metal block, using calibrated Anschütz thermometers. Infrared spectra were run in KBr discs using a Perkin-Elmer Infracord Model 157G with a grating monochromator. Infrared spectra were routinely recorded and are in agreement with the expected structures. Mass spectra were recorded on an AEI MS-30 mass spectrometer. The ionizing energy was maintained at 70 eV and the temperature of the source at 200°C.

Synthesis. Compounds having a methoxy group (*i.e.* compounds No. 3, 5, 7, 9, and 11) were prepared as follows. *N*-Formylanthranilic acid, *N*-acetylanthranilic acid, or *N*-propionylanthranilic acid (0.01 mol) was condensed with 2-methoxy-6-methylaniline [3] or 2,6-dimethoxyaniline [3] (0.01 mol) in the presence of phosphorus trichloride (0.005 mol) as earlier described.[2] Compounds 2, 4, 6, 8, 10, and 12 were prepared from the corresponding methoxy derivatives by boiling with an excess of 48 % hydrobromic acid for 1.5 h.

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On the Stereochemistry of the Interaction between Nucleic Acids and Basic Protein Side Chains

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Interactions between nucleic acids and basic proteins play an important role in cell chemistry and it would appear to be of interest to establish the stereochemistry of these interactions at the atomic level. We thought that some information might be obtained by X-ray analysis of single crystals of salts between phosphate diesters and various organic bases simulating arginine and lysine side chains. Such complexes may serve as models for the contacts occurring in nucleoproteins between phosphate groups and basic amino acids. The compounds studied are the diethyl phosphates of propylguanidine (I), arginine (II) and putrescine (III). A good model should preferably contain no hydrogen bond forming groups other than those present at the contacts, and compound (II) is therefore less satisfactory than the others. The crystal structures of the three compounds have been reported elsewhere.[1-3] In the present note the patterns of hydrogen bonding will be discussed and related to the structure of complexes between DNA and polyarginine, protamine, and polylysine.

The bonding between arginine and phosphate diesters. Arginine forms salts with phosphate diesters and bonding occurs between $(RO)_2PO_2^-$ and the guanidinium cationic group $-(NH)C(NH_2)_2^+$. In Fig. 1 the surroundings of the guanidinium group in model compounds (I) and (II) are shown. Extensive hydrogen bonding occurs, the stereochemistry of which may be described as follows:

(1) The guanidinium group forms five N−H···O hydrogen bonds to oxygen atoms in neighbouring molecules. These bonds are not far from linear and lie roughly in the plane of the guanidinium group, as is to be expected. The tendency for this general pattern of hydrogen bonding is also evident in crystal structures of inorganic salts of arginine.[4] In the present structures, especially (I), in which the guanidinium group is bonded only to diester phosphate groups, some additional characteristic stereochemical features are observed:

(2) One of the five hydrogen bonds both in (I) and (II) involves an ester oxygen atom and is much weaker (length 3.08 Å and 3.09 Å, respectively) than the others, which lie within the normal range for N−H···O bonds (mean length about 2.85 Å). The direction of this bond is roughly that of the bisecting line of the P−O−C angle. Such a hydrogen bond has apparently not been observed previously.

(3) Four of the hydrogen bonds occur in two pairs of nearly parallel bonds to oxygen atoms in the same anionic group. The N···N distances in the guanidinium group (*ca.* 2.3 Å) are not far from the O···O distances in phosphates (*ca.* 2.5 Å) and carboxylates (*ca.* 2.25 Å), making it stereochemically favourable for pairs of nearly parallel bonds to be formed. The pairs are of two types, a "strong" pair involving two normal bonds to the two *oxo* oxygen atoms in the same phosphate group, and a "weak" pair of one normal and one weak bond to one *oxo* and one ester oxygen atom, respectively. The pairs are at an angle of about 120° with one another. In compound (II) the "strong" pair is formed to the carboxyl group rather than to the phosphate, but the "weak" pair exists in both structures. It may be concluded that a guanidinium group may form a strong link between two phosphate diester groups by pairs of hydrogen bonds, and that

