Carbohydrate Research, 243 (1993) 177–181
Elsevier Science Publishers B.V., Amsterdam

Note

Synthesis of some sugar cobaloximes and a trifluoroacetic acid-induced fragmentation

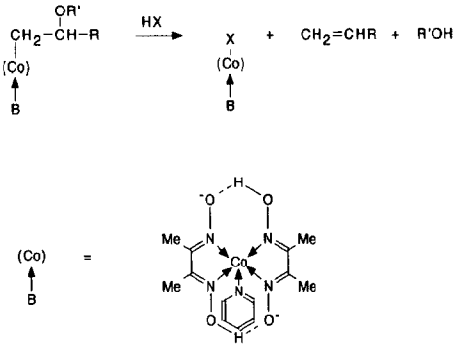
Rosaleen J. Anderson [1], Bernard T. Golding and Neil A. Hughes *

Department of Chemistry, Bedson Building, The University, Newcastle upon Tyne NE1 7RU (United Kingdom)

(Received August 5th, 1992; accepted November 2nd, 1992)

Since 2-alkoxy- or 2-hydroxy-alkyl(pyridine)cobaloximes are converted[1] into alkenes on treatment with acid (Scheme 1), sugar derivatives with a cobaloxime residue at the primary position have been synthesised and their responses to acid investigated in the context of a possible new route to terminal sugar alkenes.

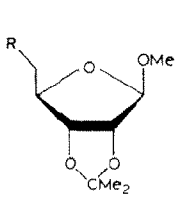
The sugar cobaloximes **2**, **4**, and **6** were synthesised from methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, and 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose by reaction of the derived primary iodides **1**[2], **3**[3], and **5**[4] with reduced (pyridine)cob(I)aloxime[5] by the sequence **9** → **10** → **11**. The D-*galacto* compound has been reported[6] as a hydrated form. Each cobaloxime was an orange solid, stable when stored in the dark, which gave



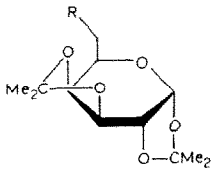
Scheme 1.

[1] Present address: School of Health Sciences, University of Sunderland, Sunderland SR2 7EE, United Kingdom.

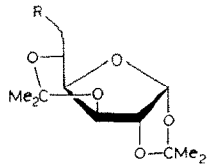
* Corresponding author.



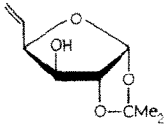
1 R = I
2 R = B-(Co)



3 R = I
4 R = B-(Co)



5 R = I
6 R = B-(Co)



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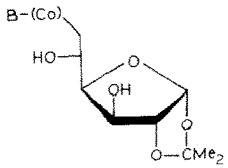

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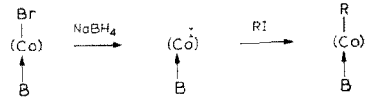

9 10 11

ions corresponding to $(M - \text{pyridine})^+$, $(M - \text{pyridine} - \text{sugar})^+$, and $(MH)^+$ in FABMS.

Treatment of **2** or **4** at room temperature with deuteriochloroform–trifluoroacetic acid resulted only in the release of ~5% of acetone after several days, presumably by hydrolysis of the isopropylidene acetal(s) by traces of water present in the solution, and no alkene was formed (NMR spectroscopy). By contrast, **6** reacted during several days to give ultimately 67% of the known[7] *gluco*-alkene **7**.

The failure of **2** and **4** to give olefins may lie in the fact that, rather than being part of alkoxy functions as in the earlier work, the oxygen atoms envisaged as taking part in the reaction are involved in acetal functions. Thus, O-4 in **2** and O-5 in **4** are part of stable furanoid and pyranoid ring systems, respectively. However, in **6**, O-5 is involved in a strained[8] 1,3-dioxane ring and reaction results in loss of this strain. Because of the strain, the 1,3-dioxane system in **6** may be hydrolysed rapidly by traces of water in the reaction medium and it is the resulting monoacetal **8** which reacts to give **7**. The latter process would be accompanied by the production of water (Scheme 1) which would enable complete hydrolysis of **6** to **7** to continue. Another consideration is that an antiperiplanar arrangement of the cobalt and the neighbouring oxygen undergoing elimination is necessary. Because of the bulk of the cobaloxime, this may be more difficult to achieve in **2**, **4**, and **6** than it is in **8** where there is less crowding in the vicinity of the cobaloxime residue.

