Removal of *O*-Benzyl Protective Groups by Catalytic Transfer Hydrogenation

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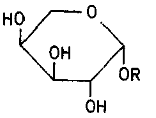
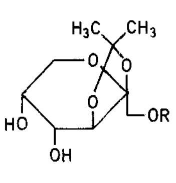
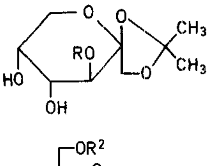
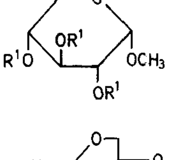
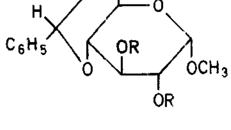
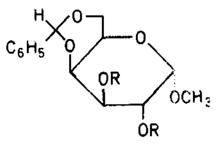
Benzyl ethers of sugars are an important class of derivatives employed in synthetic sugar chemistry[1]. Since the benzyloxy group only insignificantly participates in nucleophilic substitution reactions at the anomeric center it is increasingly used in oligosaccharide synthesis[2]. Further, the convenient methods available for the preparation of sugar benzyl ethers as well as the fact that these ethers are stable to both acids and bases but can be cleaved under relatively mild conditions have made the *O*-benzyl group particularly useful as protective group[3]. The hydroxy groups can be conveniently regenerated from the benzyl ethers by catalytic[4] or chemical hydrogenolysis[5], bromination-hydrolysis[6], or bromination-acetolysis[7].

It has been found that catalytic transfer hydrogenation utilizing palladium on carbon and formic acid[8] or palladium hydroxide on carbon and cyclohexene[9] provides an additional means for the removal of *O*-benzyl groups from carbohydrate derivatives. This procedure has the advantage of being easy and rapid; however, when formic acid is the hydrogen donor a large amount of palladium has to be used (1 g of 10% Pd/C per 0.2 mmol of substrate). The method using palladium hydroxide on carbon[9] requires the separate preparation of the catalyst[10]. Under the reported conditions,

Table. Cleavage of Benzyl Ethers and Other Derivatives of Monosaccharides by Catalytic Hydrogenation using Ammonium Formate as Hydrogen Donor (10% Palladium on Carbon, Boiling Methanol)

Educt[a]		Product[b]	Reaction Time [min]	mg Catalyst per 1 Benzyl Group in 1 mmol of **1**	Yield[c] [%]	m.p. [°C] $[\alpha]_D^{20}$	Lit. Data or Molecular Formula
	**1 a** R = Bzl	**2 a** R = H	20	600	96	157–159° +104.0° (H_2O)	158.5–160°[11] +105° (H_2O)
	**1 b** R = Bzl	**2 b** R = H	30	350	96	78–80° +19.6° (H_2O)	80°[12] +18.9° (H_2O)
	**1 c** R = Bzl	**2 c** R = H	40	350	98	119–120° −159.8° (H_2O)	120–121°[13] −158.9° (H_2O)
	**1 d** R^1 = Bzl R^2 = H	**2 d** R^1 = R^2 = H	60	400	98	167–169° +158.1° (H_2O)	167–169°[14] +157.0° (H_2O)
	1 e R^1 = Bzl R^2 = $-C(C_6H_5)_3$	**2 d** R^1 = R^2 = H (= **2 e**)	40	700	95	167–169° +158.4° (H_2O)	
	**1 f** R = Bzl	**2 f** R = H	30	1000	90	162–163° +116.2° ($CHCl_3$)	163–164°[15] +110.0° ($CHCl_3$)
	1 g R = $-CH_2-CH=CH_2$	**2 g** R = n-C_3H_7	30	180	92	69–71° +71.7° (c = 0.6, $CHCl_3$)	$C_{20}H_{30}O_6$[d,e] (366.4)
	**1 h** R = Bzl	**2 h** R = H	30	1000	91	169–171° +165.1° ($CHCl_3$)	170–172°[16] +166.5° ($CHCl_3$)

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[a] Bzl = $C_6H_5-CH_2-$.

[b] All products were characterized by m.p., α_D value, and ^1H-N.M.R. data.

[c] Yield of pure isolated product.

[d] calc. C 65.55 H 8.25
found 65.61 8.27

[e] ^1H-N.M.R. ($CDCl_3/TMS_{int}$): δ = 7.46 (m, $5H_{arom}$); 5.60 (s, 1H, $C_6H_5-C\underline{H}$); 4.85 (d, $1H_{anomeric}$, J = 3.4 Hz); 3.47 (s, 3H, $OC\underline{H}_3$); 1.58 (m, 4H, $O-CH_2-C\underline{H}_2-CH_3$); 0.97 (t, 3H, $C\underline{H}_3$, J = 7 Hz); 0.94 ppm (t, 3H, $C\underline{H}_3$, J = 7 Hz).

the commonly used *O*-benzylidene protective group is completely[8] or partly[9] removed. We have found that *O*-benzyl ethers **1** can be selectively cleaved by catalytic transfer hydrogenation using 10% palladium on carbon and ammonium formate as the hydrogen donor. Benzylidene acetal groups remain unaffected under these conditions (e.g., substrates **1f, g, h**).

$$\underset{\mathbf{1}}{R-O-CH_2-C_6H_5} \xrightarrow{10\%\ Pd/C,\ HCOONH_4,\ solvent,\ \nabla} \underset{\mathbf{2}}{R-OH}$$

As can be seen from the Table, the method may be used for the selective removal of *O*-benzyl groups in the presence of other types of *O*-protecting groups. Glycosidic methyl groups are not affected under the reaction conditions (substrates **1d–h**). The method can also be used for the cleavage of *O*-trityl groups (substrate **1e**). Cleavage of other ether groups (as in substrate **1g**) does not occur, the allyl groups of **1g** being hydrogenated to the propyl group, however, so that care should be taken with educts containing double bonds.

Cleavage of *O*-Benzyl Derivatives of Sugars (1); General Procedure: A mixture of the *O*-benzyl derivative **1** (1 mmol), ammonium formate (0.3 g), 10% palladium on carbon (Degussa, type E10N; 0.35–1.0 g per 1 benzyl group in 1 mmol of **1**, see Table), and methanol or acetone (15–30 ml) is refluxed until T.L.C. indicates complete cleavage of the benzyl ether (20–60 min). The catalyst is filtered off and washed with the solvent. The filtrate is evaporated to give the crystalline product.

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[1] See, for example:
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