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Dear Leslie,

I'm not sure that I can help much, especially with your first question. Naturally, if you were considering enzymatic DNA synthesis one could think of difficulties. For this reason one might worry whether the non-enzymatic synthesis you are interested in had a catalyst. If this were sufficiently complicated it could conceivably make a difference between P and P'. Again effects due to neighbouring base-pairs (which therefore violate the diad symmetry) might produce some difference, but one feels that they would be small and dependent on special restrictions on the base-sequence.

The second question raises some interesting possibilities. These fall, broadly, into two classes. The first class consists of a backbone whose "natural" helix is different from that due to the "natural" helix for the stacking of the bases. (Here "natural" really means unstrained). This, Aaron tells me, is likely to deform the axis of the double helix from a straight line to a helix. Incidentally, it is not known for sure that this does not happen to ordinary DNA in solution, i.e. is its axis straight or slightly bent in a systematic way? In an extreme case it might mean that short lengths were stable but longer lengths less so.

The second class consists of backbones which "terminate", or become awkward to continue, on a statistical basis. The obvious example would be a mixture of D and L deoxyribose (or ribose). Assume that (on a D template) a D monomer is preferred but that, at a lower probability, an L can be joined on, and that this makes further additions difficult or impossible. Then short oligomers would be formed but not long ones. Another possibility is some 2'-5' linkages mixed in with the 3'-5' ones.

Naturally the two mechanisms are not mutually exclusive. They certainly suggest that mixtures of different sugars should be tried, not only D and L, but also arabinose or even glucose to say nothing of deoxyglucose. I'm mildly surprised that some organic chemist has not made (homo)polymers with other phosphate sugarsbackbones to see which ones will form double helices, but perhaps they have and I haven't noticed.

What are your plans for the Summer? I assume you are going to Sicily. Is Alice coming as well? We plantto have two short holidays during January and February but otherwise to remain here. Chromatin is progressing but nothing dramatic yet.

Happy New Year,

F.H.C. Crick