In its present form, the method has very limited scope for the synthesis of sugar alkenes.

EXPERIMENTAL

General methods.—The melting points for cobaloximes **2**, **4**, and **6** are not given because they were variable owing to decomposition. NMR spectra were recorded at 200 MHz (^{1}H) and 50 MHz (^{13}C) for solutions in $CDCl_3$. Column chromatography was performed on Kieselgel (Merck, 7734), using 96:3:1 CH_2Cl_2–MeOH–pyr for the sugar cobaloximes.

Methyl 5-deoxy-2,3-O-isopropylidene-β-D-ribofuranos-5-yl(pyridine)cobaloxime (**2**).—A suspension of bromo(pyridine)cobaloxime (0.49 g, 1.1 mmol) in EtOH (40 mL) was degassed and flushed with N_2 for 30 min. A suspension of $NaBH_4$ (0.13 g, 3.3 mmol) in EtOH (2 mL) was added during 2 min and the mixture was stirred until a dark blue-green solution was obtained (1 h). A solution of methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside[2] (**1**; 0.37 g, 1.2 mmol) in EtOH (2 mL) was added, the mixture was stirred under N_2 in the dark for 2 h, then aerated for 30 min, and the solvent was evaporated. The residue was purified by column chromatography on silica gel (50 g). Removal of solvent and exposure to high vacuum, to remove traces of pyridine, left **2** as orange crystals (0.45 g, 70%); $[\alpha]_D$ −45° (*c* 1, MeOH). NMR data: ^{1}H, δ 8.56 (d, 2 H, α-pyr), 7.73 (t, 1 H, γ-pyr), 7.32 (t, 2 H, β-pyr), 4.74 (s, 1 H, H-1), 4.48 (d, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.26 (d, H-3), 3.57 (dd, 1 H, $J_{4,5a}$ 4.0, $J_{4,5b}$ 10.4 Hz, H-4), 3.25 (s, 3 H, OMe), 2.14 (s, 6 H, dmgH), 2.13 (s, 6 H, dmgH), 1.68 (dd, 1 H, $J_{5a,5b}$ 9.1 Hz, H-5a), 1.43 (t, 1 H, H-5b), 1.41 (s, 3 H, Me), and 1.27 (s, 3 H, Me); ^{13}C, δ 149.8 (s, C=N), 149.7 (s, C=N), 149.6 (d, α-pyr), 137.6 (d, γ-pyr), 125.1 (d, β-pyr), 111.2 (s, CMe_2), 108.9 (d, C-1), 89.3, 85.9, 84.4 (3 d, C-2,3,4), 54.3 (q, OMe), 27.7 (bt, C-5), 26.5, 25.0 (2 q, CMe_2), 11.9 and 11.8 (2 q, dmgMe) (Found: C, 47.40; H, 5.92; N, 12.37. $C_{22}H_{34}CoN_5O_8$ calcd: C, 47.57; H, 6.17; N, 12.61%).

6-Deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl(pyridine)cobaloxime (**4**).—6-Deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[3] (**3**; 0.39 g, 1.0 mmol) was allowed to react with reduced bromo(pyridine)cobaloxime (1.01 g, 2.3 mmol) using the above procedure except that, after bubbling air through the solution and removing the solvent, water was added and the product was extracted into CH_2Cl_2. Removal of the solvent and column chromatography gave **4** as deep-orange crystals (0.34 g, 53%), $[\alpha]_D$ −164° (*c* 0.99, MeOH). NMR data: ^{1}H, δ 8.53 (d, 2 H, α-pyr), 7.67 (t, 1 H, γ-pyr), 7.25 (t, 2 H, β-pyr), 5.29 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 4.39 (dd, 1 H, $J_{2,3}$ 2.2, $J_{3,4}$ 7.9 Hz, H-3), 4.11 (dd, 1 H, H-2), 3.99 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 3.41 (dt, 1 H, $J_{5,6a}$ 5.8, $J_{5,6b}$ 6.3 Hz, H-5), 2.07 (s, 6 H, dmgH), 2.06 (s, 6 H, dmgH), 1.81 (dd, 1 H, $J_{6a,6b}$ 9.5 Hz, H-6a), 1.54 (s, 3 H, Me), 1.43 (dd, 1 H, H-6b), 1.33 (s, 3 H, Me), and 1.23 (s, 6 H, 2 Me); ^{13}C, δ 150.3 (s, C=N), 150.0 (d, α-pyr), 137.5 (d, γ-pyr), 125.2 (d, β-pyr), 108.3 (s, CMe_2), 107.8 (s, CMe_2), 96.6 (d, C-1), 73.6, 71.4, 70.5, 69.2 (4 d, C-2,3,4,5), 26.4, 26.3, 25.2, 24.9 (4 q, 2

