2. Teorell, T., 1962, Excitability phenomena in artificial membranes, *Biophysic. J.*, **2,** No. 2, pt. 2, 27.
3. Baker, P. F., Hodgkin, A. L., and Shaw, T. I., 1962, Replacement of the axoplasm of giant nerve fibres with artificial solutions, *J. Physiol.*, **164,** 330.
4. Tosteson, D., and Hoffman, J. F., 1960, Regulation of cell volume by active cation transport in high and low potassium sheep red cells, *J. Gen. Physiol.*, **44,** 169.
5. Solomon, A. K., and Sidel, V. W., 1957, Entrance of water into human red cells under an osmotic pressure gradient, *J. Gen. Physiol.*, **41,** 243.

R. P. Rand
A. C. Burton
Biophysics Department
University of Western Ontario
London, Ontario

Non-Planar Distribution of Nitrogen Atom Bonds in Nucleosides

Dear Sir:

In a recent paper from this laboratory (1) it was pointed out that in some nucleosides the atoms of the base and the atoms substituted on the base were not coplanar. In particular, in the case of 5-fluoro-2′-deoxy-β-uridine (FUDR) atoms N1 and C1′ were out of the plane of the other atoms in the pyrimidine ring.[1] In calcium thymidylate C1′ and O2 were both out of the plane of the base and on opposite sides of that plane (2). In adenosine-5′-phosphate, C1′ was out of the plane of the base (3). In the paper on FUDR it was suggested that most of these displacements were due to steric hindrance between neighboring atoms. However, it was not possible to explain the displacement of N1 from the plane of the base in FUDR in this way.

Results recently obtained in this laboratory have prompted a revision of our view of the importance of steric hindrance in explaining these displacements. These results are as follows:

In 5-iodo-2′-deoxy-β-uridine it was found that C1′ was in the plane of the ring but O2′ was out of the plane by 0.07 A (4 standard deviations) (4). In addition, N1 and N3 were out of the mean plane, each by 0.04 A (3 standard deviations) and on the same side of the plane.

In the rubidium salt of 5-fluoroorotic acid N1 and N3 were accurately in the mean plane of the pyrimidine ring but C2 was out of the plane by 0.09 A (3 standard deviations) and O2 was out of the plane by 0.18 A (6 standard deviations) (5).

All of these observations could be explained if the nitrogen atom were to form bonds which were not in the same plane; *i.e.*, if the spatial distribution of bonds formed by the nitrogen atom were intermediate between that expected for an atom in sp^2 hybridization and that expected for an atom in sp^3 hybridization.

It is not yet clear under what conditions the nitrogen atom will adopt this pyramidal distribution of bonds. It should be emphasized that nitrogen atoms do not invariably assume this configuration, since in thymine monohydrate (6) and in azaguanine monohydrate (7) the atoms of the base are strictly coplanar.

---

[1] The atom numbering system used in this communication is the same as that used in reference 1.

The pyramidal configuration in the nitrogen atom is not caused solely by steric effects, as is shown by the fact that in the fluoroorotate ion the O2 atom is very far out of the mean plane even though there is no glycosydic CH group in that molecule to interfere with it.

It is now proposed that formation of a pyramidal distribution of bonds at nitrogen atom is responsible to a large extent for the observed deviation of atoms from the mean plane in the above purine and pyrimidine systems, with steric hindrance being a contributary effect. Of course this idea has relevance only to tervalent nitrogen atoms.

In calcium thymidylate C7 (the methyl carbon atom) and O6 are both out of the pyrimidine plane and on opposite sides. In 5-iodo-2′-deoxy-β-uridine, iodine is out of the plane in the pyrimidine ring by 0.05 A. In these two cases the effect is probably due largely to steric hindrance.

While the formation of a pyramidal distribution of the nitrogen atom bonds in purines and pyrimidines is not a universally observed phenomenon, the observations mentioned above indicate that it is much more probable that such a distribution may be formed than was previously thought. Thus in the construction of nucleic acid models purine and pyrimidine bases can be given a flexibility which has not previously been assumed.

Received for publication, August 20, 1964.

REFERENCES

1. Harris, D. R., and MacIntyre, W. M., *Biophysic. J.*, 1964, **4**, 203.
2. Trueblood, K. N., Horn, P., and Luzatti, V., *Acta Cryst.*, 1961, **14**, 965.
3. Kraut, J., and Jensen, L. H., *Acta Cryst.*, 1963, **16**, 79.
4. Werkema, G., 1965, Doctoral Thesis, University of Colorado.
5. MacIntyre, W. M., and Zirakzadeh, M., *Acta Cryst.*, 1964, **17**, in press.
6. Gerdil, R., *Acta Cryst.*, 1961, **14**, 333.
7. Singh, P., and MacIntyre, W. M., data to be published.

Walter M. MacIntyre
Department of Chemistry
University of Colorado
Boulder, Colorado