conditions applied. As seen from the table, **9** and **10**, which are susceptible to self-condensation under basic conditions, gave DL-threonine and β-hydroxy DL-leucine in good yield, even under these mild reaction conditions.

Detailed investigations of this reaction and those with complexes composed of other metal species and the application of these complexes to the synthesis of polyhydroxy amino acids and related compounds are now in progress in our laboratory.

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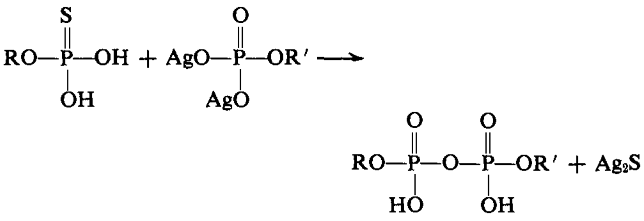
Synthesis of Nucleotide Coenzymes *via* Nucleoside 5′-Phosphorothioate Intermediates

Sir:

Unsymmetrical diesters of pyrophosphoric acid, to which class the nucleotide coenzymes belong, have been synthesized *via* nucleoside phosphoromorpholidates,[1] phosphoroimidazolidates,[2] phosphorochloridates,[3] diphenylphosphoric anhydrides,[4] and *S*-ethyl phosphorothioates.[5] We now wish to report a synthesis of nucleotide coenzymes *via* nucleoside 5′-phosphorothioate intermediates as shown in the following equation.



$$\mathrm{RO-\overset{S}{\overset{\|}{\underset{OH}{\underset{|}{P}}}}-OH + AgO-\overset{O}{\overset{\|}{\underset{AgO}{\underset{|}{P}}}}-OR' \longrightarrow RO-\overset{O}{\overset{\|}{\underset{HO}{\underset{|}{P}}}}-O-\overset{O}{\overset{\|}{\underset{OH}{\underset{|}{P}}}}-OR' + Ag_2S}$$

R = nucleoside residue
R′ = nucleoside or sugar residue

When 1 equiv of the bis[tri-*n*-butyl]ammonium salt of 2′,3′-*O*-dibenzoyluridine 5′-phosphorothioate[6] was treated with 1.2 equiv of the disilver salt of α-D-glucose 1-phosphate in dry pyridine at room temperature for 5 hr, uridine diphosphoglucose (UDPG) [$\lambda_{max}^{H_2O}$ 262 mμ (ϵ 10,000)] was isolated in 70% yield as the dilithium salt after removal of protecting group.

According to this method, uridine diphosphogalactose (UDPGal) [$\lambda_{max}^{H_2O}$ 262mμ (ϵ 10,000)], flavin adenine dinucleotide (FAD) [$\lambda_{max}^{H_2O}$ 264, 375, 450 mμ; $\lambda_{260}/\lambda_{375} = 4.00$; $\lambda_{375}/\lambda_{450} = 0.95$; $\lambda_{260}/\lambda_{450} = 3.80$], P^1-*p*-nitrophenyl P^2-uridine 5′-pyrophosphate [$\lambda_{max}^{H_2O}$ 267 mμ (ϵ 14,000)], P^1-*p*-nitrophenyl P^2-adenosine 5′-pyrophosphate [$\lambda_{max}^{H_2O}$ 262 mμ (ϵ 18,400)], and P^1-*n*-butyl P^2-adenosine 5′-pyrophosphate [$\lambda_{max}^{H_2O}$ 260 mμ (ϵ 15,400)] were obtained in 63, 51, 86, 54, and 61% yields, respectively. The structures were confirmed by paper electrophoresis, paper chromatograms, and ultraviolet spectra, and by detection of the corresponding nucleotides on hydrolysis.

It is noted that this method has three advantageous points, namely: (1) no symmetrical diester of pyrophosphoric acid was detected when only 1.2 equiv of disilver salt of nucleotide was treated with 1 equiv of nucleoside 5′-phosphorothioate; (2) satisfactory yields of nucleotide coenzymes and their analogs are maintained even when the relatively insoluble disilver salts of nucleotides, such as flavin mononucleotide (FMN), are empolyed; (3) these coenzymes and their analogs can be prepared on a relatively large scale by conventional organic techniques.

A complete report of these results will be published later.

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(6) (a) F. Eckstein, *ibid.*, **88**, 4292 (1966). (b) Uridine 5′-phosphorothioate was first prepared by Eckstein[6a] by way of thiophosphorylation using triimidazolyl-1-phosphine sulfide. In this experiment, the nucleoside 5′-phosphorothioates were conveniently prepared in high yields (73–89%) from nucleosides and thiophosphoryl chloride by modification of Murray's method.[7]

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MINDO/2 Study of the Cope Rearrangement

Sir:

As Doering and Roth[1] first pointed out, the Cope rearrangement of biallyl (I) can take place by either of two geometrically distinct reaction paths, the corresponding transition states II and III being analogous to the chair and boat forms of cyclohexane. The reaction is of considerable topical interest since, whereas both processes are "allowed" in terms of arguments based on the conservation of orbital symmetry,[2,3] that proceeding *via* II should be favored in terms of the treatment of electrocyclic reactions based on aromaticity of the transition state,[5] for the interaction between the AO's of the "para" carbon atoms, a and b, in III is predicted to be antibonding. The course of the reaction indicates[1] that the transition state does indeed have the "chair" geometry II.

Recent work[6] in these laboratories has led to the

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(1) W. von E. Doering and W. R. Roth, *Tetrahedron*, **18**, 67 (1962).

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(3) In a recent review,[4] Woodward and Hoffmann tried to account for the differences in energy between II and III in terms of orbital correlations during hypothetical dimerizations of two allyl radicals. This rather forced explanation is open to several obvious criticisms; in any case, it is clear that no simple interpretation is possible in terms of orbital correlations during the rearrangement of I.

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