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Vitamin B_{12} and BF_3-etherate as catalysts in synthesis of some C_4-C_{12}-alkyl β-D-xylopyranosides

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Two methods are presented for synthesis of some C_4-C_{12}-alkyl β-D-xylopyranosides. The first method is the vitamin B_{12}-catalyzed reaction of glycosylation of acetobromoxylose with alkanols (ROH) (C_4-C_{12}). The reaction is carried out with 2 mol% of vitamin B_{12}, with respect to xylosyl bromide**,** under argon at room temperature. Under these conditions peracetylated C_4-C_{12}-alkyl β-D-xylopyranosides are obtained. Following chromatographic purification these products are de-esterified with a mixture of methanol-triethylamine-water (2:1:1) to give corresponding alkyl β-D-xylopyranosides in 50-60% yield. In all cases 3,4-di-O-acetyl- D-xylal is obtained, as the product of reductive elimination of peracetylated xylosyl bromide (15-25%). The second method is synthesis of C_4-C_{12}-alkyl β- D-xylopyranosides performed by glycosylation of corresponding alkanols with tetra-O-acetyl β- D-xylopyranose in the presence of BF_3-etherate, as a Lewis acid catalyst. This glycosylation proceeds in only moderate yield (45-55%), but simplicity of this method and avoidance of expensive heavy metal catalysts make such procedure attractive.

Keywords: Xylopyranosides, vitamin B_{12}, glycosylation, cyanocobalamin

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Cyanocob(III)alamin (vitamin B_{12}) is a complex compound active in human beings which is named "pigment of life". Intracellular vitamin B_{12} can be converted to the two coenzyme forms namely, methylcobalamin and 5′-deoxyadenosylcobalamin and promoted a series of biochemical transformations *in vivo*; these coenzymes are essential for cell growth and replication[1,2]. Cyanocob(III)alamin is also chiral and non-toxic reagent in organic chemistry which has been used as catalyst for various types of reactions[3,4]. The catalytically active species in these reactions is cob(I)alamin obtained by electrochemical or chemical reduction (with activated Zn dust or with $NaBH_4$) of vitamin B_{12} [Co(III) to Co(I)]. The cob(I)alamin, obtained in this way, is a very powerful nucleophile[5] and reacts rapidly with alkyl or alkenyl halides to form organocob(III)alamins (from kinetic studies Schrauzer and Deutch[6] concluded that the rate law corresponds to an S_N2 type substitution at carbon). Finally, cleavage of the Co-C bond of this intermediate affords products of the following reactions: reductive C-C bond formation, reductive elimination, hydrogenation, oxidation and substitution[7,8] independent of the structure of the substrates and reaction conditions (**Figure 1**).

Results and Discussion

In recent years we have studied the reactions of organic halides catalyzed by organocob(III)alamin (vitamin B_{12})[10-12] and reactions like glycosylation of xylose peracetate[13]. In continuation of this investigation the behaviour of brominated β-D-xylose peracetate in the B_{12}-catalyzed reaction of glycosylation has been examined. Reactions of glycosylation of mono- or disaccharides are particularly interesting in synthesis of biodegradable surfactants, detergents and emulsifiers[9].

The reaction was started with 2 mol% of vitamin B_{12}, with respect to xylosyl bromide **1**, and with $NaBH_4$, as a reducing agent. Then xylosyl bromide, dissolved in the corresponding alkanol (ROH) **3**, was added to the reaction mixture under argon atmosphere at room temperature. The mechanism of this reaction[14,15] proceeds *via* a xylosecob(III)alamin intermediate **2** which with alkanols (ROH) **3a-h** (C_4-C_{12}) gave peracetylated alkyl β-D-xylopyrano-

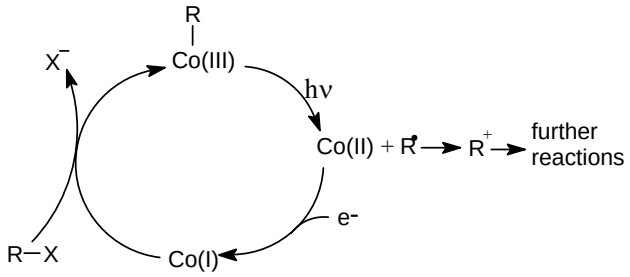


Figure 1

sides **4a-h**. Products **4a-h** were isolated by flash chromatography (yield 55-70%) and characterized by spectroscopic methods. Their ^1H and ^{13}C NMR spectral data were in agreement with structures assigned in previous work[13]. After de-esterification of **4a-h**, alkyl β-D-xylopyranosides **6a-h** were obtained in 50-60% yied (**Table I**). In all the cases 3,4-di-O-acetyl-D-xylal **5** was obtained (15-25%) as the product of reductive elimination of peracetylated-xylosyl bromide (**Scheme I**). ^1H NMR characteristics of **5** were identical with those of a commercial sample.

