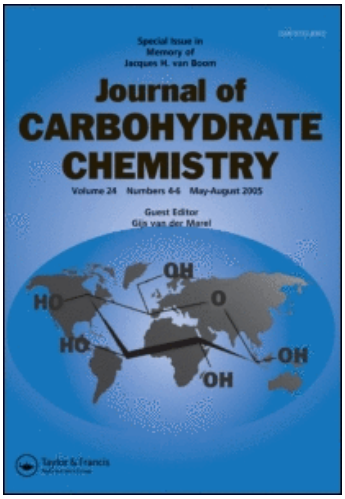

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Potassium Cyanide as Catalyst for Deesterification of Acid- and Base-Sensitive D-Galactopyranosides

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POTASSIUM CYANIDE AS CATALYST FOR DEESTERIFICATION OF ACID- AND BASE-SENSITIVE D-GALACTOPYRANOSIDES

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ABSTRACT

β-D-Galactopyranosides which suffered galactosidic bond cleavage upon treatment with bases that are normally used for deesterification, were successfully deesterified with KCN in 95% ethanol. Also α-D-galactopyranosides bearing acid- or base-sensitive substituents were deesterified using the same reagent without damage to those substituents.

INTRODUCTION

Esters like acetates and benzoates are often used to protect hydroxyl groups of monosaccharides in oligosaccharide syntheses, especially in synthesis of β-D-glycosides which require an ester on C-2 as a neighboring participating group. Traditionally esters are removed by transesterification methods that employ strong bas-

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es, usually metal alkoxides. These conditions sometimes eliminate needed protecting groups and have also been observed to cleave some β-D-galactopyranosidic bonds.

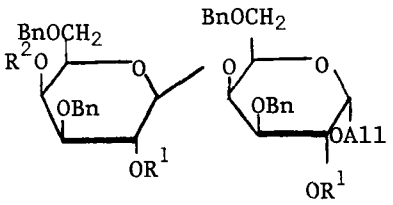
In previous publications from our laboratory, it was reported that O-debenzoylation of a β-D-(1→6)-linked galactotetrasaccharide[1] and a β-D-(1→2)-linked galactotrisaccharide[2] with sodium methoxide in methanol produced almost no yield of the O-debenzoylated oligosaccharides because of the cleavage of the glycosidic bond. The above oligosaccharides were O-debenzoylated with $Ba(OMe)_2$ in methanol giving 87% yield of the O-debenzoylated tetrasaccharide and 50% yield of the O-debenzoylated trisaccharide. On the other hand a β-D-(1→6)-linked galactotrisaccharide was O-debenzoylated with sodium methoxide in methanol without observable degradation.[3] In this publication a more general deesterification method that can be used with acid- or base-sensitive glycosides is presented.

RESULTS AND DISCUSSION

We are now involved in the synthesis of oligosaccharides having β-D-galactopyranoside units, and we have prepared allyl 4-O-(4-O-acetyl-2-O-benzoyl-3,6-di-O-benzyl-β-D-galactopyranosyl)-2-O-benzoyl-3,6-di-O-benzyl-α-D-galactopyranoside (1) and allyl 2-O-benzoyl-4-O-(2-O-benzoyl-3,6-di-O-benzyl-4-O-chloroacetyl-β-D-galactopyranosyl)-3,6-di-O-benzyl-α-D-galactopyranoside (2) in reasonably good yield and with complete stereoselectivity.[4] We have tried the common deesterification methods using dilute solu-

tions of $Mg(OMe)_2$, NaOMe or $Ba(OMe)_2$ in methanol at room temperature to remove the ester groups from compounds 1 and 2. The reaction was followed by thin layer chromatography (TLC) using ethyl acetate-hexanes mixtures (1:1) as eluant. Slow-moving and stationary spots were observed after adding the base. After all the starting material was consumed, the products were separated by silica gel high pressure liquid chromatography (HPLC) using a mixture of ethyl acetate-hexanes (1:1). Only 20% of the products were disaccharides, while 80% had suffered galactosidic bond cleavage when $Ba(OMe)_2$ was used. Among the products, we were able to identify allyl 3,6-di-O-benzyl-α-D-galactopyranoside (3). The ^1H NMR spectrum of 3 matched that of an authentic sample obtained by O-debenzoylation of allyl 2-O-benzoyl-3,6-di-O-benzyl-α-D-galactopyranoside (4) under the same conditions. Structure of 3 was confirmed by its ^{13}C NMR (assigned in relation to recently reported chemical shift values[5]) which showed no signals for carbonyl carbons but showed signals for both the allyl and benzyl groups, and a downfield shift of both C-1 and C-3 compared to C-1 and C-3 of 4 as a result of elimination of the benzoyl group from C-2. Compound 3 can be formed from 1 only as a result of β-D-galactosidic bond cleavage. We also tried other milder basic conditions using ethylamine, diethylamine, and triethylamine solutions in aqueous ethanol, but a slow degradation occurred and the β-D-galactosidic bond was broken even before the benzoate was removed. This was confirmed by the separation and identification of allyl 2-O-benzoyl-3,6-di-O-benzyl-α-D-galactopyranoside (4) which

