Carbohydrate Research, 135 (1985) C17–C21
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

Higher-carbon sugars: on the stereochemistry of the oxidation of some unsaturated carbohydrate derivatives with osmium tetraoxide

JOHN S. BRIMACOMBE*, RODERICK HANNA, and (in part) FRANK BENNETT
Chemistry Department, Dundee University, Dundee DD1 4HN (Great Britain)
(Received October 12th, 1984; accepted for publication, October 22nd, 1984)

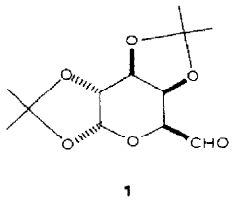
Traditionally, higher-carbon sugars have been prepared by one-carbon extension of the chain of the next lower aldose, usually *via* the cyanohydrin or nitromethane methods[1]; in recent times, other methods[2] have permitted extension of the sugar chain by two or more carbon atoms in a single step. In connection with the synthesis of higher-carbon sugars of biological interest, we have examined the osmium tetraoxide oxidation of a number of carbohydrate derivatives, including (*E*)- and (*Z*)-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enopyranose (**3** and **6**), the 8-*O*-benzyl derivative **4** of **3**, methyl (*Z*)-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enopyranuronate (**5**), 7,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-oct-7-enopyranose[3] (**15**), and (*Z*)-6,7,8-trideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enopyranose[4,5] (**18**). In adopting this approach, we were influenced by recent observations[6] that the osmylation of allylic alcohols and their derivatives proceeds with moderate to marked stereoselectivity which can be predicted on an empirical basis.

All the carbohydrate derivatives examined were prepared in a straightforward manner from 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[7] (**1**). Thus, **1** reacted with formylmethylenetriphenylphosphorane** in refluxing benzene to give the (*E*)-enal **2** (90%), m.p. 94.5–95.5° [from light petroleum (b.p. 60–80°)], $[\alpha]_D$ −137° (*c* 1, chloroform) {lit.[8] m.p. 97.5–99.5°, $[\alpha]_D$ −135° (*c* 1, chloroform)}, which, on reduction with di-isobutylaluminium hydride in dichloromethane at 0°, afforded **3**, b.p. ~145° (bath)/0.03 mmHg, $[\alpha]_D$ −108° (*c* 1, chloroform), in 70% yield. Conventional benzylation of **3** gave **4**, b.p. ~157° (bath)/0.01 mmHg, $[\alpha]_D$ −100° (*c* 1.1, chloroform). The reaction between **1** and (methoxycarbonylmethylene)triphenylphosphorane in methanol at ~4° furnished the (*Z*)-olefin **5** (92%), b.p. ~96° (bath)/0.01 mmHg, $[\alpha]_D$ −121° (*c* 0.6, chloroform), which, on reduction with lithium aluminium hydride in tetrahydrofuran at room temperature, gave **6***** (67%), b.p. ~140° (bath)/-0.05 mmHg, $[\alpha]_D$ −110° (*c* 1, chloroform). Literature procedures were used in preparing **15**[3] and **18**[4] from **1**.

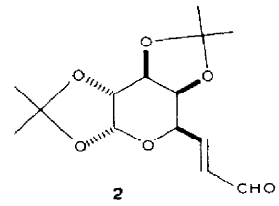
*To whom enquiries should be addressed.

Other workers[8] claimed that **1 failed to react with this Wittig reagent in refluxing benzene, although they were successful in preparing **2** by another route.

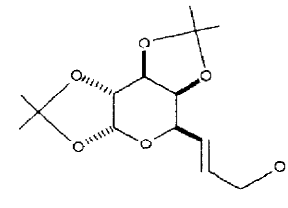
***The geometric isomers **3** and **6** are distinguishable by ^{1}H-n.m.r. spectroscopy.