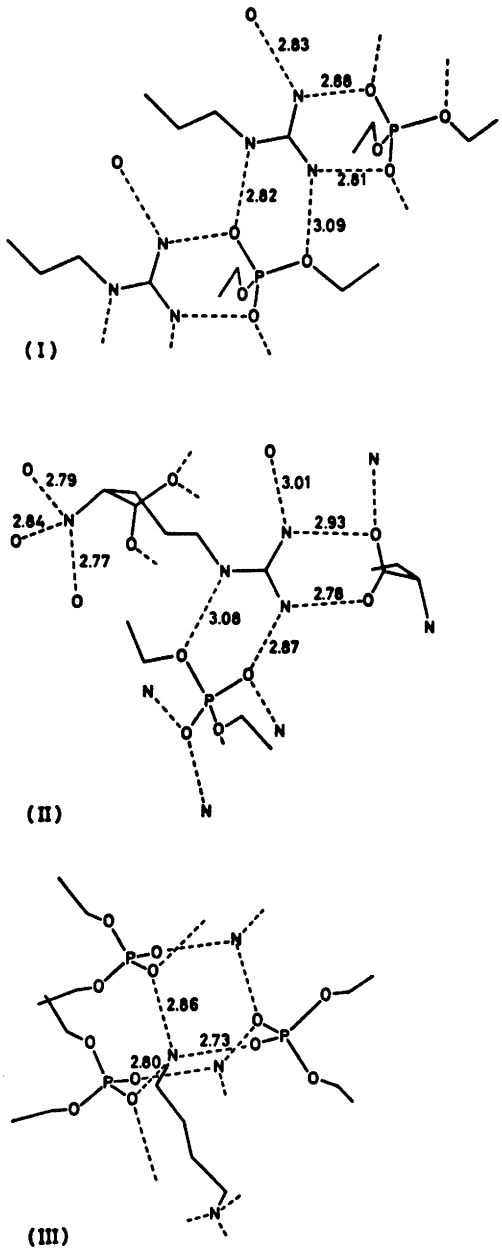

Fig. 1. Hydrogen bonds (broken lines) in diethyl phosphates of propylguanidine (I), arginine (II), and putrescine (III). Hydrogen atoms are not shown.

a phosphate diester group may be linked to two arginines, as shown by structure (I).

(4) The angles between the N–H···O bonds and the adjacent P–O (*oxo*) bonds lie in the range 108°–137°, the mean value being 123°. The hydrogen bonds of the "weak" pairs nearly lie in the O–P–O plane of the acceptor oxygen atoms, whereas the bonds of the "strong" pair form an angle of about 25° with it. In other structures this angle may be greater, but it seems likely that the general direction of any pair will be so as to point away from the oxygen atoms to which they are not bonded.

The stereochemical features described above in (1)–(4) are likely to persist at contacts between phosphate diesters and arginines in general and should be taken into account when formulating structural models of nucleoproteins and related complexes at the atomic level.

As an example, the hydrogen bonding in DNA-polyarginine and DNA-protamine complexes will be discussed on this basis. A general model of the structure of these complexes has been proposed, in which the polypeptide chain winds helically around the DNA molecule in the small groove.[6] The stereochemistry of the phosphate/guanidinium interactions was, however, not described. We have studied the stereochemical fit between DNA and polyarginine by wire models (scale 1 Å = 4 cm) using the coordinates of Arnott and Hukins [5] for B-DNA. We assume that the ten-fold symmetry is maintained in a general way on complex formation, as indicated by the X-ray fibre diagrams,[6,7] and that only minor modifications in the position and orientation of the phosphate groups occur. The different stable arginine conformations [4] were considered, and also the fact that the Cα carbon atoms have to lie less than about 10 Å from the ten-fold axis because of the symmetry (dipeptide length < 7.2 Å).

There are several feasible ways of linking the arginines to the phosphates in B-DNA by hydrogen bonds. In view of the bonding observed in the model compounds it appears, however, likely that both *oxo* oxygen atoms of the phosphates are engaged in the formation of a "strong" pair of hydrogen bonds to a guanidinium group, and satisfactory models can be built on this basis. The other pair from the guanidinium groups points away from the complex and may form cross-links to phosphates in the complementary helix in neighbouring complexes. This bonding pattern is similar to the one observed in compound (I). The distances between complexes in fibres of DNA-polyarginine and DNA-protamine [6,7] are consistent with the existence of such guanidinium bridges.

