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INTRODUCTION

Nucleic acids and their components are of such great importance in biology that even the most significant contributions made by chemists in this area are sometimes overshadowed, especially by contributions from molecular biologists. This situation is often reflected in the content of papers given at international conferences on nucleic acids. However, conferences dealing with recent developments in the more chemical aspects of nucleic acid research do take place and it is intended that the subject matter of this Symposium-in-Print should correspond as closely as possible to the proceedings of such a conference were it to be held at the present time.

Nucleoside chemistry is a fascinating branch of organic chemistry which is well worth studying for its own intrinsic interest. However, much of the stimulus for the vast amount of work which has been carried out particularly on the synthesis of nucleosides comes from the possibility that analogues of natural nucleosides might have antibiotic, antiviral or antitumour activity. The four articles on nucleoside chemistry in this Symposium are all concerned with synthesis. Two of the articles (by K. A. Watanabe, J. J. Fox *et al.*, and by M. J. Robins *et al.*) deal with nucleoside base- and sugar-residue modification, respectively. The other two articles (by J. G. Buchanan *et al.*, and by M. Ohno *et al.*) deal with the enantioselective synthesis of nucleosides from chiral and achiral starting materials, respectively. Thus the studies described in the latter two papers are very much in the mainstream of contemporary organic synthesis. The ingenious use of pig liver esterase to promote kinetic asymmetric transformations in M. Ohno's paper is particularly noteworthy.

Two of the articles deal with nucleotide analogues. One of them (by J. G. Moffatt *et al.*) contains a comprehensive account of the synthesis of phosphonate analogues of nucleoside 3′-phosphates. The other article (by W. J. Stec *et al.*) is concerned with the stereospecific synthesis of nucleoside 3′,5′-cyclic phosphorothioates and dinucleoside phosphorothioates from 2′-deoxyribonucleoside 3′-aryl phosphoranilidates. The diastereoisomerically pure phosphorothioate analogues of nucleotides and dinucleoside phosphates have proved to be valuable substrates in the elucidation of the mechanisms of action of phosphorolytic and phosphoryl transfer enzymes. W. J. Stec's methodology is additionally important in that nucleoside phosphoranilidates may also be used in the stereospecific synthesis of chiral phosphate esters containing heavy isotopes of oxygen.

In the light of its overall importance in present day nucleic acid research, it is arguably quite reasonable that a significant proportion of the articles in this Symposium should, in some way, be concerned with oligonucleotide synthesis. A successful approach to oligonucleotide synthesis depends primarily on the choice of suitable protecting groups and an effective phosphorylation method. In one article (by W. Pfleiderer *et al.*), a most interesting unified approach to protecting groups in oligonucleotide synthesis is presented. The 2-(4-nitrophenyl)ethyl group is used to protect both the internucleotide linkages and the 4- and 6-oxo-groups, respectively, of uracil(thymine) and guanine residues; it is also used, in the form of a 2-(4-nitrophenyl)ethoxycarbonyl group, to protect the amino functions of adenine and cytosine residues. Protecting groups also feature prominently in an article (by T. Hata *et al.*) concerned with the synthesis, in solution, of a nonaribonucleotide sequence starting with 5′-protected *S*,*S*-diphenyl ribonucleoside 3′-phosphorodithioate building blocks.

There are two other articles dealing with the phosphotriester approach in solution. One of them (by J. H. van Boom *et al.*) is concerned with the use in oligodeoxyribonucleotide synthesis, of the powerful bifunctional phosphorylating agent prepared from 2-chlorophenyl phosphorodichloridate and two molecular equivalents each of 1-hydroxybenzotriazole and pyridine. The efficient synthesis of all sixteen dinucleoside phosphates and two longer sequences is described. In the

other article (by M. Ikehara *et al.*) the synthesis of a tritriacontaribonucleotide (33-mer) sequence of *E. coli* $tRNA^{Gly}$ is described. The research group concerned has thereby shown that its present phosphotriester methodology stands up to the stringent test of being effective in the synthesis of almost one-half of a tRNA molecule.

The rapid synthesis of oligonucleotides on a solid support is now the method of choice when biological quantities of these compounds are required. Two articles which deal mainly with this subject are included, and solid phase synthesis also features in two other articles. In one article (by M. H. Caruthers *et al.*), the synthesis of two oligodeoxynucleotide sequences by the phosphite triester approach on a silica gel support is described. Nucleoside 3′-methyl dimethylphosphoramidite building blocks are used and the oligonucleotides are prepared on an exceptionally large scale. Two procedures for the preparation of dinucleoside methylphosphonates in solution are reported in the same article. In another article (by H. Köster *et al.*), solid support synthesis of oligodeoxyribonucleotides both by the phospho triester and phosphite triester approaches is described. Controlled pore glass is used as the solid support. It would seem clear that now that stable nucleoside phosphoramidite building blocks are readily available, the solid support phosphite triester approach to oligonucleotide synthesis of oligodeoxyribonucleotides both by the phosphotriester and phosphite *et al.*) in which solid phase synthesis is also involved is concerned mainly with the use of the 1,1-dimethyl-2,2,2-trichloroethyl group for the protection of internucleotide linkages. Novel features in this interesting article include the use of phosphite triester block synthesis both in solution and on a solid support (silica gel), and the removal of oligonucleotides from a solid support without concomitant unblocking of the internucleotide linkages.

There are two remaining articles involving oligonucleotide synthesis and both of them have a wider physico-chemical significance. The first of them (by R. A. Jones *et al.*) is concerned with the influence of the purine 2-amino group on DNA conformation and stability. The oligonucleotide substrates, which contain 2,6-diaminopurine residues, are synthesized by the phosphotriester approach on a highly functionalised Merrifield resin. The final article (by L. E. Orgel *et al.*) in this section of the Symposium is concerned with the temperature dependence of the template-directed synthesis of oligoguanylic acids. This is one of several most interesting studies, carried out by L. E. Orgel and his coworkers, which demonstrate how complementary templates can direct the ordered synthesis of oligonucleotides from activated monomers both in the presence and absence of heavy metal ions.

The last part of the Symposium consists of two articles on tRNA chemistry. The first of them (by G. Lowe and G. Tansley) is concerned with the stereochemistry of the tyrosinyl-tRNA synthetase catalyzed activation of tyrosine by ATP. This is a very good example of this research group's use of chiral phosphate esters in the solution of stereochemical problems in biology. The final article (by S. M. Hecht *et al.*) is concerned with a study in which a number of chemically synthesized 2′(3′)-*O*-acyl derivatives of the dinucleotide, pCpA are attached enzymatically (by T4 RNA ligase) to *E. coli* $tRNA^{Phe}$ from which the 3′-terminal dinucleotide has been deleted. This work clearly demonstrates the power of organo-chemical methods in molecular biology.

I hope that this relatively short Symposium will clearly reveal some of the excitement and diversity of current research in this fascinating and important field. I very much enjoyed reading all of the contributions and should like to record my gratitude to the authors. I should also like to thank the reviewers for their help.

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