Preliminary communication

Amination of sugar derivatives with a mixture of phthalimide, triphenylphosphine, and diethyl azodicarboxylate

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A common procedure for the synthesis of amino sugars involves the conversion of a hydroxyl group into a good leaving group, such as a sulfonic ester or halogen group, followed by a displacement reaction with a nitrogen-containing nucleophile, such as ammonia, hydrazine, or azide ion[1,2]. Recently, Mitsunobu *et al.*[3] reported a stereospecific, one-stage formation of *N*-alkylphthalimides from alcohols by treatment with phthalimide, diethyl azodicarboxylate ($C_2H_5OOCN{=}NCOOC_2H_5$), and triphenylphosphine. In this Communication we describe some preliminary results which demonstrate that the reaction provides a convenient route to certain amino sugars.

Treatment of several carbohydrate derivatives containing "isolated" hydroxyl groups with equimolar amounts of phthalimide, diethyl azodicarboxylate, and triphenylphosphine in tetrahydrofuran at room temperature[3] is shown to afford the corresponding deoxyphthalimido derivatives in good yields. The progress of each reaction was monitored by t.l.c.; usually, reaction times of 24–48 h were employed. The reaction mixtures were concentrated to dryness, and the products were isolated by chromatography on silica gel. The amino sugars were obtained by the reaction of the phthalimido derivatives with *n*-butylamine in methanol at reflux temperature.

1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose[4] (**1**) was converted into 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-phthalimido-α-D-galactopyranose (**2**), yield 66.3%; m.p. 145–146°; ν_{max}^{nujol} 1620, 1715 and 1775 (C=O), 725 cm^{-1} (*o*-disubstituted Ph), no OH absorption. The n.m.r. spectrum (chloroform-*d*) revealed a pattern of signals similar to those given by known[5] 6-substituted derivatives of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. The phthaloyl group was removed to give the previously reported[6] 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**3**), which was converted into the 6-acetamido derivative[6] **4** by treatment with acetic anhydride–pyridine. Methyl 5-deoxy-2,3-di-*O*-*p*-tolylsulfonyl-α-L-*arabino*-hexofuranoside[7] (**5**) was converted into the 6-deoxy-6-phthalimido derivative **6**; yield 66.6%; m.p. 155–156°; ν_{max}^{nujol} 1600, 1715 and 1770 (C=O), 725 cm^{-1} (*o*-disubstituted Ph), no OH absorption.

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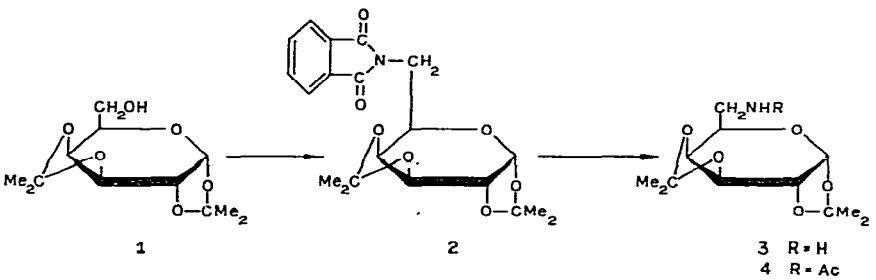

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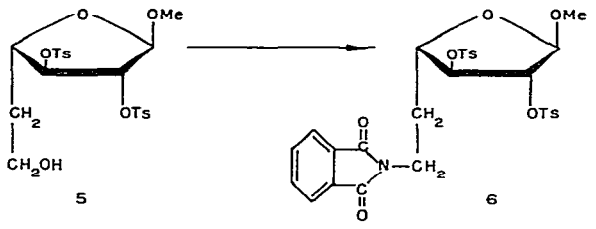

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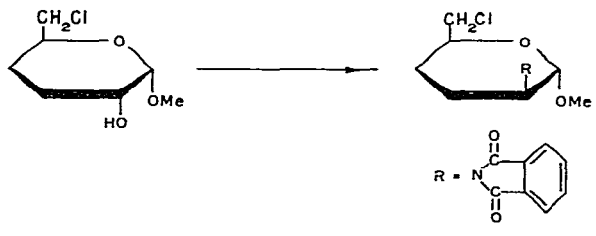

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An example of the application of the method to a carbohydrate derivative containing an "isolated" secondary hydroxyl group was provided by the conversion of methyl 6-chloro-3,4,6-trideoxy-α-D-*erythro*-hexopyranoside[8] (**7**) into a 2-deoxy-2-phthalimido derivative, yield 47%; m.p. 105–106°; ν_{max}^{nujol} 1615, 1715 and 1775 (C=O), 720 cm^{-1} (*o*-disubstituted Ph), no OH absorption. Mitsunobu *et al.*[3] have reported that their reactions of optically active alcohols with phthalimide or carboxylic acids in the presence of diethyl azodicarboxylate and triphenylphosphine proceeded stereospecifically with (nearly) complete inversion of the configuration of the alkyl group. The product of the reaction with **7** is tentatively assigned, therefore, the D-*threo* configuration as shown in structure **8**; n.m.r. (chloroform-*d*): τ4.82 [doublet, $J_{1,2}$ 6.5 Hz, H-1 of **8** in the *1C*(D) conformation].

The formation of phthalimido derivatives could not be observed when the reaction was attempted with 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (1 week at ~25°, followed by 18 h at reflux), methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (48 h at ~25°, followed by 1 h at reflux), or methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (6 days at ~25°, followed by 18.5 h at reflux).

Full details of the reactions described in this Communication and of other examples will be published later.

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