

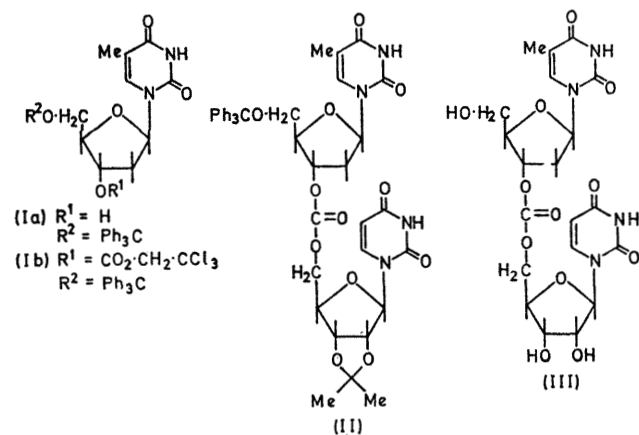
## The Preparation of Dinucleoside Carbonates

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**Summary** Dinucleoside carbonates have been prepared by means of a simple trans-esterification reaction.

RECENTLY, Mertes and Coats<sup>1</sup> described the preparation of pyrimidine dinucleoside carbonates in which the carbonate bridge between adjacent carbohydrate residues was formed by reaction of the nucleosides with phosgene. We report an alternative method involving the reaction of a 5'-O-protected deoxyribonucleoside 3'-O-carbonate active ester [*e.g.* (Ib)]



with a 2',3'-O-protected ribonucleoside. The method has been used successfully in the preparation of pyrimidine and

purine dinucleoside carbonates in good yield and is illustrated by the following preparation of 3'-O-thymidinyl-5'-O-uridinyl carbonate.

5'-O-Tritylthymidine (Ia) was treated with 2,2,2-trichloroethoxycarbonyl chloride (1.25 mol.) in anhydrous pyridine at room temperature for 3 days. After removal of the solvent (25°; 12 mm.), the residue was crystallised from ethanol to give 3'-O-2,2,2-trichloroethoxycarbonyl-5'-O-tritylthymidine (Ib) as white needles. [60%; m.p. 189—190°; λ<sub>max</sub> (EtOH) 267 nm, ε 9300]. This (Ib) was added to a solution of 2',3'-O-isopropylideneuridine (1 mol.) and sodium hydride (1 mol.) in anhydrous *NN*-dimethylformamide and left at room temperature for 24 hr. The solvent was removed (25°; 0.1 mm.) and the resulting mixture was separated by silicic acid chromatography (chloroform:ethanol 9:1). 3'-O-(5'-O-Tritylthymidinyl)-5'-O-(2',3'-O-isopropylideneuridinyl) carbonate (II), the major product, crystallised from ethanol as white needles. [70%; m.p. 190—191°, softening 160°; λ<sub>max</sub> (EtOH) 263 nm, ε 17,300]. Treatment of the protected carbonate (II) with 80% aqueous acetic acid (100°; 1 hr.) gave a single substance isolated as an amorphous powder after silicic acid chromatography (chloroform:ethanol 8:2). Recrystallisation from aqueous ethanol gave 3'-O-thymidinyl-5'-O-uridinyl carbonate, (III), as white needles. [66%; m.p. 176—178°, softening 148°; λ<sub>max</sub> (EtOH) 264 nm, ε 16,000]. Alkaline hydrolysis of (III) gave equimolar amounts of thymidine and uridine.

The structures of (Ib), (II), and (III) were confirmed by elemental analysis, n.m.r., and i.r. spectroscopy.

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\* M. P. Mertes and E. A. Coats, *J. Medicin. Chem.*, 1969, **12**, 154.