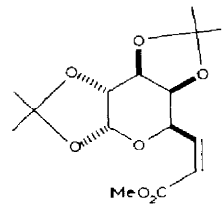
1



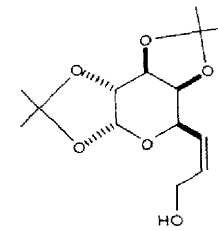
2



3 R = H
4 R = Bzl



5



6

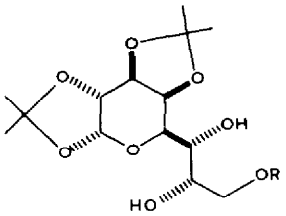
When subjected to oxidation with osmium tetraoxide under catalytic conditions[9]†, **3** gave a mixture of 1,2:3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octopyranose (**7**) and the D-*threo*-α-D-*galacto* isomer **8** in the ratio ~7:1, respectively, and in a combined yield of 56.5%. In this and subsequent oxidations, the ratio of the products was determined by integration over the resonances for the anomeric protons in the ^{1}H-n.m.r. spectra ($CDCl_3$). The stereochemistry of the major product was established by the isolation of L-*threo*-D-*galacto*-octitol (**11**, 45%), m.p. 233–236° (from water)††, following acid hydrolysis (CF_3CO_2H–H_2O) of the mixture of **7** and **8**, and reduction ($NaBH_4$) of the resulting octoses. In agreement with the symmetry of **11**, only four resonances, of roughly equal intensity, were observed in its ^{13}C-n.m.r. spectrum [$(CD_3)_2SO$]. Acetylation of **11** gave the octa-acetate **12**, m.p. 143–145° (from aqueous ethanol), $[\alpha]_D$ –40° (*c* 1.1, chloroform) {lit. (D enantiomer)[10] m.p. 141° (corrected), $[\alpha]_D$ +40.4° (*c* 1.2, chloroform)}. Catalytic osmylation of **4** was less stereoselective, affording a mixture (92%) of **9** and **10** in the ratio ~3:1.

Catalytic osmylation of **6** produced a mixture (67%) of 1,2:3,4-di-*O*-isopropylidene-D-*erythro*-α-D-*galacto*-octopyranose (**13**) and the L-*erythro*-α-D-*galacto* isomer **14** in the ratio 7:1, from which **13**, m.p. 117–118° (from ethyl acetate–hexane), $[\alpha]_D$ –61° (*c* 0.75, chloroform), readily crystallised. Since **13** (79%) was also obtained as the preponderant (even exclusive) product on similar osmylation of **15**[3], its stereochemistry is rigorously established. Acid hydrolysis of **13** afforded the new octose **16**, namely D-*erythro*-D-*galacto*-octose, m.p. 180–181.5° (from aqueous ethanol), $[\alpha]_D$ +42°

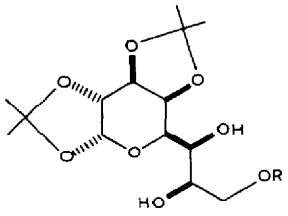
---

†The following general procedure was used: the substrate (1 equiv.), *N*-methylmorpholine *N*-oxide (2 equiv.), and osmium tetraoxide (~0.05 equiv.) in acetone–water (8:1; 5mL/mmol of substrate) were stirred at room temperature until t.l.c. indicated that the reaction was complete.

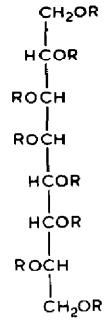
††The octitol **11** has no measurable optical rotation in saturated aqueous solution. The D enantiomer[10] has m.p. 230° (corrected).



7 R = H
9 R = Bzl



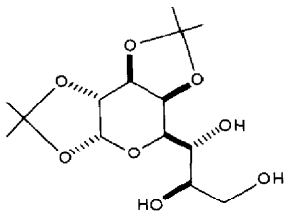
8 R = H
10 R = Bzl



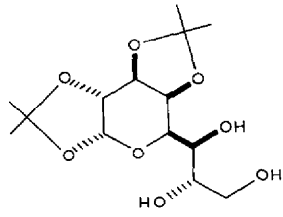
11 R = H
12 R = Ac

(7 min) → +62° (equil.; *c* 1.1, water), in 60% yield, which was reduced in a straightforward manner to the octitol **17** (80%, isolated as the monohydrate), m.p. 168–169° (from aqueous ethanol), $[\alpha]_D$ +2.5° (*c* 0.7, water). The oxidation of **18**[4] with osmium tetraoxide, as with aqueous potassium permanganate[5], yielded a single crystalline product identified as 8-deoxy-1,2:3,4-di-*O*-isopropylidene-D-*erythro*-α-D-*galacto*-octopyranose (**19**, 78%), m.p. 152–153° [from chloroform–light petroleum (b.p. 60–80°)], $[\alpha]_D$ −55.5° (*c* 1, chloroform) {lit.[5] m.p. 151–152°, $[\alpha]_D$ −57° (*c* 1.4, chloroform)}.

