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O-BENZYL PROTECTING GROUPS AS HYDROGEN DONORS IN CATALYTIC TRANSFER HYDROGENOLYSIS. SELECTIVE DEBENZYLATION OF 1,6-ANHYDRO HEXOSES.

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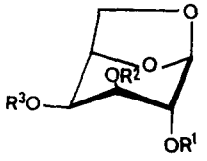
Summary.- O-Benzyl protecting groups may act as hydrogen donors in heterogeneous catalytic transfer hydrogenolysis. Hydrogenolysis of compounds 1 - 4 demonstrated that this hydrogen transfer occurs when adjacent cis-disposed benzylated hydroxyl groups are present.

Heterogeneous catalytic transfer hydrogenolysis may potentially afford enhanced selectivity in deprotection of O-benzyl ethers of polyols.[1,2] O-Benzyl protection is widely used in synthetic organic chemistry[3] and, particularly, in carbohydrate chemistry.[4] Catalytic hydrogen-transfer cleavage of O-benzylated carbohydrates has been observed[5-7] by using Pd/C and formic acid[5] or 2-propanol,[7] and Pearlman's catalyst[8] with cyclohexene as hydrogen donor.[6] O-Benzyl groups were selectively removed in the presence of O-benzylidene groups when the systems Pd/C-2-propanol[7] or $Pd(OH)_2$/C-cyclohexene[6] were used, and some partial selectivity in the removal of O-benzyl groups was also observed by using Pd/Al_2O_3-2-propanol.[7]

We now report preliminary results on the catalytic transfer hydrogenolysis of 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-galacto- (1), manno- (2), gulo- (3), and gluco- (4) pyranose. Heterogeneous catalytic transfer hydrogenolysis seems to be structure sensitive[2] and 1,6-anhydrohexoses constitute a group of available, well known, conformationally rigid molecules whose partially protected derivatives are of interest in organic synthesis. Our results indicate that, in the reaction conditions, conveniently orientated benzyl groups can act as hydrogen donors and partially O-benzoylated and O-benzylated derivatives can be isolated from the reaction mixture.

Treatment of 1 with 10% Pd/C in refluxing 2-propanol for 5 h, gave 1,6-anhydro-3-O-benzoyl-β-D-galactopyranose [5, 70%, m.p. 146-148°, $[\alpha]_D^{20}$ -22° (c 0.4 chloroform); lit[9], m.p. 145-147°, $[\alpha]_D^{20}$ -25° (c, 0.8 chloroform)] and 1,6-anhydro-β-D-galactopyranose (6). 1,6-Anhydro-3,4-di-O-benzyl-β-D-galactopyranose [7, 20%, m.p. 68-70°,

$[\alpha]_D^{20}$ -35.2° (c 0.52 chloroform; lit[10], m.p. 70-71°, $[\alpha]_D^{23}$ -36.9 (c 1.4 chloroform)] and 1,6-anhydro-3-O-benzoyl-2-O-benzyl-β-D-galactopyranose [8, 20%, $[\alpha]_D^{20}$ -64° (c 0.24 chloroform)] could also be isolated from the hydrogenolysis mixture when the reaction was stopped after 3 h. The IR spectrum of 8 showed a C=O band at 1720 cm^{-1} and the 300 MHz ^1H NMR spectrum presented a low field signal (δ 5.46, dd, 1H), assigned to H-3. The concentration of both 7 and 8 decreased as that of 5 increased in the reaction mixture (t.l.c.). Acetylation of 5, 7 and 8 yielded the acetyl derivatives 9, 10 and 11 respectively. Their spectral properties were in agreement with the proposed structures.

