Carbohydrate Research, 65 (1978) 139–143

Note

The preparation of aldonolactones and lactols by oxidation of aldoses with ruthenium(VIII) oxide

RICHARD H. HALL AND KARL BISCHOFBERGER
National Chemical Research Laboratory, South African Council for Scientific and Industrial Research, Pretoria 0001 (South Africa)

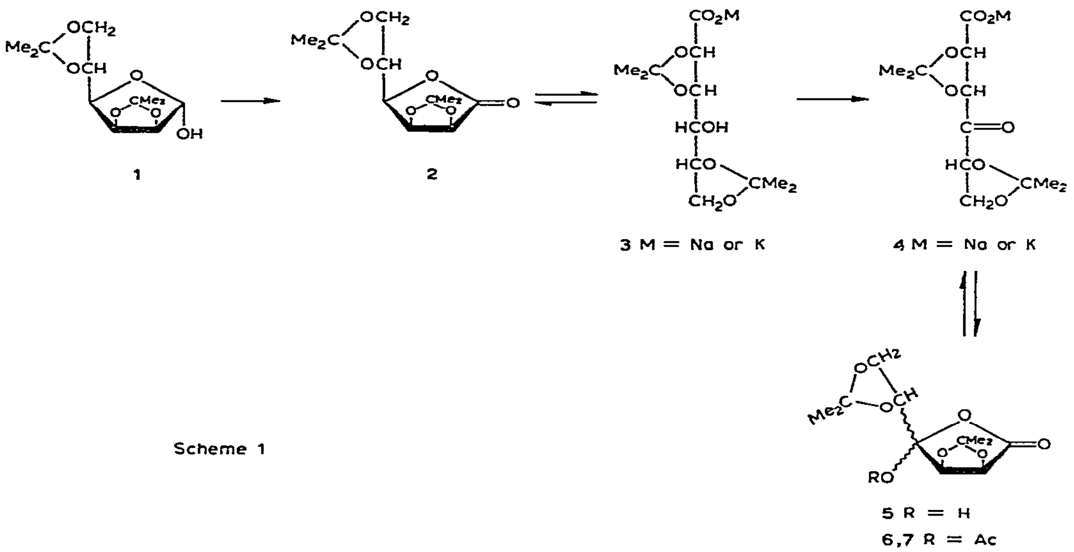
(Received July 19th, 1977; accepted for publication, September 25th, 1977)

Work in these laboratories required large amounts of 2,3:5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**2**) and 2,3:5,6-di-*O*-isopropylidene-D-allono-1,4-lactone (**9**). The most direct route to **2** and **9** is *via* acetonation of D-mannose and D-allose to give 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**1**) and 2,3:5,6-di-*O*-isopropylidene-β-D-allofuranose (**8**), respectively, followed by oxidation of the isolated hemiacetal groups of **1** and **8**. The conversion of **1** and **8** into **2** and **9**, respectively, has been effected by oxidations with dimethyl sulphoxide–acetic anhydride[1,2], silver carbonate on Celite[3], and alkaline permanganate (with subsequent lactonization)[4,5]. However none of these methods is entirely suitable for preparing **2** and **9** on a moderate scale; the dimethyl sulphoxide–acetic anhydride method is time-consuming and unpleasant[1,2,6], the silver carbonate-on-Celite method requires large amounts of oxidant and solvent[3,7], and the permanganate method is time-consuming and gives the products in only moderate yields[4,5]. Horton and Jewell[1] have shown that oxidation of **1** with dimethyl sulphoxide–acetic anhydride gives **2** in 96% yield, but no significant oxidation was effected with lead tetraacetate in pyridine, and use of the Pfitzner–Moffatt reagent[8] gives **2** in only low yield.