Vitamin B_{12}-catalyzed conversion of xylosyl bromide to alkyl β-D-xylopyranosides, described herein, illustrates that cob(I)alamin is a very strong nucleophile and cyanocob(III)alamin is powerful, natural and non-toxic catalyst which is now applied in complex carbohydrate chemistry.

For activation with a Lewis acid, exclusively the β-D-xylose tetraacetate **7** is required. The reaction with alkanols, ROH (C_4-C_{12}) **3a-h** and BF_3-etherate, as a Lewis acid, gives corresponding *trans*-linked alkyl xylosides **4β**. Namely, under these conditions the presence of BF_3-etherate leads to the formation of 1,2-acetoxonium intermediate[13] **8**. Addition of alcohol (ROH) at room temperature under anhydrous conditions gives *trans*-linked xylosides **4β**, as in previous reaction with $SnCl_4$ (ref. 13). The formation of the β-products **4** is kinetically controlled. Extension of reaction period leads to increasing proportions of the α-xylosides **4α** due to anomerization. The acetylated alcohols (ROAc) are formed as side products in this reaction.

Following chromatographic purification the peracetylated products **4β** are de-esterified with sodium methoxide in anhydrous methanol (40 mL) under reflux and subsequently neutralized with ion-exchange resin (Amberlite IR 120 H^+) to give alkyl β-D-xylosides **6a-h** in moderate yield (45-55%) (**Scheme II)**.

Table I — Vitamin B_{12} and BF_3-etherate as catalysts in synthesis of some C_4-C_{12}-alkyl β-D-xylopyranosides **6a-h**

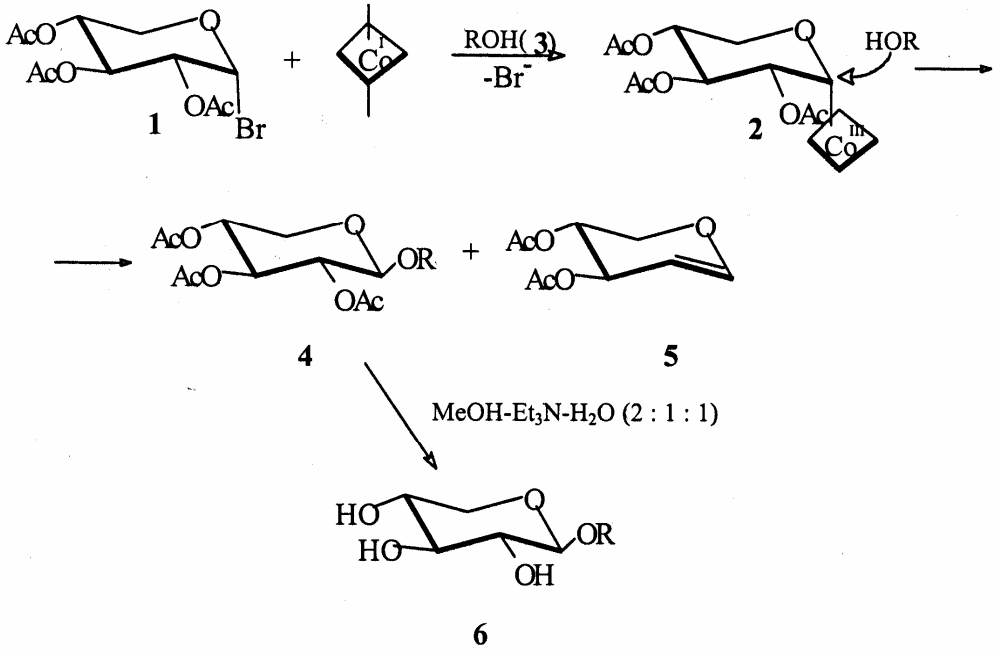
ROH (**3**)	R	Products[a]	
3a	$CH_3(CH_2)_3$	**4a**	**6a**
3b	$CH_3(CH_2)_6$	**4b**	**6b**
3c	$CH_3(CH_2)_7$	**4c**	**6c**
3d	$CH_3(CH_2)_3CH(C_2H_5)CH_3$	**4d**	**6d**
3e	$CH_3(CH_2)_8$	**4e**	**6e**
3f	$CH_3(CH_2)_9$	**4f**	**6f**
3g	$CH_3(CH_2)_{10}$	**4g**	**6g**
3h	$CH_3(CH_2)_{11}$	**4h**	**6h**

[a]Structures were determined on the basis of ^1H NMR and ^{13}C NMR spectral data[13]