was indistinguishable from a synthetic sample.[4] Resistance of the benzoate group to these conditions in a related series has been observed before.[2]



1 R^1 = Bz, R^2 = Ac

2 R^1 = Bz, R^2 = ClAc

5 R^1 = H, R^2 = H

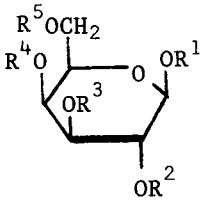
6 R^1 = Bz, R^2 = H

These results indicate that β-D-galactopyranosides have different sensitivities toward bases, and in our hands β-D-(1→4) galactopyranosides are the most sensitive. Birch et al.[6] reported KCN in 95% ethanol to be a good transesterification catalyst. They proposed that the reaction presumably occurs through an acyl cyanide intermediate, which reacts with the large excess of ethanol present.

$$RCO_2Me \rightleftharpoons RCOCN \rightleftharpoons RCO_2Et$$

Later Mori et al. used KCN to deesterify α,β-conjugated esters with minimum cis-trans isomerization of the double bonds[7] and also to deesterify a compound having an acetal linkage.[8] More recently Hanessian et al. used the same reagent to deesterify a carbohydrate derivative.[9] Deesterification of disaccharides 1 and 2

using the same reaagent gave the triol 5 (67% yield) and the partially deesterified disaccharide 6 (11% yield). The ^{1}H NMR spectrum of compound 5 showed no signals for the benzoyl group, but showed two anomeric protons; H-1, α as doublet at δ4.95, $J_{1,2}$ = 4 Hz and H-1', β as doublet at δ 4.26, $J_{1,2}$ = 8 Hz. The β-D-galactopyranosides 7, 8, and 9 were also debenzoylated with KCN in 95% ethanol in quantitative yield.



7 R^1 = Bn, R^2 = Bz, R^3 = H, R^4, R^5 = PhCH

8 R^1 = Me, R^2 = Bz, R^3 = R^4 = Bn, R^5 =H

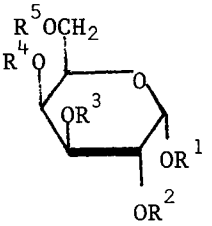
9 R^1 = All, R^2 = Bz R^3 = R^4 = Bn, R^5 = H

10 R^1 = Bn, R^2 = R^3 = H, R^4, R^5 = PhCH

11 R^1 = Me, R^2 = R^5 = H, R^3 = R^4 = Bn

12 R^1 = All, R^2 = R^5 = H, R^3 = R^4 = Bn

The same deesterification method was applied to a number of α-D-galactopyranosides which have different ester groups as well as other protecting groups located at different positions. The purpose was to test the efficiency of the reagent in removing different esters from different positions and also to determine the stability of the acid- and base-sensitive groups.



