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Preliminary communication

A convenient method for the preparation of *C*-phosphino derivatives of D-glucose by a substitution reaction using SDMA as the key reagent

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A few articles have reported formation of a phosphorus–carbon bond by the reaction of phosphorus compounds with alkyl halides in the presence of sodium dihydrobis-(2-methoxyethoxy)aluminate (SDMA)[1–3]. The reaction of phosphorus compounds in the presence of SDMA with *p*-toluenesulfonates, as well as with halides[4], was found to afford a C–P bond. The procedure seems to be a simple and convenient method, because it is homogeneous. Some *C*-phosphino derivatives were prepared by the reaction of metal phosphides with *O*-*p*-tolylsulfonyl or deoxyhalo derivatives of carbohydrates[5–7]. This communication deals with a facile method for preparing *C*-phosphino and *C*-phosphinyl derivatives of D-glucose by the use of SDMA.

To a stirred solution of diphenylphosphine (1.3 g) in oxolane (10 mL) at room temperature was added dropwise a solution of SDMA (8.3 g) in oxolane (10 mL) under a nitrogen atmosphere. When all of the hydride solution had been added, stirring was continued for several minutes, until complete consumption of the phosphine was shown by t.l.c. A solution of 1,2:3,5-di-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (1) (1.5 g) in oxolane (10 mL) was added, and the solution was boiled for 4 h under reflux. After processing by addition of water (1 mL) and neutralization of the base with hydrochloric acid, the insoluble material was filtered off, and washed with ether. Evaporation of the filtrate plus washings *in vacuo* gave 6-deoxy-6-*C*-(diphenylphosphino)-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (2) (1.4 g, 90% yield). The same reaction of compound 1 with diphenylphosphine oxide in oxolane for 10 h at 65° gave the corresponding *C*-diphenylphosphinyl derivative (3) in 46% yield.

The reaction of methyl 6-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (4) with diphenylphosphine in the presence of SDMA in oxolane gave 6-deoxy-6-*C*-(diphenylphos-

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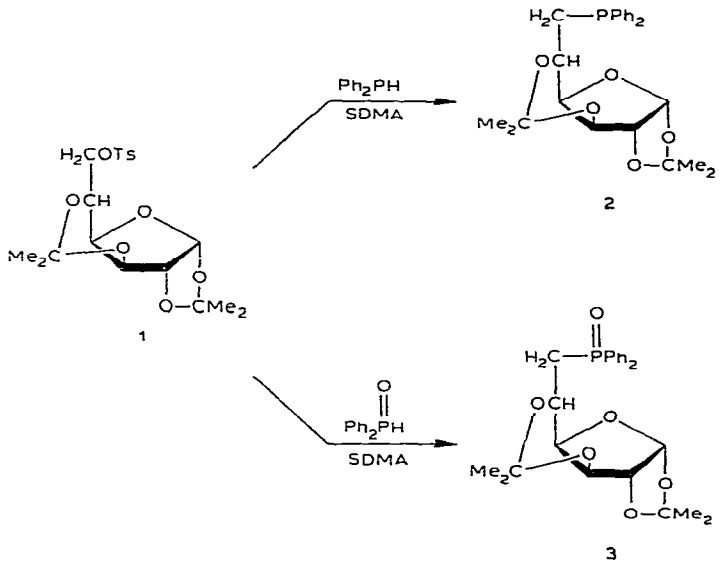

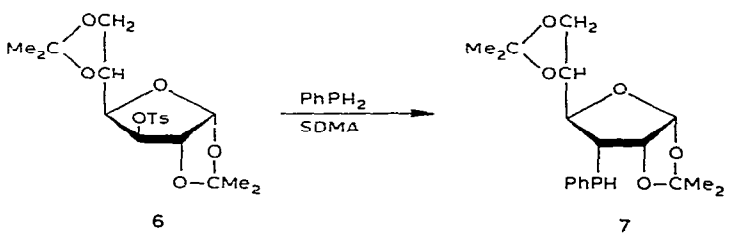

phino)-α-D-glucopyranose (5) in 77% yield. The reaction of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (6) with phenylphosphine in diglyme in the presence of SDMA afforded 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-(phenylphosphino)-α-D allofuranose (7) in 80% yield. The data for these reactions are summarized in Table I.

4-*O*-*p*-Tolylsulfonyl, 4-*O*-(trifluoromethylsulfonyl), and 4-chloro-4-deoxy derivatives of methyl 2,3-*O*-isopropylidene α,β-D-lyxopyranoside also gave 4-*C*-(phenylphosphino) derivatives when the reactions were conducted in diglyme under reflux.

These data suggest that this procedure provides a facile and convenient method for introducing a C—P bond, not only on a primary but also on a secondary carbon atom of carbohydrates. The method has an additional advantage, in that certain phosphorus esters could be used instead of phosphines as phosphide precursors.

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TABLE 1

C-PHOSPHINO AND *C*-PHOSPHINYL DERIVATIVES FROM D-GLUCOSE

Substrate	*Phosphorus compound*	*Reaction conditions*	*Product*	*Yield (%)*	*^{1}H-n m r. data ($CDCl_3$)*	*(m/z)*
1	Ph_2PH	4 h at 56° in oxolane	2[a]	90	1 06, 1 34 (2 s, 6 H, CMe_2), 1 26, 1 45 (2 s, 6 H, CMe_2), 2.02 (d, 2 H, *J* 13.0 Hz, H-6,6'), 3 30–5.00 (m, 4 H, H-2–5), 5.92 (d, 1 H, *J* 4 0 Hz, H-1), 7.15–7.90 (m, 10 H, 2 Ph)	428 (M^+)
1	$Ph_2\overset{O}{\overset{\|}{P}}H$	10 h at 56° in oxolane	3[b]	46	1 16, 1.23 (2 s, 6 H, CMe_2), 1.23, 1 40 (2 s, 6 H, CMe_2), 2.02–2.75 (m, 2 H, H-6,6'), 3 25–4.46 (m, 3 H, H-3–5), 4.50 (d, 1 H, *J* 5.1 Hz, H-2), 5 89 (d, 1 H, *J* 5 1 Hz, H-1), 6.80–7 93 (m, 10 H, 2 Ph)	444 (M^+)
4	Ph_2PH	4 h at 56° in oxolane	5	77	1.86 (d, 2 H, *J* 13 5 Hz, H-6,6') 3 0–3.9 (m, 8 H, H-2–5, OH-1–4), 5 72 (s, 1 H, H-1), 7 15–7.95 (m, 10 H, 2 Ph)	–[c]
6	$PhPH_2$	165 h at 115° in diglyme	7	80[d]	–[e]	–[e]

[a] $[\alpha]_D^{16}$ +2.1° (*c* 1.0, EtOH). Analysis of the oxide gave a satisfactory result (C, ±0 08%, H, ±0 18%). [b] $[\alpha]_D^{23}$ +29.9° (*c* 4.55, $CHCl_3$). [c] No molecular-ion peak was observed. [d] Crude yield. [e] Isolation and identification were performed after the oxidation of compound 7 with hydrogen peroxide to the corresponding phenylphosphinic acid derivative.

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