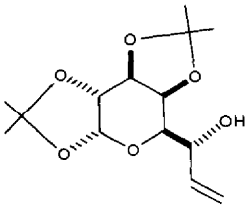
According to Kishi's empirical rule[6] for osmylation, the relative stereochemistry between the pre-existing hydroxyl or alkoxyl group and the adjacent, newly-introduced hydroxyl group of the major product is *erythro*. If, for compounds **3**, **4**, **6**, and **18**, the



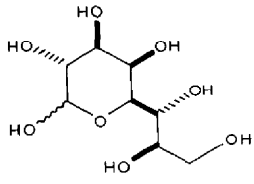
13



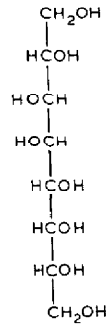
14



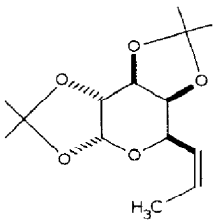
15



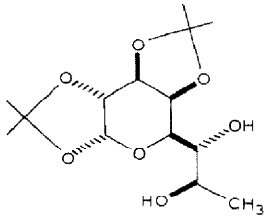
16



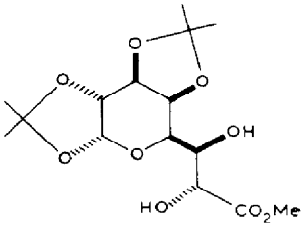
17



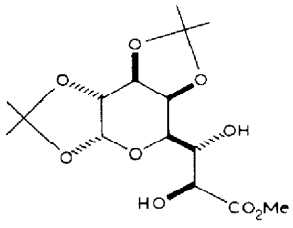
18



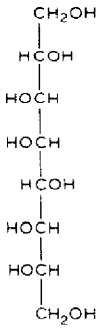
19



20



21



22

oxygen atom of the pyranoid ring exerts the same influence as that of an alkoxyl group, then the stereochemical outcome of the foregoing oxidations follows Kishi's formulation. However, the catalytic osmylation of **5** is exceptional, since it gave a mixture (83.5%) of methyl 1,2:3,4-di-*O*-isopropylidene-L-*erythro*-α-D-*galacto*-octopyranuronate (**20**) and the D-*erythro*-α-D-*galacto* isomer **21** in the ratio 4:1. Reduction of this mixture with lithium aluminium hydride in tetrahydrofuran at room temperature gave **14** and **13** (ratio 4:1), which, on acid hydrolysis (CF_3CO_2H–H_2O) and reduction ($NaBH_4$) of the resulting octoses, afforded L-*erythro*-D-*galacto*-octitol (**22**, 43%), m.p. 153–154.5° (from aqueous ethanol), $[\alpha]_D$ −2.5° (*c* 0.6, water) {lit. (D enantiomer)[11] m.p. 153–154°, $[\alpha]_D$ +2.4° (*c* 4, water)}. Kishi *et al.*[6] have pointed out that the empirical rule for osmylation should be applied with caution to conjugated carbonyl compounds, since there are exceptions.

The ability to predict the stereochemical outcome of reactions used in the synthesis of higher-carbon sugars is unquestionably important. We envisage that, after suitable manipulation of the non-reducing segment of the sugar chain, such compounds as **9** could be transformed into decose derivatives of predictable stereochemistry.

New compounds had elemental analyses and/or spectroscopic properties in agreement with the structures assigned.

ACKNOWLEDGMENT

We thank J. A. Chudek for recording the ^1H- and ^{13}C-n.m.r. spectra.

REFERENCES

1 J. M. Webber, *Adv. Carbohydr. Chem.*, 17 (1962) 15–63.
2 H. Paulsen, K. Roden, V. Sinnwell, and P. Luger, *Justus Liebigs Ann. Chem.*, (1981) 2009–2027; T. Suami, H. Sasai, and K. Matsuno, *Chem. Lett.*, (1983) 819–822; J. A. Secrist, III, and K. D. Barnes, *J. Org. Chem.*, 45 (1980) 4526–4528, provide some recent examples.
3 G. B. Howarth, D. G. Lance, W. A. Szarek, and J. K. N. Jones, *Can. J. Chem.*, 47 (1969) 75–79; R. Hems, D. Horton, and M. Nakadate, *Carbohydr. Res.*, 25 (1972) 205–216.
4 D. G. Lance and W. A. Szarek, *Carbohydr. Res.*, 10 (1969) 306–310.
5 D. G. Lance, W. A. Szarek, J. K. N. Jones, and G. B. Howarth, *Can. J. Chem.*, 47 (1969) 2871–2874.
6 J. K. Cha, W. J. Christ, and Y. Kishi, *Tetrahedron*, 40 (1984) 2247–2255.
7 R. E. Arrick, D. C. Baker, and D. Horton, *Carbohydr. Res.*, 26 (1973) 441–447.
8 D. Horton, A. Liav, and S. E. Walker, *Carbohydr. Res.*, 28 (1973) 201–212.
9 V. Van Rheenen, R. C. Kelly, and D. Y. Cha, *Tetrahedron Lett.*, (1976) 1973–1976.
10 W. D. Maclay, R. M. Hann, and C. S. Hudson, *J. Am. Chem. Soc.*, 60 (1938) 1035–1040.
11 R. M. Hann, A. T. Merrill, and C. S. Hudson, *J. Am. Chem. Soc.*, 66 (1944) 1912–1921.