OPTICAL PROPERTIES AND CONFORMATION OF PURINE NUCLEOSIDES IN SOLUTION **

G.T. Rogers and T.L.V. Ulbricht

Twyford Laboratories Ltd., Elveden Road, London, N.W.10,
England.

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SUMMARY: The relationship between the sign and magnitude of the long wave-length Cotton effect in the ORD of purine nucleosides and their conformation is illustrated by means of a projection diagram.

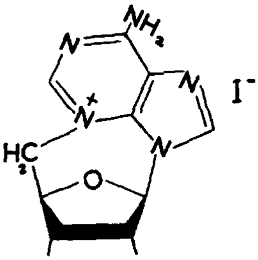
In an earlier paper in this series[1] we pointed out that purine nucleosides give Cotton effects of lower amplitude than pyrimidines, which is undoubtedly related to the fact that rotation about the glycosidic bond is less restricted.[2] Consequently, the ORD of purine nucleosides is more likely to be sensitive to small changes of structure than is the case with pyrimidine nucleosides.

We have confirmed that 9-β-D-glycofuranosyl derivatives of substituted purines not containing other chromophores give negative Cotton effects; α-D- and β-L-compounds give positive Cotton effects, as expected. N.m.r. studies have shown meanwhile that purine nucleotides exist in solution in a conformation close to *anti*;[3-5] it is, therefore, clear that the negative Cotton effect of purine-β-D-nucleosides is associated with such a conformation.

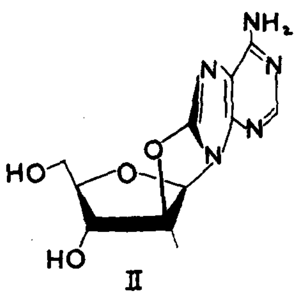
Controversy over the conformation of purine-β-nucleosides has undoubtedly resulted from oversimplified conclusions drawn from a series of cyclonucleosides.

**Optical Rotatory Dispersion of Nucleic Acid Derivatives Part XI. Part X: G.T. Rogers and T.L.V. Ulbricht, Biochem. Biophys. Res. Comm., Preceding paper.

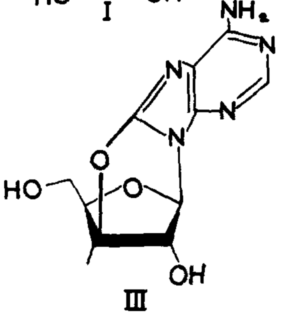
N^3-5'-Cycloadenosine (I) must have a *syn* conformation, yet it has a large negative Cotton effect.[6] On the other hand, the cyclic derivatives of 8-hydroxy-β-D-adenosine, in which the 8-hydroxy oxygen is linked to the 2'-, 3'- and 5'-carbon atoms of the sugar respectively (II, III, IV) all give *positive* Cotton effects, and the α-anomers, negative Cotton effects.[7]



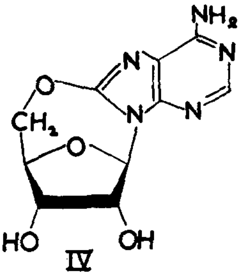
I



II



III



IV

We believe that an *anti* conformation can be associated with either a positive or negative Cotton effect, and this is shown in a projection diagram of the cyclonucleosides I - IV (Fig. 1), similar to that described for pyrimidine nucleosides in the preceding paper.[8]

In this case the line dividing the circle into positive and negative Cotton effects appears to be in line with the C$^{1'}$ - O bond (ϕ_{CN} = 180°). The most likely conformation of the majority of purine-β-nucleosides is close to the dotted line, i.e., a *small negative* Cotton effect would be associated with a predominantly *anti* conformation. This structure would permit hydrogen bonding between 2' - OH and N-3, as has been suggested for ribose derivatives.[3] Moreover, such a conformation in a dinucleotide would enable the phosphate group to occupy a position close to the H-8 proton of the purine and account for the deshielding observed in n.m.r. studies of these compounds.[5] An extreme anti conformation (ϕ_{CN} = -30°) is associated with a large positive Cotton effect as shown by 8, 5'-cyclo-8-hydroxyadenosine (IV).

A syn conformation for those purine β-D-nucleosides which give a negative Cotton effect was suggested by Klee and Mudd[9] because they found that derivatives which had a sulphur containing group attached at C-5' gave positive Cotton effects, and they considered that a large group at C-5' would make the syn conformation sterically unfavourable. However, reference to Fig. 2 shows that an anti conformation can indeed be associated with a positive Cotton effect. Moreover, adenosine derivatives with a 5'-acetoxy group give a negative Cotton effect like adenosine itself.[1] We suggest that an interaction between the sulphur atom at C-5' and the purine ring may be responsible for a change either in the conformation or in the electronic transitions and account for the ORD observed in 5'-methylthioadenosine and related compounds.

8-Bromoguanosine gives a positive Cotton effect.[10] Because of the size of the 8-substituent, it cannot have the anti conformation, and in the solid state, it has the syn conformation[11] with ϕ_{CN} = 127°. However, we suggest that in aqueous solution the conformation of 8-bromoguanosine is probably opposite to that of normal purine β-nucleosides, i.e., with ϕ_{CN} about -150° (see Fig. 1).

The validity of a comparison between cyclo- and non-cyclopurine nucleosides requires further investigation. Meanwhile, the projection diagram (Fig. 1) should prove useful in further studies of the relationship between the conformation and sign and magnitude of the Cotton effect in purine nucleosides.

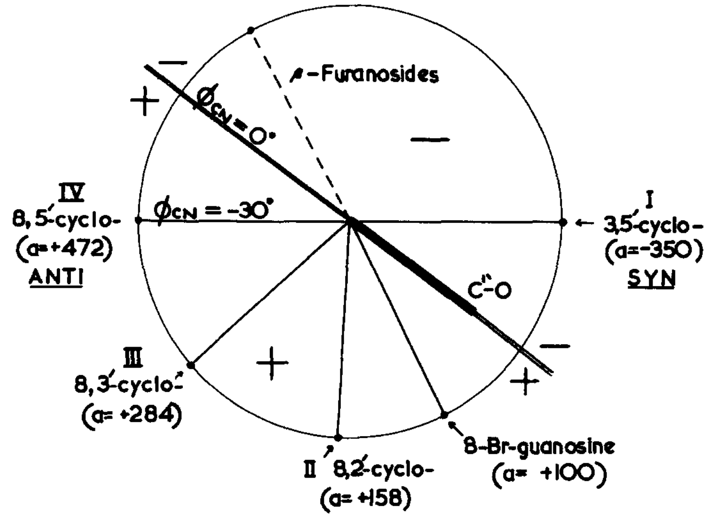


FIG. 1. RELATIONSHIP BETWEEN ϕ_{CN} AND THE SIGN OF THE C.E. IN CYCLOADENOSINES AND OTHER PURINES

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