

THE USE OF A PURINE CYCLONUCLEOSIDE FOR THE SYNTHESIS
OF A DINUCLEOSIDE PHOSPHATE*

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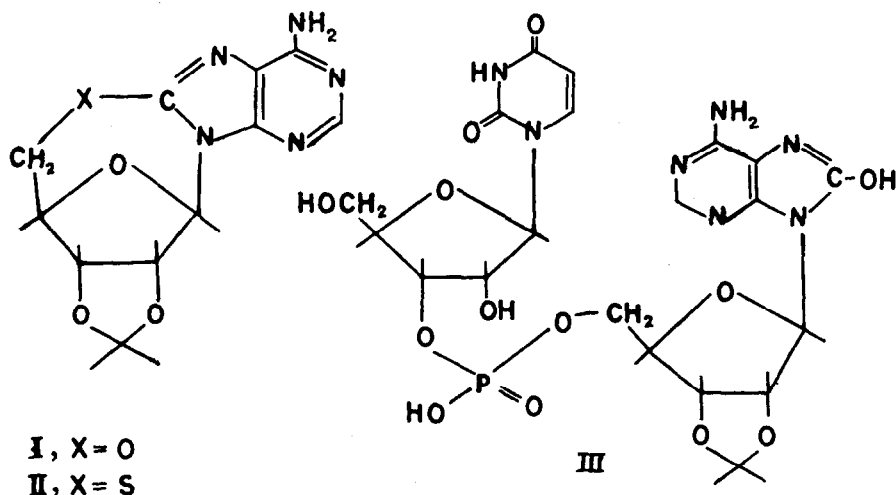
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Pyrimidine cyclonucleosides have been used in the synthesis of inter-nucleotide bonds (1,2,3,4,5). We now report the synthesis of the purine cyclonucleoside, 8,5'-anhydro-2',3'-O-isopropylideneadenosine (I) and its successful use in the synthesis of a dinucleoside phosphate, uridyl-(3'-5')-8-hydroxy-2',3'-O-isopropylideneadenosine (III).

Our initial plan envisaged the preparation of 8,5'-anhydro-2',3'-O-isopropylidene-8-mercaptoadenosine (II) and the synthesis of dinucleoside phosphates by attack of a nucleoside phosphate anion at the 5'-C of the anhydro linkage in this molecule. For the preparation of II, it was intended to tosylate 8-bromo-2',3'-O-isopropylideneadenosine (6), and convert the 5'-O-tosylate to II by successive treatment with thiourea and a base. 8-Bromo-2',3'-O-isopropylideneadenosine was therefore treated with tosyl chloride (1.1 eq.) in pyridine as previously described for the preparation of 2',3'-isopropylidene-5'-O-tosyladenosine (7) but 8-bromo-2',3'-O-isopropylidene-5'-O-tosyladenosine, λ_{\max} 263 $m\mu$ was obtained in a yield of

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only 11%. The major product being 8-bromo- N^3 , 5'-cycloadenosine tosylate, λ_{\max} 276 $m\mu$. These two products could be purified by chromatography over Florisil (elution solvents chloroform-ethanol (95:5) and chloroform-ethanol (90:10) respectively).



To avoid the occurrence of N^3 , 5' cyclisation, attention was directed to the synthesis of I. This compound was readily obtained by stirring a dioxan solution of 2',3'-O-isopropylidene-8-bromoadenosine with one equivalent of sodium hydride overnight at 27° and then at 50° for 3 hr. The product crystallized from chloroform, m.p. 222-4°; yield, 46%; R_f , 0.87 (8); Found: C, 51.45; H, 5.32; N, 22.63. Anal. Calcd. for $C_{13}H_{15}N_5O_4$, C, 51.15; H, 4.91; N, 22.94%. Its U-V absorption [λ_{\max} , H_2O -261 $m\mu$ (14,700); 0.1N NaOH-260 $m\mu$ (17,540) and 0.1N HCl-259 $m\mu$ (16,230)] is similar to that of

the known 8-methoxyadenosine (9) and its m.p. is depressed to 197-200° on admixture with 2',3'-O-isopropylideneadenosine.

The dinucleoside phosphate (III) was prepared by refluxing I with 1.5 equivalents of tri-n-butyl ammonium 3'-uridyate in dry dimethyl formamide for 15 hr. Removal of solvent, followed by preparative paper chromatography on Whatman 3 MM paper yielded a product, R_f , 0.57 (8); yield 47%; λ_{max} , 0.1N HCl-292 m μ ; Found: C, 42.32; H, 4.86; N, 16.04. Anal. Calcd. for $C_{22}H_{28}N_7O_{13}P$, C, 41.97; H, 4.45; N, 15.59. Formic acid hydrolysis of this product gave uracil and 8-hydroxyadenine (10) and paper chromatography of the pancreatic ribonuclease hydrolysate revealed the presence of uridine-3'-phosphate and another substance which is presumably 8-hydroxy-2', 3'-O-isopropylideneadenosine.

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