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STUDIES OF PHOSPHORYLATION. IV[1)]
A SELECTIVE PHOSPHORYLATION OF 5'-HYDROXY GROUP OF NUCLEOSIDES BY MEANS OF TIRS(8-QUINOLYL) PHOSPHATE

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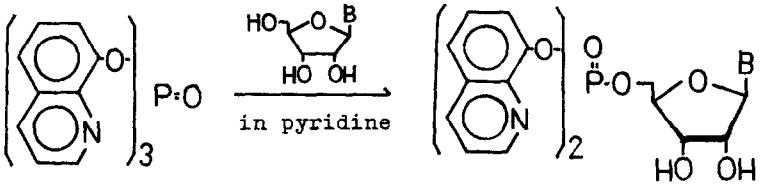
In the syntheses of nucleotides and oligonucleotides, it is desirable to develop selective phosphorylation of unprotected nucleosides.

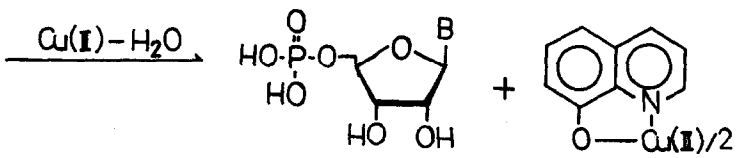
A number of laboratories have reported the direct phosphorylation of unprotected nucleosides.[2-7)] For example, the reaction of unprotected deoxyribonucleosides and 2-cyanoethyl dihydrogen phosphate with dicyclohexylcarbodiimide resulted in the formation of the corresponding nucleoside 5'-phosphate as a major product.[2)] Yoshikawa, et al.[6)] have reported that the reaction of unprotected nucleosides with phosphoryl chloride in trialkyl phosphates gave nucleoside 5'-phosphates.

In previous papers, phosphorylation of alcohols, phosphates and 2',3'-O-isopropylidenenucleosides by means of 8-quinolyl phosphates has been reported.[1,8,9]

In this paper, we wish to report a selective phosphorylation of the 5'-hydroxy group of nucleosides by means of tirs(8-quinolyl) phosphate (I). A phosphorylating reagent, tris(8-quinolyl) phosphate (I), was prepared from 8-hydroxyquinoline and phosphoryl chloride in 75% yield.[9]



(I) (II)



(III)

B: adenine, guanine, uracil, or cytosine

For example, when a mixture of adenosine (1 mmole) and tris(8-quinolyl) phosphate (I) (3 mmole) in dry pyridine (2 ml) was heated at 80°C for 8 hr, the corresponding adenosine 5'-bis(8-

quinolyl) phosphate (IIa) was formed. The phosphate (IIa), without isolating, was treated with aqueous solution of cupric chloride (4.5 mmole) at 100°C for 1 hr. The reaction mixture was concentrated and the residue was dissolved in water. After removal of an insoluble material (8-hydroxyquinoline-copper complex), the solution was concentrated and applied to a column (10 × 200 mm) of Dowex-1-(× 2) resin (formate form; 100-200 mesh) and eluted with 0.1M- and 4M-formic acid. Adenosine 5'-phosphate (IIIa) was obtained in 61% yield and a trace of 2'(3'),5'-diphosphate was detected.

Table 1. Yield and Paper Chromatography and Spectral Properties of Nucleoside 5'-phosphates (III).

Compounds	Yield (%)	Rf*		UV Spectral data (pH 2)	
		(A)	(B)	$\lambda_{max}^{H_2O}$ ($10^{-3}\varepsilon$)	$\lambda_{min}^{H_2O}$ (mμ)
Adenosine 5'-phosphate (IIIa)	61	0.34	0.15	257 (15.0)	230
Guanosine 5'-phosphate (IIIb)	55	0.48	0.07	256 (12.2)	228
Uridine 5'-phosphate (IIIc)	60	0.67	0.10	262 (10.1)	230
Cytidine 5'-phosphate (IIId)	43	0.70	0.13	280 (13.2)	241

* Paper chromatography was preformed by the descending technique using Toyo Roshi No. 51 paper. The solvent systems used were solvent (A), isopropyl alcohol-saturated ammonium sulfate-water (2:79:19, v/v); solvent (B), isopropyl alcohol-concentrated ammonium hydroxide-water (7:1:2, v/v).

In a similar manner, guanosine (IIIb), uridine (IIIc) and

cytidine 5'-phosphate (IIId) were obtained as shown in Table 1.

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