sulfurization of III (1.5 g.) proceeded at 100° in a refluxing ethanol–Methyl Cellosolve solution in the presence of a 15-fold weight of catalyst to give 0.8 g. (67%) of crude 2′,3′-dideoxyadenosine. After three recrystallizations from ethanol, colorless crystals of IV (0.25 g.) were obtained, chromatographically homogeneous. Pure 2′,3′-dideoxyadenosine (IV) melted at 184–186°, $[\alpha]^{25}D$ −25.2° (*c* 1.01, H_2O); λ_{max}^{MeOH} 259.5 mμ (ε 14,800). *Anal.* Calcd. for $C_{10}H_{13}N_5O_2$: C, 51.1; H, 5.54; N, 29.8. Found: C, 50.9; N, 5.32; N, 29.6; R_f 0.45, $R_{Adenine}$ 1.80 (NH_4OH:DMF:*i*-PrOH, 10:25:65); R_f 0.36, $R_{Adenine}$ 1.19 (*n*-BuOH saturated with H_2O). The proton magnetic resonance spectrum of IV in D_2O showed a complex multiplet corresponding to four protons at δ 2.0 to 2.8 (C-2′ and C-3′ protons) and no absorption at δ 4.63 in the region of the C-3′ proton in 2′-deoxyadenosine in the same solvent.

These procedures are presently being applied to the preparation of other novel purine deoxy- and polydeoxynucleosides utilizing the commercially available deoxynucleosides obtained from DNA.

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Synthesis of Deoxyribonucleoside-3′,5′ Cyclic Phosphates by Base-Catalysed Transesterification

Sir:

Hydrolysis of *p*-nitrophenyl thymidine-3′ phosphate in *aqueous* sodium hydroxide produces both thymidine-3′ and thymidine-5′ phosphates, thymidine-3′,5′ cyclic phosphate being an intermediate in the reaction.[1] This communication describes the reaction of *p*-nitrophenyl esters of deoxyribonucleotides with base in *anhydrous* solvents where deoxyribonucleoside-3′,5′ cyclic phosphates are produced in excellent yields.

5′-O-Di-*p*-methoxytritylthymidine[2,3] was reacted with *p*-nitrophenyl phosphate and dicyclohexylcarbodiimide in dimethylformamide–pyridine[4] to yield, after acetic acid treatment, *p*-nitrophenyl thymidine-3′ phosphate. The nucleotide (20 μmoles) as its ammonium salt in dimethyl sulfoxide (2.0 ml.)[5] was treated with molar potassium *t*-butoxide in *t*-butyl alcohol (1.0 ml.)[6] at 20°. Immediately an intense yellow color developed and chromatography in isopropyl alcohol–concentrated ammonia–water (7:1:2) indicated that formation of thymidine-3′,5′ cyclic phosphate was quantitative and complete in less than 5 min. The nucleotide was isolated by ion-exchange chromatography on diethylaminoethyl cellulose[7] and characterized by its spectral properties, paper chromatography in three systems, electrophoresis at pH 7.5, and hydrolysis to thymine in molar hydrochloric acid at 50°.[7-9]

Although *p*-nitrophenyl uridine-5′ phosphate is not hydrolysed by aqueous alkali *via* the nucleoside-3′,5′ cyclic phosphate,[1] the reaction of *p*-nitrophenyl thymidine-5′ phosphate (sodium salt) was next examined. Under the conditions described above, conversion to thymidine-3′,5′ cyclic phosphate was complete in 60 min.[10] Similarly, *p*-nitrophenyl deoxyadenosine-5′ phosphate[11] was completely converted to deoxyadenosine-3′,5′ cyclic phosphate, although the reaction proceeded at about 80% of the rate of the thymidine-5′ nucleotide. Deoxyadenosine-3′,5′ cyclic phosphate was characterized by its ion-exchange, spectral, chromatographic, and electrophoretic properties, by its resistance to molar hydrochloric acid at 50°, and by its hydrolysis by the adenosine-3′,5′ cyclic phosphate diesterase of brain.[7,12]

When formamide was substituted for dimethyl sulfoxide as solvent,[13] there was no detectable reaction of *p*-nitrophenyl thymidine-5′ phosphate after 60 min. In dimethylformamide, thymidine-3′,5′ cyclic phosphate was produced at about 75% of the rate in dimethyl sulfoxide.