13 R^1 = All, R^2 = R^3 = R^5 = Bz, R^4 = H

14 R^1 = All, R^2 = R^3 = R^4 = Ac, R^5 = Bn

15 R^1 = All, R^2 = R^3 = R^4 = Bz, R^5 = Bn

16 R^1 = All, R^2 = R^3 = R^5 = Bz, R^4 = Ac

17 R^1 = All, R^2 = Bz, R^3 = R^5 = Bn, R^4 = Ac

18 R^1 = All, R^2 = Bz, R^3 = R^5 = Bn, R^4 = ClAc

19 R^1 = All, R^3, R^4 = i-Prop, R^2 = Bz, R^5 = Bn

20 R^1 = All, R^2 = R^3 = R^4 = R^5 = H

21 R^1 = All, R^2 = R^3 = R^4 = H, R^5 = Bn

22 R^1 = All, R^2 = R^4 = H, R^3 = R^5 = Bn

23 R^1 = All, R^2 = H, R^3, R^4 = i-Prop, R^5 = Bn

24 R^1 = Me, R^2 = R^5 = Ac, R^3, R^4 = i-Prop

25 R^1 = Me, R^2 = R^5 = Tosyl, R^3 = R^4 = Ac

26 R^1 = Me, R^2 = R^5 = Tosyl, R^3, R^4 = i-Prop

27 R^1 = Me, R^2 = R^5 = H, R^3, R^4 = i-Prop

28 R^1 = Me, R^2 = Tosyl, R^3, R^5 = Anh

Ac = acetyl, All = allyl, Anh = anhydro, Bz = benzoyl, Bn = benzyl, ClAc = chloroacetyl, i-Prop = isopropylidene, Me = methyl, and Tosyl = p-tolylsulfonyl.

The following transformations took place in 8 to 12 h, usually in quantitative, in all cases in better than 90% yield: 7 → 10; 8

→ 11; 9 → 12; 13 → 20; 14 → 21; 15 → 21; 16 → 20; 17 → 22; 18 → 22; 19 → 23; 24 → 27; 25 → 28; 26 → 26.

We conclude that KCN in 95% ethanol is a more general deesterifying reagent that can be applied to base-sensitive D-galactopyranosides and probably to acid-sensitive D-galactopyranosides like 2-acetamido-2-deoxy-β-D-galactopyranosides.[10] Both acid-sensitive groups like the isopropylidene group and base-sensitive groups like the tosyl group, which was lost upon treatment of 26 with a catalytic amount of NaOMe in methanol overnight, were stable under the reaction conditions.

EXPERIMENTAL

General. Instrumental and chromatographic procedures were the same as described previously.[1]

Attempted deesterification of allyl 4-O-(4-acetyl-2-O-benzoyl-3,6-di-O-benzyl-β-D-galactopyranosyl)-2-O-benzoyl-3,6-di-O-benzyl-α-D-galactopyranoside (1).

A- Using $Mg(OMe)_2$- A solution of 1 (100 mg) in absolute methanol (15 mL) was cooled to 0 ° and treated with 1 mL of M $Mg(OMe)_2$ solution. The reaction was followed by TLC using a 1:1 mixture of ethyl acetate - hexanes. The starting material remained unchanged during the first 6 h. After 12 h four spots in addition to the starting material spot were observed: a slightly dark stationary spot, indicating a highly polar decomposition product, followed by three spots at R_f = 0.25, 0.13, and 0.08, which correspond to par-

tially deesterified intermediates. After 24 h, the starting material spot and the spot at R_f = 0.25 became less intense, while the stationary spot increased in intensity. After 48 h, only the stationary spot was detected, indicating complete decomposition of the disaccharide.

B- Using $Ba(OMe)_2$- The reaction was carried out as described for $Mg(OMe)_2$. The TLC showed that after 72 h most of the starting material was consumed, and two moving spots in addition to a stationary one were formed. The solvent was evaporated under vacuum, the products were extracted in chloroform, the chloroform layer was washed with water, and dried over anhydrous magnesium sulfate. After the chloroform was evaporated, the products were isolated on silica gel HPLC using 1:1 mixture of ethyl acetate-hexanes. Three fractions were isolated. The first was the starting material, and the second fast-moving fraction was allyl 3,6-di-O-benzyl-α-D-galactopyranoside (3); ^{1}H NMR ($CDCl_3$): δ 7.3 (s, 10 H, $CH_2C_6H_5$), 6.33-5.63 (m, 1 H, CH=), 4.98 (d, 1 H, $J_{1,2}$ = 4.8 Hz, H-1), 4.72 (s, 2H, $CH_2C_6H_5$), 4.65 (s, 2 H, $CH_2C_6H_5$), 2.32 (bs, 2 H, 2 OH D_2O exchangeable). ^{13}C NMR ($CDCl_3$), p.p.m. 138.4 (CH=); 134.0, 128.8, 128.7, 128.1, 127.9 ($C_6H_5CH_2$); 118.0 (CH_2=); 98.0 (C-1); 78.8 (C-3); 69.7 (C-4), 68.8 (C-6); 67.5 (C-2); and 73.8, 72.3, 69.7 ($CH_2C_6H_5$ and CH_2CH=). The third fraction was identified as allyl 3,6-di-O-benzyl-4-O-(3,6-di-O-benzyl-β-D-galactopyranosyl)-α-D-galactopyranoside (5). ^{1}H NMR ($CDCl_3$): δ 7.6-7.05 (2s, 20 H, 4 $CH_2C_6H_5$), 6.1-5.68 (m, 1 H, CH=), 5.4-5.08 (m, 2 H, CH_2=), 4.92 (d, 1 H, $J_{1,2}$ = 4Hz, H-1), 4.77 (m, 4H,

$2CH_2C_6H_5$), 4.45 (m, 4 H $2CH_2CH_{65}$), 3.25 (d, 1 H, $J_{1,2}$ = 8 Hz, H-1', β). Yield 20.7% $[\alpha]_D^{24}$ = +68° (c 1, $CHCl_3$).