This bonding scheme is stereochemically compatible with placing the polypeptide chain in either of the DNA grooves, although the large groove appears to be the more favourable one. X-Ray evidence indicates, however, that the small groove is the site of binding in the DNA-protamine complex.[6,7]

It is also possible from a stereochemical point of view that the guanidinium groups link together consecutive phosphates along the DNA helices, as has been proposed.[7] The "strong" pair of hydrogen bonds can, however, in this case not be formed without strain, and we consider this possibility less likely than the one described above.

The bonding between lysine and phosphate diester. The $-NH_3^+$ group of protonated lysine would be expected to form, if possible, three hydrogen bonds in roughly tetrahedral arrangement, as observed in compound (III) (Fig. 1) and also in crystals of amino acids. The P–O···N angles in (III) lie in the range 110–135° and the mean length of the three bonds is 2.80 Å.

The oxygen atoms receiving hydrogen bonds from an NH_3^+ group are at distances of about 5 Å. The most favorable hydrogen bonding scheme in B-DNA-polylysine complexes would appear to be that the lysine NH_3^+ groups are linked to an *oxo* oxygen atom (O3) in one phosphate and, by a weak bond, to an *ester* oxygen atom (O4) in the next phosphate along the helix, these atoms being at a distance of 5.0 Å. *Oxo* oxygen atoms of consecutive phosphates seem to be too far apart. The third bond would then be formed to an *oxo* oxygen atom in the complementary helix in a neighbouring complex. The distance between complexes in fibres is consistent with this view.

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Algal Carotenoids. XI.* New Carotenoid Epoxides from *Trentepohlia iolithus*

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A recent re-examination of the carotenoids of the green alga *Trentepohlia iolithus*[1] demonstrated the natural occurrence of carotenoids containing 2-hydroxylated β-rings. Structures *1*, *2*, and *3* (Scheme 1) were established from full spectroscopic characterization. The absolute stereochemistry has subsequently been confirmed.[2]

We now report the natural occurrence of the epoxides *4a* and *7* (probably *7a*) of β,ε-caroten-2-ol (*1*) and of β,β-caroten-2-ol (*2*), comprising 0.2 % (0.4 mg) and 0.3 % (0.6 mg), respectively, of the total carotenoids of *T. iolithus*.

In order to include stereochemical considerations the partial synthesis of the 5,6-epoxides *4a* and *4b* from β,ε-caroten-2-ol (*1*, 3.6 mg) by *m*-chloroperbenzoic acid,[3] Scheme 2, will be discussed first. Reported data for relevant cyclohexene model substances reveal a directive effect of a hydroxy substituent, resulting in preferential epoxidation *cis* to the hydroxy substituent, explained by hydrogen bonding between the hydroxy group and the peracid.[4] Similar results are observed with an acetoxy substituent.[5] Thus zeaxanthin (β,β-caroten-3,3′-diol) diacetate gives preferentially *cis* products (*cis* relationship between the epoxy and acetoxy groups) on epoxidation.[5]

On epoxidation of β,ε-caroten-2-ol (*1*) two diastereomeric products *4a* (60 % of total) and *4b* (40 % of total) were obtained. Both *4a* and *4b* exhibited λ_{max} (acetone) 419, 441.5, and 470 nm and *m/e* 568 (M), fragment ions M–16, M–80, 181, and 221 consistent with carotenoid epoxides, as well as common fragment ions M–92, M–106, M–16–92, M–16–106, M–80–92 ascribed to eliminations from the polyene chain, combined with losses of 16 and 80 mass units.[6a] Relative yields and adsorptive properties support the stereochemistry assigned to the epoxidic products *4a* and *4b*, see Scheme 2. Thus *4a* was chromatographically less strongly retained than *4b*, compatible with intramolecular hydrogen bonding, and *4a* indeed showed the predicted hydrogen bonding in IR (predominantly associated hydroxyl at 3509 cm^{-1} as expected for conformation A Scheme 2, *cf.* Ref. 6b).

On furanoid rearrangement with hydrogen chloride in ether the epoxide *4a*, referred to

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