Experiments to determine the utility of this reaction in the synthesis of other deoxyribonucleoside-3′,5′ cyclic phosphates,[7] ribonucleoside-3′,5′ cyclic phosphates,[14] and internucleotide linkages are in progress.

(1) A. F. Turner and H. G. Khorana, *J. Am. Chem. Soc.*, **81**, 4651 (1959).

(2) H. Schaller, G. Wiemann, B. Lerch, and H. G. Khorana, *ibid.*, **85**, 3821 (1963).

(3) M. Smith, D. H. Rammler, I. H. Goldberg, and H. G. Khorana, *ibid.*, **84**, 430 (1962).

(4) This solvent system was first described by R. K. Ralph, W. J. Connors, H. Schaller, and H. G. Khorana, *ibid.*, **85**, 1983 (1963), and was used here because *p*-nitrophenyl phosphate is insoluble in anhydrous pyridine.

(5) Dimethyl sulfoxide is a useful solvent in nucleotide chemistry; see J. G. Moffatt, *Can. J. Chem.*, **42**, 599 (1964).

(6) R. B. Clayton, H. B. Henbest, and M. Smith, *J. Chem. Soc.*, 1982 (1957).

(7) G. I. Drummond, M. W. Gilgan, E. J. Reiner, and M. Smith, *J. Am. Chem. Soc.*, **86**, 1626 (1964).

(8) G. M. Tener, H. G. Khorana, R. Markham, and E. H. Pol, *ibid.*, **79**, 430 (1957).

(9) These criteria do not exclude the possibility of anomerization (at the glycosidic linkage). However, other experiments involving *t*-butoxide catalysis indicate that this is improbable. See R. Letters and A. M. Michelson, *J. Chem. Soc.*, 1410 (1961); A. M. Michelson and W. E. Cohn, *Biochemistry*, **1**, 490 (1962).

(10) Thymidylyl-(5′→3′)-thymidine is unaffected under the same conditions (unpublished results).

(11) Kindly donated by Dr. W. E. Razzell.

(12) G. I. Drummond and S. Perrot-Yee, *J. Biol. Chem.*, **236**, 1126 (1961).

(13) Formamide was used as solvent in the potassium *t*-butoxide catalysed transesterification of ribonucleic acid to ribonucleoside-2′,3′ cyclic phosphates; see D. Lipkin and P. T. Talbert, *Chem. Ind.* (London), 143 (1955).

(14) M. Smith, G. I. Drummond, and H. G. Khorana, *J. Am. Chem. Soc.*, **83**, 698 (1961).

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Heat of Hydrogenation of Bicyclo[2.2.2]octa-2,5,7-triene

Sir:

In view of recent commentary on the question of delocalization energy in bicyclo[2.2.2]octa-2,5,7-triene ("barrelene"),[1] the author wishes to report the value obtained in this laboratory for the heat of hydrogenation of this substance. A purified sample, kindly provided by Dr. H. E. Zimmerman, was reduced in acetic acid solution at 25° with the uptake of 2.99 molar equivalents of hydrogen. The heat of hydrogenation was −93.78 ± 0.31 kcal./mole.

Since the heat of hydrogenation of bicyclo[2.2.2]-octa-2,5-diene is −56.21 ± 0.10 kcal./mole,[2] the heat evolved in reduction of the first double bond of barrelene

(1) H. E. Zimmerman and G. L. Grunewald, *J. Am. Chem. Soc.*, **86**, 1434 (1964), footnote 2.

(2) R. B. Turner, W. R. Meador, and R. E. Winkler, *ibid.*, **79**, 4116 (1957).