten, Sletten & Jensen, 1969); in theophylline, III (Sutor, 1958), and in purine itself, IV (Watson, Sweet & Marsh, 1965).



(II)



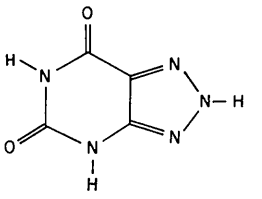
(III)



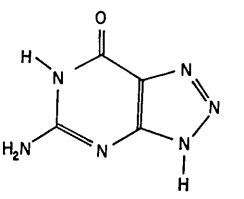
(IV)

A different situation, on the other hand, obtains in the case of 8-azapurine deviations. In xanthazole, V (Nowacki & Bürki, 1955; Mez & Donohue, 1969), the hydrogen atom is localized on N(8), while in 8-azaguanine, VI (Sletten, Sletten & Jensen, 1968), it is localized on N(9).

Although it might be possible by the use of quantum mechanical calculations to predict which tautomers should be preferred (provided, of course, that the correct answer is known in advance), it would seem more prudent to adopt



(V)



(VI)

only those which have been directly observed. While it could be argued that a particular crystal structure, because of a specific hydrogen bonding scheme, might lead a molecule to adopt one or another tautomeric form, it seems unlikely that this would happen unless these forms were of very nearly equal energies to begin with. It is interesting that McConnell, Sharma & Marsh (1964), who found that isocytosine co-crystallizes with two tautomeric forms of itself in a 1:1 ratio concluded that 'this result strongly suggests that they are of about equal stability'. Unless additional information to the contrary is found then the formulas I(*c*) and II–VI should be taken as the stable forms of those respective molecules.

This work was supported by the National Science Foundation. Some of the calculations were carried out by Mr Neal Schultz.

References

Brown, G. M. (1967). Minneapolis Meeting, ACA, Abstract D3.

Donohue, J. (1966). In *Structural Chemistry and Molecular Biology*. A. Rich & N. Davidson. San Francisco: Freeman.

McConnell, J. F., Sharma, B. D. & Marsh, R. E. (1964). *Nature, Lond.* **203**, 339.

Mez, H.-C. & Donohue, J. (1969). *Z. Kristallogr.* To be published.

Nowacki, W. & Bürki, H. (1955). *Z. Kristallogr.* **106**, 339.

Sletten, E., Sletten, J. & Jensen, L. H. (1969). To be published; cited by Sletten *et al.* (1968).

Sletten, J., Sletten, E. & Jensen, L. H. (1968). *Acta Cryst.* B**24**, 1692.

Srinivasan, R. & Chandrasekharan, R. (1968). *Acta Cryst.* B**24**, 1698.

Sutor, D. J. (1958). *Acta Cryst.* **11**, 83.

Watson, D. G., Sweet, R. M. & Marsh, R. E. (1965). *Acta Cryst.* **19**, 573.