CMe_2), 25.4 (bt, C-6), 12.2 and 12.1 (2 q, dmgMe) (Found: C, 48.72; H, 6.16; N, 11.38. $C_{25}H_{38}CoN_5O_9$ calcd: C, 49.10; H, 6.26; N, 11.45%).

6-Deoxy-1,2:3,5-di-O-isopropylidene-α-D-glucofuranos-6-yl(pyridine)cobaloxime (**6**).—6-Deoxy-6-iodo-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose[4] (**5**; 0.22 g, 0.6 mmol) and reduced bromo(pyridine)cobaloxime (0.47 g, 1.05 mmol) were reacted, as described in the previous experiment, to give **6** as an orange crystalline solid (0.29 g, 85%); $[\alpha]_D$ −52° (*c* 0.88, MeOH). NMR data: ^1H, δ 8.48 (d, 2 H, α-pyr), 7.66 (t, 1 H, γ-pyr), 7.24 (t, 2 H, β-pyr), 5.80 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1), 4.38 (d, 1 H, H-2), 3.97 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 3.85 (dd, 1 H, $J_{4,5}$ 5.6 Hz, H-4), 3.15 (dd, 1 H, $J_{5,6a}$ 4.4, $J_{5,6b}$ 6.8 Hz, H-5), 2.041 (s, 6 H, dmgH), 2.038 (s, 6 H, dmgH), 1.59 (m, 2 H, H-6a,6b), 1.38 (s, 3 H, Me), 1.25 (s, 3 H, Me), 1.20 (s, 3 H, Me), and 1.16 (s, 3 H, Me); ^{13}C, δ 149.9 (s, C=N), 149.8 (d, α-pyr), 137.5 (d, γ-pyr), 125.1 (d, β-pyr), 111.5 (s, CMe_2), 105.6 (d, C-1), 89.9 (s, CMe_2), 83.9, 83.8, 73.8, 73.6 (4 d, C-2,3,4,5), 30.4 (bt, C-6), 27.0, 26.5, 25.2, 24.9 (4 q, 2 CMe_2), 12.2 and 12.1 (2 q, dmgMe) (Found: C, 49.48; H, 6.32; N, 11.64. $C_{25}H_{38}CoN_5O_9$ calcd: C, 49.10; H, 6.26; N, 11.45%).

Acid-catalysed cleavage reactions.—Trifluoroacetic acid (8 μL, 0.1 mmol) was added to a degassed solution of the sugar cobaloxime (0.1 mmol) in $CDCl_3$ (0.6 mL) in an NMR tube. The tubes were kept at room temperature in the dark and any changes were followed by ^1H NMR spectroscopy.

With **2** and **4**, no change was observed after several days except for the appearance of a weak signal at δ 2.1 for acetone (~5%). The same signal appeared in the mixture containing **6**, but more strongly and accompanied by signals in the region δ 5.8–5.5. After 3 days, more trifluoroacetic acid (4 μL, 0.05 mmol) was added and, after a further day, the reaction was complete. Light petroleum was added, the mixture was filtered, and the solvent was evaporated. Column chromatography (1:1 EtOAc–light petroleum) of the residue gave 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose[7] (**7**; 13 mg, 67%), mp and mixture mp 60–62°C.

ACKNOWLEDGMENTS

We thank S.E.R.C. and British Petroleum for a CASE studentship (to R.J.A.). NMR spectra were recorded by Dr. N.M.S. Hill and Mr. I. McKeag, the mass measurements were determined by Mr. P. Kelly and Mr. S. Addison, and the microanalyses were performed by Mr. D. Dunbar.

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