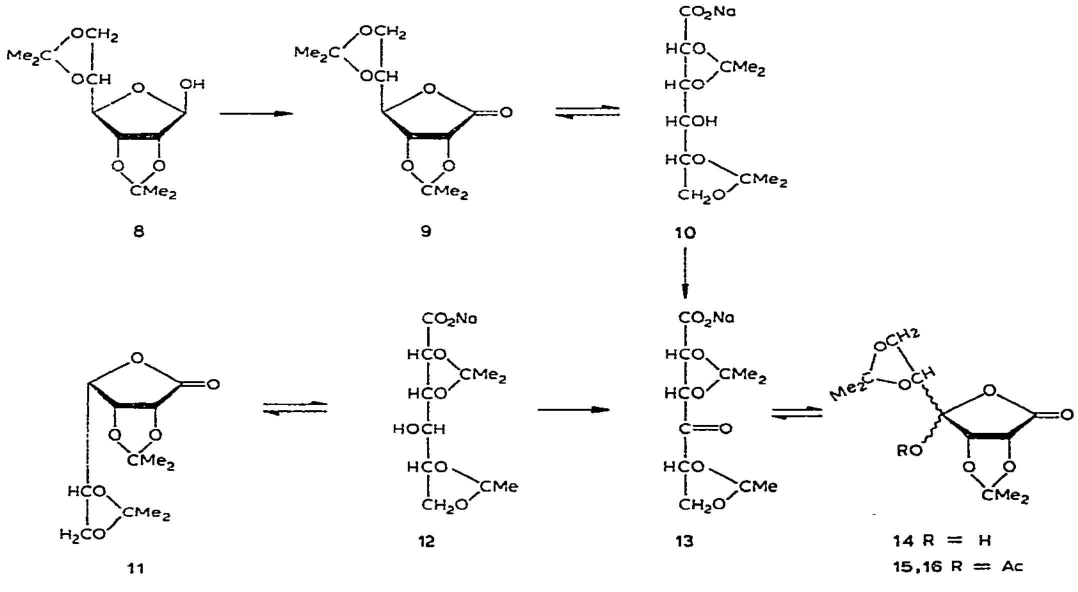
Ruthenium(VIII) oxide has proved an effective oxidant with many carbohydrate derivatives for the conversion of isolated secondary hydroxyl groups into carbonyl functions[9]. The method is amenable to preparations on a large scale[10] and is economical; the oxidant can be recovered [as ruthenium(IV) oxide] and, in many instances, catalytic amounts of the oxidant can be used. Surprisingly, oxidation of isolated hemiacetal groups of carbohydrate derivatives with ruthenium(VIII) oxide has not been reported. We therefore decided to investigate the reaction with **1** and **8**.

By a catalytic procedure, **1** and **8** (20 g of each) were converted into **2** (73%) and **9** (92%), respectively, during 1–1.5 h and, after several preparations, considerable stocks of **2** and **9** were quickly accumulated.

During the preparation of **2**, it was observed that a more-polar product was slowly being formed. The oxidation was repeated, but with the addition of a large excess of sodium metaperiodate for a period of 30 h; the reaction rate fell considerably after 1–1.5 h. During this time, small volumes of aqueous sodium hydrogencarbonate were added periodically to keep the mixture alkaline. Processing gave crystalline, 2,3:5,6-di-*O*-isopropylidene-D-*lyxo*-4-hexulosono-1,4-[(*R*) or (*S*)]-lactol (5) in 13% yield. Similar oxidation of **2** and potassium 2,3:5,6-di-*O*-isopropylidene-D-mannonate[4] [(3), *M* = *K*] during 15 h also gave **5** in 36 and 17% yield, respectively,



Scheme 1



Scheme 2

indicating that the oxidation pathway is as shown in Scheme 1. Compound **5** was readily identified by conventional spectral and analytical techniques, and its structure was confirmed by the formation of two mono-acetates (**6**) and (**7**) on acetylation, Compound **9** was over-oxidized during 40 h to give 2,3:5,6-di-*O*-isopropylidene-D-*ribo*-4-hexulosono-1,4-[(*R*) and (*S*)]-lactol (**14**) in 23% yield, and its C-4 epimer, 2,3:5,6-di-*O*-isopropylidene-D-gulono-1,4-lactone[11] (**11**), gave **14** in 52% yield during 15 h (Scheme 2). Again, the structure of **14** was confirmed by the preparation of two, mono-acetates (**15** and **16**).

The ease of conversion of **2**, **9**, and **11** into **5** and **14** must be determined by the accessibility of the C-4 hydroxyl groups of **3**, **10**, and **12** to the oxidizing agent. In every case, the yields of **5** and **14** were increased by acidifying the mixture before isolation, presumably by converting **4** and **13** into the free acids, which then form the lactols **5** and **14**, respectively.

The results indicate that, despite possible over-oxidation[12], oxidation with a catalytic amount of ruthenium (VIII) oxide is the method of choice for the preparation, on a moderate scale, of **2** and **9** from **1** and **8**, respectively.

EXPERIMENTAL

For general experimental procedures, see ref. 13.