Anal. Calcd for $C_{43}H_{50}O_{11}$: C, 69.52; H, 6.78. Found: C, 69.53; H, 6.99.

C- Using triethylamine.- A solution of the disaccharide 1 in 95% ethanol was treated with triethylamine and left at room temperature under nitrogen. After 36 h TLC showed no starting material, but showed a very intense stationary spot and a light spot slower moving than the starting material. The solvent was evaporated and the products were extracted in chloroform, washed with N HCl, water and dried over anhydrous magnesium sulfate. The chloroform was evaporated to leave a dark syrup which was partially soluble in 1:1 ethyl acetate-hexanes. The soluble part was purified using HPLC to give a compound identical to the synthetic allyl 2-O-benzoyl-3,6-di-O-benzyl-α-D-galactopyranoside,[4] $[\alpha]_D^{24}$ = 117° (c, 1.2, $CHCl_3$), ^1H NMR ($CDCl_3$): δ 8.14-8.0 (m, 2 H, COC_6H_5, o), 7.61-7.22 (m, 13 H, 2 $CH_2C_6H_5$, COC_6H_5, m.p.), 6.1-5.0 (m, 5 H, CH=, H-1, and H-2), 4.2 (s, 2H, $CH_2C_6H_5$), 4.1 (s, 2H, $CH_2C_6H_5$) 2.3 (bs, 1 H, OH, D_2O exchangeable).

D- Using KCN in 95% aqueous ethanol.- A solution of the disaccharide 1 (90 mg) in 30 mL of 2% KCN solution in 95% aqueous ethanol was heated in a thermostated water-bath at 55 °C for 12 h. The ethanol was then removed under vacuum, the products were extracted in chloroform (3 x 100 mL) and washed with water. The chloroform layer was dried over anhydrous magnesium sulfate and evaporated under vacuum. The products were separated on silica gel HPLC

using 1:1 mixture of ethyl acetate-hexanes as eluent. Two main fractions were separated, the fast moving fraction was identified as allyl 2-O-benzoyl-4-O-(2-O-benzoyl-3,6-di-O-benzyl-β-D-galactopyranosyl)-3,6-di-O-benzyl-α-D-galactopyranoside (6) (14 mg, 11%). ^{1}H NMR of 6 showed no acetyl peak, but showed two benzoyl groups: δ8.1 (4H, $2COC_6H_5$, o). The second fraction was the desired allyl 3,6-di-O-benzyl-4-O-(3,6-di-O-benzyl-β-D-galactopyranosyl)-α-D-galactopyranoside (5) (35 mg, 67%).

The same procedure was followed for the deesterification of all other compounds listed above.

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REFERENCES

1. V. K. Srivastava and C. Schuerch, Carbohydr. Res. 106, 217 (1982).

2. R. Eby and C. Schuerch, Carbohydr. Res., 92, 149 (1981).

3. V. K. Srivastava, S. J. Sondheimer, and C. Schuerch, Carbohydr. Res., 36, 203 (1980).

4. H. A. El-Shenawy and C. Schuerch, Carbohydr. Res., 131, 227, 239 (1984).

5. K. Bock and C. Pedersen, Adv. Carbohydr. Chem. Biochem., 41, 27 (1983).

6. A. J. Birch, J. E. T. Connie, P. L. McDonald, and G. Subba Rao, J. Chem. Soc., Perkin Trans. I, 1186 (1972).

7. K. Mori and M. Sasaki, Tetrahedron Lett., 1329 (1979).

8. K. Mori, and M. Toominaga, T. Takigawa, and M. Matsui, Synthesis, 740 (1973).

9. S. Hanessian, J. R. Pougny and J. K. Boessenkool, J. Am. Chem. Soc., 104, 6164 (1982).

10. H. J. Jennings and C. Lugowski, Can. J. Chem., 58, 2610 (1980).