

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*-benzenesulphonyl² 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, $-\text{PO}(\text{OCH}_2\text{Ph})_2$,³ and the trifluoroacetyl⁴ 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. Newman⁵ has employed *N*-trifluoroacetyl as a blocking group in the synthesis of steroid glycosides of amino-sugars using for this purpose the glycosyl bromide of a 3,4,6-trideoxy-3-methylamino-hexose.

1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy- β -D-glucose⁶ 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°, $[\alpha]_D^{25} -13^\circ$ (*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 trimethylsilylthymine⁸ 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°, $[\alpha]_D^{25} -48^\circ$ (*c.*, 2.43 in chloroform), λ_{max} (EtOH) 265 m μ . 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°, $[\alpha]_D^{25} +35^\circ$ (*c.*, 2.34 in water), λ_{max} (H₂O) 265 m μ .

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³ Si-Oh Li and R. E. Eakin, *J. Amer. Chem. Soc.*, 1955, **77**, 1866.

⁴ F. Weygand and E. Scendes, *Angew. Chem.*, 1952, **64**, 136.

⁵ H. Newman, *J. Org. Chem.*, 1965, **30**, 1287.

⁶ M. Bergmann and L. Zervas, *Ber.*, 1931, **64**, 975.

⁷ Unless otherwise noted, all new compounds reported herein were crystalline, were homogeneous by thin-layer chromatography, and gave satisfactory elemental analyses.

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