*2,3:5,6-Di-O-isopropylidene-*D*-mannono-1,4-lactone* (**2**). — A freshly prepared, aqueous solution (350 ml) of sodium metaperiodate (26 g) was added to a vigorously stirred mixture of **1** (20 g) in carbon tetrachloride (200 ml), ethanol-free chloroform (30 ml), saturated aqueous sodium hydrogencarbonate (30 ml), and ruthenium dioxide (100 mg) at such a rate that the colour of the mixture rapidly alternated between yellow and black. The organic layer was periodically tested by t.l.c., with 4:1 chloroform–ethyl acetate as eluant, and, when all the starting material (**1**) had reacted (~1 h), propan-2-ol (10 drops) was added to the mixture. The mixture was then filtered through a thin pad of Celite, and the two layers were separated. The aqueous layer was saturated with sodium chloride, and extracted with chloroform (3 x 100 ml). The chloroform extracts were combined with the original organic layer, and the solution was washed with a saturated solution of sodium thiosulphate (100 ml), and finally dried (magnesium sulphate). Removal of the solvents *in vacuo* gave a solid that was recrystallized from ethyl acetate–hexane to give the lactone **2** (14.5 g, 73%), m.p. 125–126° (lit.[1,4] m.p. 126°).

*2,3:5,6-Di-O-isopropylidene-*D*-allono-1,4-lactone* (**9**). — Compound **8** (20 g) was similarly oxidized (~1.5 h) to give, after recrystallization from ethyl acetate–hexane, compound **9** (18.4 g, 92%), m.p. 71–72° (lit.[5,14] m.p. 72–73°, 72–74°).

*Preparation of 2,3:5,6-di-*O*-isopropylidene-*D-lyxo*-4-hexulosono-1,4*[(R) *or* (S)]-*lactol* (**5**). — (*a*) *From* **1**. Small aliquots of an aqueous solution (500 ml) of sodium metaperiodate (33 g) [fresh solutions (50 ml) were made up each time] were added during a total of 30 h (the unfinished reaction may be left overnight) to a mixture containing **1** (10 g) and made up as described for the preparation of **2**. Small volumes of saturated aqueous sodium hydrogencarbonate were added periodically to keep the mixture alkaline. After 30 h, the mixture was adjusted to pH 5 with acetic acid and processed, as described for the preparation of **2**, to give a solid. Recrystallization from ethyl acetate–hexane gave **5** (1.84 g, 13%), m.p. 94–96°, $[\alpha]^{20}_{D}$ +63°; ν_{max} 3535 (OH) and 1795 cm^{-1} (lactone); *m/e* 259 ($M^+ - CH_3$); n.m.r. data: τ 5.12 and 5.35 (2d, $J_{2,3}$ 6 Hz, H-2,3), 50 (br. s), disappeared on addition of D_2O, OH), ~5.83 (m, H-5,6,6′), and 8.48, 8.58, and 8.68 (3 s, 4 Me).

Anal. Calc. for $C_{12}H_{18}O_7$: C, 52.6; H, 6.6. Found: C, 52.8; H, 6.8.

(*b*) *From* **2**. Compound **2** (5.16 g) was similarly oxidized during 15 h (15 g of sodium metaperiodate) to give, after recrystallization, **5** (1.96 g, 36%), m.p. and mixed m.p. 94–96°.

(*c*) *From* **3** ($M = K$). Compound[4] **3** (M = K, as the monohydrate) (6.64 g) was similarly oxidized during 15 h (15 g of sodium metaperiodate) to give, after recrystallization, 920 mg (17 %) of **5**, m.p. and mixed m.p. 94–96°.

*Preparation of 2,3:5,6-di-O-isopropylidene-*D-ribo*-4-hexulosono-1,4-*[(R) *and* (S)]*-lactol* (**14**). — (*a*) *From* **9**. Compound **9** (5.16 g) was oxidized as described for **2** during 40 h (15 g of sodium metaperiodate) to give, after recrystallization from ethyl acetate–hexane, compound **14** (1.4 g, 23%), m.p. 96–99°; ν_{max} 3520 (OH) and 1795 cm^{-1} (lactone); *m/e* 299 ($M^+ - CH_3$); n.m.r. data: τ 5.09–6.10 (6-proton multiplet) and 8.48–8.64 (12-proton multiplet). The n.m.r. spectrum indicated that both 4-epimers were present.

Anal. Calc. for $C_{12}H_{18}O_7$: C, 52.6; H, 6.6. Found: C, 52.7; H, 6.8.

(*b*) *From* **11**. — Compound[11] **11** (5.16 g) was similarly oxidized during 15 h (15 g of sodium metaperiodate) to give, after recrystallization, compound **14** (3.1 g, 55%), m.p. 93–105°.