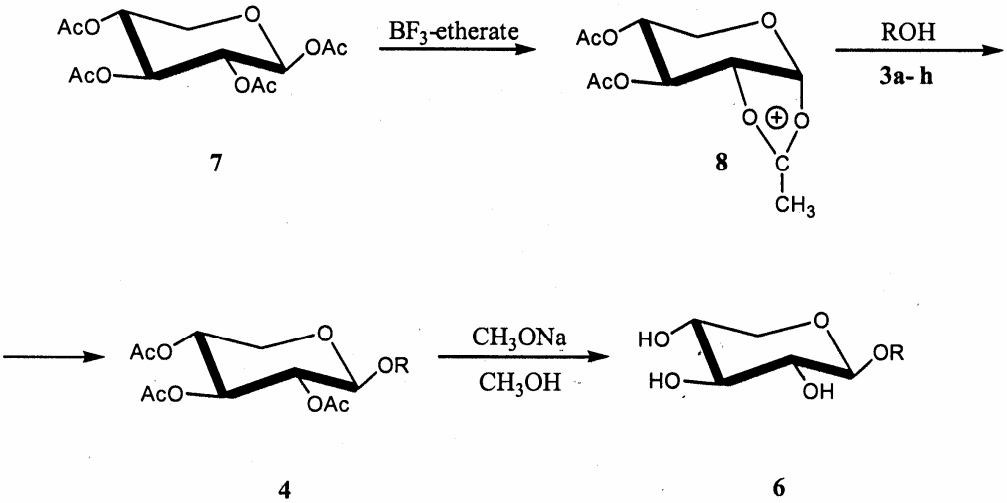
Experimental Section

Flash column chromatography was carried out on Merc silica gel (particle size 0.04-0.06 mm) using dichloromethane and ethyl acetate as eluents. TLC was performed on Merck TLC aluminium sheets of silica gel 60 F_{254}. Spots were visualized by spraying with 10% sulfuric acid in ethanol (carbohydrates) and with 1% anisaldehyde and 2% sulfuric acid in glacial acetic acid (non-carbohydrate compounds), respectively, and subsequent heating. ^1H and ^{13}C NMR spectra were run on a Varian Gemini 200 (200 MHz) or Bruker AC 250 (250 MHz) spectrometer in $CDCl_3$ with TMS as internal standard (chemical shifts in δ, mol ppm) All solvents were purified by distillation.

General procedure for preparation of alkyl xylosides catalyzed by vitamin B_{12}. A 100 mL flask, containing 20 mL of alkanol (ROH) **3** (C_4-C_{12}; **3a-h**), equipped with a magnetic stirrer bar under Ar, was charged with 0.16 g (0.12 mmole) of vitamin B_{12} and 0.09 g (2.4 mmole) of $NaBH_4$. After stirring for 30 min, the colour changed from red to dark green which indicates that Co(III) from vitamin B_{12} is reduced to Co(I). Then tri-O-acetyl-D-xylopyranosyl bromide **1** (2.58 g, 8 mmoles) (freshly prepared from peracetylated xylose **7** with hydrobromic acid in glacial acetic acid[16,17]) dissolved in 5 mL of alkanol (ROH), was added to this mixture. The colour immediately changed to red [xylose-Co(III)]. After stirring for 20 hr at room temperature, the dark red mixture was washed with cold saturated solution of NaCl and extracted with dichloromethane (3×25 mL). The combined organic phases were washed twice with water (2×25 mL), filtered over celite and evaporated



Scheme I



Scheme II

in vacuo. Most of the unreacted alkanol was removed by repeated evaporations of the syrup at 70°C on an oil pump in vacuum. The resulting syrup was purified by dry column chromatograhy (silica gel 60 (Merck) and dichloromethane-ethyl acetate (4:1) to give the products **4a-h** in the yield ranging from 55-70% (based on the peracetylated β-D-xylose) which were characterized by spectroscopic methods. In all the cases 3,4-di-O-acetyl-D-xylal **5** was obtained as the minor product (15-25%) as a result of reductive elimination of peracetylated xylosyl bromide **1**. Following chromatographic purification the peracetylated products **4a-h** were de-esterified with a mixture of methanol-triethylamine-water (2:1:1) to give alkyl β-D-xylopyranosides **6a-h** in 50-60% yield.

General procedure for preparation of alkyl xylosides in the presence of BF_3-etherate. A solution of β-D-xylose tetraacetate (0.64 g, 2.01 mmoles) in anhydrous dichloromethane (20 mL) was stirred for 1-2 hr with molecular sieves (0.4 nm, 1-2 g) at room temperature and under argon atmosphere. The solution was treated with boron trifluoride etherate (4-20 mmoles) and then with the alcohol **3** (4-10 mmoles) dissolved in anhydrous dichloromethane (20 mL); the preparation of β-xylosides **4** required 2-3 days. Then the mixture was poured into saturated

$NaHCO_3$ solution (50 mL), the organic layer was separated and aqueous phase was extracted with dichloromethane (3×40 mL). The combined organic phases were washed twice with water (2×40 mL), filtered over Celite and evaporated *in vacuo*. Most of the unreacted alkanol was removed by repeated evaporations of the syrup at 70°C on an oil pump vacuum. Flash chromatography (toluene-ethyl acetate) of the resulting syrups afforded **4β** (yield 50-65%), which were characterized by spectroscopic methods. The acetylated alcohol was also isolated from the reaction mixture.

The resulting materials **4β** were deacetylated by treatment with sodium methoxide in anhydrous methanol (40 mL) under reflux and subsequently neutralized with ion-exchange resin (Amberlite IR 120 H^+) to give alkyl β-xylosides **6a-h** in 45-55% yield.

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