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Preliminary communication

A novel synthesis of aryl glycosides

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Aryl glycosides may be synthesised[1] by displacement with a phenol of an anomeric substituent such as a halogen atom (Koenigs–Knorr reaction) or acyloxy group (Helferich reaction) in the presence of an appropriate catalyst. A new method is now reported, namely, the condensation of a sugar derivative containing an unsubstituted anomeric hydroxyl group with phenols in the presence of diethyl azodicarboxylate and a trivalent phosphorus compound.

The betaine formed from diethyl azodicarboxylate and triphenylphosphine can effect the alkylation of phenols by simple alcohols[2], hydroxysteroids[3], and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[3]. 2,3:5,6-Di-*O*-isopropylidene-D-mannofuranose (**1**) was chosen as a model compound for glycosylation, and was treated in tetrahydrofuran with *p*-substituted phenols in the presence of diethyl azodicarboxylate (**2**) and triphenylphosphine (**3**), tributylphosphine (**4**), or triethyl phosphite (**5**). When phenol was used, the ratio of phenyl 2,3:5,6-di-*O*-isopropylidene-α- and -β-D-mannofuranoside was found (t.l.c., g.l.c.) to be 3:7 when **3** was employed as the phosphine component, 6:4 with **5**, and 8:2 with **4**. The highest yields of **6**–**11** were obtained when **4** was used as the phosphine component, whereas the *p*-nitro- and *p*-cyano-phenyl glycosides were obtained in significant yield only when **5** was used.

Compounds **6**–**13** (Table I) gave correct elemental analyses and exhibited the expected spectral properties. The remaining phenyl glycosides were identified by comparison with authentic samples.

The phenol–tributylphosphine–diethyl azodicarboxylate mixture was also tested on other sugar substrates. Thus, 4,6-di-*O*-acetyl-D-*erythro*-hex-2-enopyranose[4] was converted into the phenyl α-glycoside, m.p. 38°, $[\alpha]_{578}^{20}$ +176° (chloroform), in good yield, and 2,3,4,6-tetra-*O*-acetyl-D-mannopyranose afforded exclusively the phenyl α-glycoside, m.p. 79–80°, $[\alpha]_{578}^{20}$ +76° (chloroform).

A most striking property of the new glycosylating system is its ability to transfer a phenoxy residue on to an unprotected carbohydrate molecule. Thus, D-mannose reacted completely in 15 min when treated with 2 mol. of phenol, together with **2** and **4** in *N*,*N*-dimethylformamide at room temperature. The single carbohydrate product (>80%) isolated

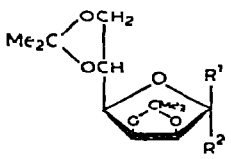

TABLE I

DATA ON PHENYL GLYCOSIDES

	R^1	R^2	*Yield (%)*	*M.p. (degrees)*	$[\alpha]_{578}^{20}$ *($CHCl_3$) (degrees)*
6	H	OPh	67	93–95	+116
7	OPh	H	16	97	–47.5
8	H	OC_6H_4Br-*p*	46	63	+141
9	OC_6H_4Br-*p*	H	33	69–70	–73
10	H	OC_6H_4Me-*p*	58	38	+116
11	H	OC_6H_4OMe-*p*	52	77	+117.5
12	H	$OC_6H_4NO_2$-*p*	12	81–83	+186
13	H	OC_6H_4CN-*p*	16	116	+115

by p.l.c. (silica gel, 1-butanol–acetic acid–diethyl ether–water, 45:30:15:15) was phenyl α-D-mannopyranoside. Likewise, 2-deoxy-D-*arabino*-hexose was converted into the phenyl α-glycoside. On the other hand, D-ribose gave a product which, after acetylation, was shown (t.l.c.) to be practically pure phenyl β-D-ribopyranoside. D-Glucose afforded ~70% of phenyl αβ-D-glucopyranoside, in which the β anomer preponderated. These results indicate a strong preference for the formation of phenyl glycopyranosides having the substituents at positions 1 and 2 *trans*-oriented. Arylation at positions other than the glycosidic centre did not occur during glycosylation of the above-mentioned free sugars.

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REFERENCES

1 W. G. Overend, in W. Pigman and D. Horton (Eds.), *The Carbohydrates*, Vol. 1A, Academic Press, New York, 1972, pp. 279–353.
2 S. Bittner and Y. Assaf, *Chem. Ind. (London)*, (1975) 281.
3 M. S. Manhas, W. H. Hoffman, B. Lal, and A. K. Bose, *J. Chem. Soc., Perkin Trans. I*, (1975) 461–463.
4 B. Fraser-Reid and B. Radatus, *J. Am. Chem. Soc.*, 92 (1970) 5288–5290.
5 W. Z. Antkowiak and W. J. Krzyzosiak, *J. Chromatogr.*, 90 (1974) 399–401.