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Preliminary communication

Synthesis of a chiral phosphine and a phosphinite from carbohydrates and application to asymmetrical hydrogenation

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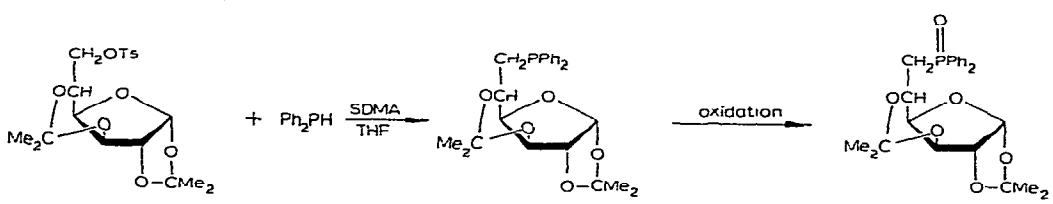
The formation of a C–P bond is the most important step in the synthesis of phospho sugars (sugars having a phosphorus atom in the hemiacetal ring), and several methods for forming a C–P bond have been investigated[1–5]. Only a few studies concerning homogeneous, asymmetrical hydrogenation reactions of alkenes in the presence of a rhodium catalyst, using a sugar framework as an asymmetrical component, are known[6–9]; however, the optical yields obtained were not always satisfactory. In this communication, we report the simple synthesis of novel carbohydrates having a diphenylphosphino group on a carbon or oxygen atom, as well as their application to the homogeneous, asymmetrical hydrogenation of prochiral alkenes with rhodium complexes.

1,2:3,5-Di-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (1) was added at room temperature to a solution, in oxolane (THF), of diphenylphosphide anion [produced by the reaction of diphenylphosphine with sodium dihydrobis(2-methoxyethoxy)-aluminate (SDMA) in THF under a nitrogen atmosphere].



1 2 3

The reaction mixture was heated for 4 h at 65°, followed by addition of a small amount of water, and neutralization of the base with hydrochloric acid. Filtration of the mixture, and evaporation of the filtrate *in vacuo*, gave 6-deoxy-6-*C*-(diphenylphosphino)-1,2;3,5-di-*O*-isopropylidene-α-D-glucofuranose (2) in 90% yield; $[\alpha]_D^{16}$ +2.1° (*c* 1.0, EtOH); n.m.r. ($CDCl_3$): δ 1.06, 1.31 (2s, 6 H, CMe_2), 1.26, 1.45 (2s, 6 H, CMe_2),

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TABLE I

ASYMMETRICAL HYDROGENATION[a] OF PROCHIRAL ALKENES BY $Rh_2Cl_2(C_8H_{12})_2$

Chiral phosphine	*Substrate*	*Product*[b]	*Time (h)*	*Chemical yield (%)*	*$[\alpha]_D^A$ (degrees)*	*Optical*[c] *yield (%)*	*Configuration*
2	α-Acetamido-cinnamic acid	*N*-Acetylphenylalanine ethyl ester	24	99	−1.3 (*c* 1.3, EtOH)	9	(*R*)
	Methyl α-acetamidocinnamate	*N*-Acetylphenylalanine methyl ester	24	99	−0.4 (*c* 1.8, MeOH)	2	(*R*)
	α-Benzamido-cinnamic acid	*N*-Benzoylphenylalanine ethyl ester	24	72	−0.8 (*c* 1.0, MeOH)	2	(*S*)
	Itaconic acid	Methylsuccinic acid	24	96	−2.4 (*c* 1.0, EtOH)	14	(*R*)
	Tiglic acid	2-Methylbutyric acid	24	98	−0.3 (*c* 2.0, EtOH)	2	(*R*)
5	α-Acetamido-cinnamic acid	*N*-Acetylphenylalanine ethyl ester	24	99	−8.8 (*c* 1.2, EtOH)	67	(*R*)
	Methyl α-acetamidocinnamate	*N*-Acetylphenylalanine methyl ester	24	99	−6.6 (*c* 2.2, MeOH)	29	(*R*)
	α-Benzamido-cinnamic acid	*N*-Benzoylphenylalanine ethyl ester	24	85	−12.8 (*c* 1.0, MeOH)	32	(*S*)
	Itaconic acid	Methylsuccinic acid	24	99	−8.4 (*c* 1.0, EtOH)	49	(*S*)
	Tiglic acid	2-Methylbutyric acid	24	99	−11.9 (*c* 2.8, EtOH)	62	(*R*)

[a] The ratios of substrate to rhodium complex, and of compound 2 or 5 to rhodium complex, were 25 : 1 and 4 : 1, respectively. [b] Determined by ^{1}H-n.m.r. spectroscopy. [c] Calculated on the basis of the value reported for the optically pure compound: *N*-acetyl-(*R*)-phenylalanine ethyl ester[10], $[\alpha]_D^{20}$ −13.1° (*c* 2.0, EtOH); *N*-acetyl-(*R*)-phenylalanine methyl ester[10], $[\alpha]_D^{25}$ −21.4° (*c* 1.9, MeOH); *N*-benzoyl-(*S*)-phenylalanine ethyl ester[11], $[\alpha]_D^{26}$ −40.3° (*c* 1.0, MeOH); methyl-(*R*)-succinic acid[6], $[\alpha]_D^{18}$ +17.01° (*c* 4.41, EtOH); and 2-methyl-(*R*)-butyric acid[12], $[\alpha]_D^{18}$ −19.33°.

