Trifluoroacetyl as *N*-Blocking Group in Amino-sugar Nucleoside Synthesis

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THIS laboratory has been concerned with the synthesis of nucleosides of 2-amino-2-deoxy-sugars and for this purpose suitable *N*-blocking groups are required. We have utilized the *N*-acetyl, *N*-2,4-dinitrophenyl,[1] and *N*-benzenesulphonyl[2] functions to this end but these all offer difficulties in deblocking, especially in the presence of a neighbouring hydroxyl group which is configurationally *trans*. The bis(benzyloxy)phosphinyl group, $-PO(OCH_2Ph)_2$,[3] and the trifluoroacetyl[4] function have been attached to the nitrogen in amino-acids. We report herein a successful application of the latter in nucleoside synthesis. Experiments with the former are in progress. Newman[5] has employed *N*-trifluoroacetyl as a blocking group in the synthesis of steriod glycosides of amino-sugars using for this purpose the glycosyl bromide of a 3,4,6-trideoxy-3-methylaminohexose.

1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucose[6] was treated with trifluoroacetic anhydride in pyridine and methylene chloride to give 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trifluoroacetamido-D-glucose,[7] (I), yield 90%, m.p. 167°, $[\alpha]_D^{22}$ −13° (*c*., 2·43 in chloroform). This substance was converted to its syrupy glycosyl chloride with hydrogen chloride in acetic anhydride and methylene chloride and the product was immediately fused, at 150° and under reduced pressure, with trimethylsilylthymine[8] to yield the blocked nucleoside, 1-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-D-glucosyl)thymine, yield 56% from (I), m.p. 235—236°, $[\alpha]_D^{22}$ −48° (*c*, 2·43 in chloroform), λ_{max} (EtOH) 265 mμ. This product was completely deblocked by treatment with methanol and hydrogen chloride at room temperature to yield 1-(2-amino-2-deoxy-D-glucopyranosyl)thymine hydrochloride, yield 85%, m.p. 301—304°, $[\alpha]_D^{22}$ +35° (*c*, 2·34 in water), λ_{max} (H_2O) 265 mμ.

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