4-[(R) *or* (S)]*-O-Acetyl-2,3:5,6-di-O-isopropylidene-*D-lyxo*-4-hexulosono-1,4-*[(R) *or* (S)]*-lactol* (**6**) *and its 4-epimer* (**7**). — Compound **5** (500 mg) was acetylated conventionally with acetic anhydride in pyridine and processed to give an oil. Chromatography with 4:1 chloroform–ethyl acetate as eluant gave a solid that was recrystallized from ethyl acetate–hexane to give **6** (160 mg, 28%), m.p. 164–165°, $[\alpha]^{20}_{D}$ −3°; ν_{max} 1800 (lactone) and 1750 cm^{-1} (ester); *m/e* 301 ($M^+ - CH_3$); n.m.r. data: τ 4.89 and 5.15 (2d, $J_{2,3}$ 6 Hz, H-2,3), 5.15 (dd, $J_{5,6}$ 7.5 $J_{5,6'}$ 5.5 Hz, H-5), 5.84 (dd, $J_{6',6}$ 9, H-6′), 5.99 (dd, H-6), 7.88 (s, AcO), and 8.56, 8.61, 8.66, and 8.69 (4 s, 4Me).

Anal. Calc. for $C_{14}H_{20}O_8$: C, 53.2; H, 6.4. Found: C, 53.2; H, 6.3.

Further elution gave an oil (60 mg, 10%), ν_{max} 1805 (lactone) and 1750 cm^{-1} (ester); *m/e* 301 ($M^+ - CH_3$). This epimer decomposed rapidly to give a polar solid (t.l.c.).

Anal. Calc. for $C_{13}H_{17}O_8$: $M^+ - CH_3$, 301.092. Found: $M^+ - CH_3$, 301.093.

4-[(R) *or* (S)]*-O-Acetyl-2,3:5,6-di-O-isopropylidene-*D-ribo*-4-hexulosono-1,4-* [(R) *or* (S)]*-lactol* (**15**) *and its 4-epimer* (**16**). — Compound **14** (1 g) was acetylated conventionally with acetic anhydride in pyridine, and isolated as an oil. Chromatography with 4:1 chloroform–ethyl acetate as eluant gave a solid that was recrystallized from ethyl acetate–hexane to give **15** (286 mg, 25%) m.p. 81–82°, $[\alpha]^{20}_{D}$ −64°; ν_{max} 1800 (lactone) and 1750 cm^{-1} (ester); *m/e* 301 ($M^+ - CH_3$); n.m.r. data: 5.18–5.22 (m, H-2,3,5), 5.88–5.94 (m, H-6,6′), 7.88 (s, AcO), and 8.53. 8.55, 8.59, and 8.67 (4 s, 4 Me).

Anal. Calc. for $C_{14}H_{20}O_8$: C, 53.2; H, 6.4. Found: C, 53.2; H, 6.5.

Further elution gave an oil (60 mg, 5%), ν_{max} 1800 (lactone) and 1750 cm^{-1} (ester); *m/e* 301 ($M^+ - CH_3$). This epimer decomposed rapidly to give a polar solid (t.l.c.).

Anal. Calc. for $C_{13}H_{17}O_8$: $M^+ - CH_3$, 301.092. Found: $M^+ - CH_3$, 301.093.

REFERENCES

1 D. Horton and J. S. Jewell, *Carbohydr. Res.*, 2 (1966) 251–260.
2 M. Haga, M. Takano, and S. Tejima, *Carbohydr. Res.*, 14 (1970) 237–244.
3 S. Morgenlie, *Acta Chem. Scand.*, 26 (1972) 2518–2522.
4 H. Ohle and G. Berend, *Ber.*, 58 (1925) 2590–2592.
5 J. M. Ballard and B. E. Stacey, *Carbohydr. Res.*, 12 (1970) 37–41.
6 Cf. J. D. Stevens, *Methods Carbohydr. Chem.*, 6 (1972) 123–128.
7 M. Fétizon and M. Golfier, *C.R. Acad. Sci.*, 267 (1968) 900–903.
8 K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, 85 (1963) 3027–3028.
9 R. F. Butterworth and S. Hanessian, *Synthesis*, (1971) 70–88.
10 Cf. D. C. Baker, D. Horton, and C. C. Tindall, *Methods Carbohydr. Chem.*, 7 (1976) 3–6.
11 K. Iwadare, *Bull. Chem. Soc. Jpn.*, 18 (1943) 226–231.
12 Cf. R. F. Nutt, M. J. Dickinson, F. W. Holly, and E. Walton, *J. Org. Chem.*, 33 (1968) 1789–1795.
13 R. H. Hall, K. Bischofberger, S. J. Eitelman, and A. Jordaan, *J. Chem. Soc. Perkin Trans. 1*, (1977) 743–753.
14 B. D. Kohn, P. Kohn, and A. Dubin, *Carbohydr. Res.*, 18 (1971) 349–355.