TABLE II

ASYMMETRICAL HYDROGENATION OF PROCHIRAL ALKENES BY RHODIUM COMPLEXES WITH 5

Rhodium complex	*Substrate*	*Product*	*Time (h)*	*Chemical yield (%)*	$[\alpha]_D^{17}$ *(degrees)*	*Optical yield (%)*	*Configuration*
$Rh_2Cl_2(C_8H_{12})_2$	α-Acetamido-cinnamic acid	*N*-Acetylphenylalanine ethyl ester	96	78	−3.3 (*c* 0.9, EtOH)	25	(*R*)
	Itaconic acid	Methylsuccinic acid	96	100	−3.8 (*c* 1.8, EtOH)	22	(*R*)
	Tiglic acid	2-Methylbutyric acid	120	100	−2.8 (*c* 1.6, EtOH)	15	(*R*)
$RhCl(C_8H_{14})_2$	α-Acetamido-cinnamic acid	*N*-Acetylphenylalanine ethyl ester	216	88	−0.7 (*c* 1.1, EtOH)	6	(*R*)
	Itaconic acid	Methylsuccinic acid	216	100	−2.3 (*c* 1.6, EtOH)	1	(*S*)
	Tiglic acid	2-Methylbutyric acid	216	100	−1.0 (*c* 1.4, EtOH)	5	(*R*)

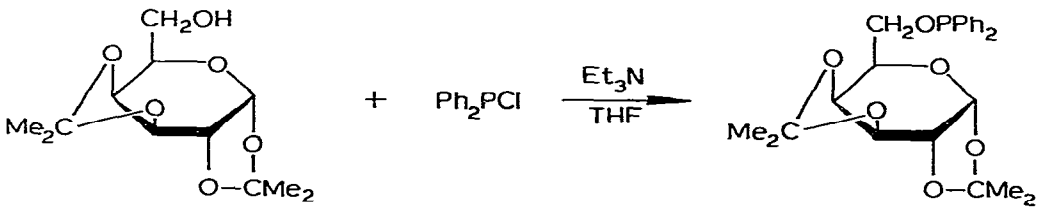
2.02 (d, 2 H, *J* 13.0 Hz, H_2), 3.30–5.00 (m, 4 H, H-2–5), 5.92 (d, 1 H, *J* 4.0 Hz, H-1), and 7.15–7.90 (m, 10 H, 2 Ph); *m/z* 428 (M^+) and 243 ($M^+ - PPh_2$).

Anal. Calc. for $C_{24}H_{29}O_6P$: C, 64.86; H, 6.58. Found: C, 64.94; H, 6.40.

Oxidation of compound 2 gave the oxide 3.

Reaction of 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (4) with diphenylphosphinous chloride in the presence of triethylamine for 24 h at room temperature, followed by isolation by column chromatography, gave 6-*O*-(diphenylphosphino)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (5) in 46% yield; $[\alpha]_D^{16}$ +47.0° (*c* 1.2, EtOH); n.m.r. ($CDCl_3$): δ 1.32, 1.42 (2s, 6 H, CMe_2), 1.32, 1.46 (2s, 6 H, CMe_2), 3.76–4.76 (m, 6 H, H-2–6'H), 5.56 (d, 1 H, *J* 5.0 Hz, H-1), and 7.16–7.72 (m, 10 H, 2 Ph); *m/z* 444 (M^+) and 243 ($M^+ - OPPh_2$):

Anal. Calc. for $C_{24}H_{29}O_6P$: C, 64.86; H, 6.58. Found: C, 64.35; H, 6.70.



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Homogeneous hydrogenation of prochiral alkenes with $Rh_2Cl_2(C_8H_{12})_2$ was conducted in the presence of chiral ligand 2, or 5, and triethylamine in dry benzene and absolute ethanol with hydrogen at atmospheric pressure and room temperature. Removal of the catalyst by means of Dowex 50W (H^+), and evaporation of the solvents *in vacuo*, gave the corresponding products, shown in Table I.

The same procedure was used for $RhCl(C_6H_{14})_2$, and the results showed that the catalyst gave poorer optical yields in the asymmetrical hydrogenation (see Table II).

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