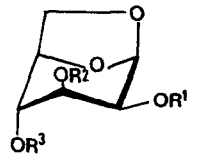


1, $R^1=R^2=R^3=Bzl$

5, $R^1=R^3=H$, $R^2=Bz$

6, $R^1=R^2=R^3=H$

7, $R^1=H$, $R^2=R^3=Bzl$



2, $R^1=R^2=R^3=Bzl$

12, $R^1=R^3=H$, $R^2=Bz$

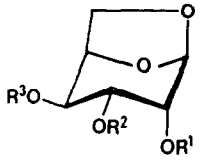
13, $R^1=R^2=R^3=H$

8, $R^1=Bzl$, $R^2=Bz$, $R^3=H$

9, $R^1=R^3=Ac$, $R^2=Bz$

10, $R^1=Ac$, $R^2=R^3=Bzl$

11, $R^1=Bzl$, $R^2=Bz$, $R^3=Ac$

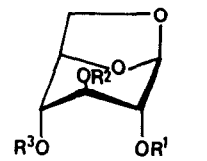


3, $R^1=R^2=R^3=Bzl$

14, $R^1=Bz$, $R^2=R^3=H$

15, $R^1=R^2=R^3=H$

16, $R^1=R^3=H$, $R^2=Bz$



4, $R^1=R^2=R^3=Bzl$

17 $R^1=R^2=R^3=H$

Hydrogenolysis of 2 under similar conditions afforded, after 4 h, 1,6-anhydro-3-O-benzoyl-β-D-mannopyranose [12, 40%, $[\alpha]_D^{20}$ -101.8° (c 0.38 chloroform)] and 1,6-anhydro-β-D-mannopyranose (13). The IR spectrum of 12 showed a band at 1720 cm^{-1}, the ^{13}C NMR spectrum showed a signal at 165.7 ppm, and the ^1H NMR spectrum presented a low field multiplet at δ 5.39 which was assigned to H-3. As in the hydrogenolysis of 1 two intermediate compounds were also detected (t.l.c.) but not isolated.

Similarly, the hydrogenolysis of 3 yielded, after 7 h, 1,6-anhydro-2-O-benzoyl-β--D-gulopyranose [14, 40%, m.p. 147-150°, $[\alpha]_D^{20}$ +92° (c 0.48 chloroform); lit.[11] m.p. 151-152°, $[\alpha]_D^{25}$ +96° (c 0.30 chloroform)] and 1,6-anhydro-β-D-gulopyranose (15). Intermediate partially benzylated compounds were also detected (t.l.c.) but not isolated. In this case, however, a monobenzoyl derivative other than 14 was also isolated in 10% yield. Interconversion of this benzoyl derivative and 14 took place in the reaction conditions (t.l.c.) and structure 16 may be tentatively assigned to this compound on these and spectroscopic basis.

Hydrogenolysis of 4 in the above conditions yielded, after 3 h, 1,6-anhydro- β -D-glucopyranose (17) and a partially benzylated derivative (30%) which was rapidly formed (t.l.c.). No benzoylated compounds were detected in the reaction mixture.

There is a paucity of kinetic, thermodynamic, and stereochemical data on transfer hydrogenation reactions and their mechanisms are poorly understood. Transfer of hydrogen can be thought to take place between adsorbed species, and oxidative addition of the hydrogen donor to palladium, followed by coordination of the substrate and transfer of hydrogen in two steps, the second one formally involving a five-membered transition state, have been postulated[2]. From the above results it may be concluded that O-benzyl protecting groups can act as hydrogen donors in heterogeneous catalytic transfer hydrogenolysis. There seem also to exist some stereochemical requirements as O-benzoyl derivatives have been isolated only in those cases in which adjacent cis-disposed benzylated hydroxyl groups are present in the starting material (compounds 1 - 3). The isolation of compounds 5 and 12 in reasonable yields may indicate that the transfer takes always place from an axially orientated O-benzyl group although care should be taken as benzoyl migration could easily occur as observed in the 1,6-anhydro-β-D-gulopyranose derivatives (compounds 14 and 16). Disproportionation and isomerization reactions have been previously observed[12] in transfer hydrogenation reactions catalyzed by Pd/C. Previous results have been reported[13] on the hydrogenolysis of the C-O bond of 1-tetrazolyl ethers of phenols with Pd as catalyst which demonstrate that direct transfer of hydrogen from the methyl groups of toluene seems to occur, and that formic acid, used as donor, is just required to maintain a supply of hydrogen to the active site. A similar process would explain our preliminary results. The scope and synthetic utility of this reaction are presently under investigation.

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