Carbohydrate Research, 162 (1987) 298–302
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Branched-chain sucrose: synthesis of 4,1′,6′-trichloro-4,1′,4′,6′-tetradeoxy-4′-*C*-methyl-*galacto*-sucrose*,†

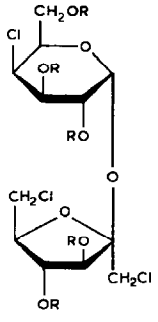
RIAZ KHAN AND GITA PATEL

Tate & Lyle Group Research and Development, Philip Lyle Memorial Research Laboratory, P.O. Box 68, Whiteknights Park, Reading RG6 2BX (Great Britain)

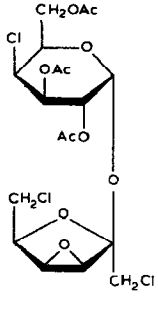
(Received August 8th, 1986; accepted for publication, November 14th, 1986)

Sugar epoxides undergo ring-opening reactions by carbon nucleophiles to give *trans*-diaxial products. Alkylmagnesium chlorides react with pyranoid and furanoid epoxides to give branched-chain hydroxy compounds[2,3]. Other carbanions which have been used are those derived from 1,3-dithiane[4], lithium dimethylcuprate[5], diethyl malonate[6], and hydrogen cyanide[7–9]. We now describe the reaction of 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-anhydro-1,6-dichloro-1,6-dideoxy-β-D-*lyxo*-hexulofuranoside (**2**) with lithium dimethylcuprate.

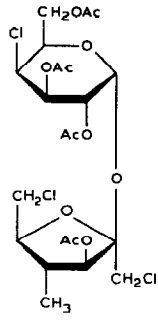
The 3′,4′-*lyxo*-epoxide **2** was synthesised by treatment of 4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose (**1**) by 6-(*tert*-butyldiphenylsilylation) followed by reaction[10] with diethyl azodicarboxylate (DEAD) and triphenylphosphine (TPP). It was necessary to block HO-6 in order to avoid the formation of the 3,6-anhydride



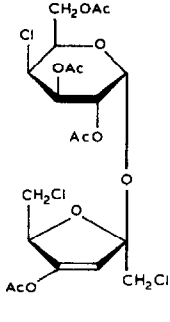
1 R = H
6 R = Ac



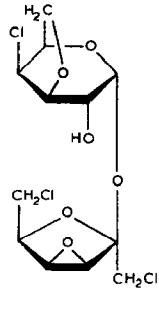
2



3



4



5

galacto-Sucrose connotes α-D-galactopyranosyl β-D-fructofuranoside.
†Sucrochemistry, Part 40. For Part 39, see ref. 1.

0008-6215/87/$ 03.50

TABLE I

^{1}H-N.M.R. DATA (250 MHz, $CDCl_3$); CHEMICAL SHIFTS (τ) AND COUPLING CONSTANTS (Hz)

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a* *H-6b*	*H-1'a* *H-1'b*	*H-3'*	*H-4'*	*H-5'*	*H-6'a* *H-6'b*	*Ac*	*Me*
2	4.69 (d) $J_{1,2}$ 4.04	4.88 (dd) $J_{2,3}$ 10.66	4.69 (dd) $J_{3,4}$ 3.67	5.40 (dd) $J_{4,5}$ 1.09	5.49 (dt) $J_{5',6'a}$ 6.25 $J_{5',6'b}$ 5.51	5.71 (dd) 5.80 (dd) $J_{6a,6b}$ 11.39	6.33 (d) 6.49 (d) $J_{1'a,1'b}$ 11.76	6.07 (d) $J_{3',4'}$ 2.57	6.10 (sdd) $J_{4',5'}$ 0.73	5.82 (sxt) $J_{5',6'a}$ 8.08 $J_{5',6'b}$ 5.51	6.39 (dd) 6.48 (dd) $J_{6'a,6'b}$ 11.35	7.87 7.93 7.97 3 Ac	
3	4.73 (d) $J_{1,2}$ 3.42	4.76 (dd) $J_{2,3}$ 10.76	4.68 (dd) $J_{3,4}$ 3.29	5.41 (dd) $J_{4,5}$ 1.33	5.46 (m)	5.72 (dd) 5.79 (dd) $J_{5,6a}$ 4.06 $J_{6a,6b}$ 11.68	6.33 (d) 6.49 (d) $J_{1'a,1'b}$ 11.59	4.77 (d) $J_{3',4'}$ 10.40	7.68 (dqt)	6.06 (dt) $J_{4',5'}$ 4.4 $J_{5',6'a}$ 5.54 $J_{5',6'b}$ 5.63	6.26 (dd) 6.28 (dd) $J_{6'a,6'b}$ 11.5	7.84 7.88 7.91 7.93 4 Ac	8.82 (d) $J_{Me,4'}$ 6.57
4	4.50 (d) $J_{1,2}$ 4.0	4.83 (dd) $J_{2,3}$ 10.7	4.69 $J_{3,4}$ 3.3	5.43 (dd) $J_{4,5}$ 1.5	5.62 (dt) $J_{5,6a}$ 5.3 $J_{5,6b}$ 8.4	5.80 (dd) 5.94 (dd) $J_{6a,6b}$ 11.4	6.29 (d) 2.39 (d) $J_{1'a,1'b}$ 11.7	3.56 (sd) $J_{3',5'}$ 1.4		5.04 (sxt) $J_{5',6'a}$ = $J_{5',6'b}$ = 6.25	6.40 (dd) 6.47 (dd) $J_{6'a,6'b}$ 10.0	7.80–8.0 4 Ac	

TABLE II

^{13}C-N.M.R. DATA (62 MHz, $CDCl_3$)[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-5'*	*C-6'*	*CH_3CO*	*CH_3CO*
2	89.9	68.0	67.4	58.7	67.2	63.4	45.7	103.4	57.1	55.0	77.5	40.4	20.7–20.6	170.2–169.6
3	89.5	67.4	66.7	59.0	68.2	63.9	46.0	103.0	78.2	39.9	83.6	44.6	20.7–20.5	170.1–169.6

[a]Chemical shifts expressed in p.p.m. downfield from the signal for Me_4Si.

5. If the epoxidation of **1** is performed in ethyl acetate with 4 mol each of DEAD and TPP below 5° for 30 min, the formation of **5** is minimised and ~80% of **2** is obtained.

Treatment of **2** with lithium dimethylcuprate in dry ether afforded, after acetylation and chromatography, the 4′-*C*-methyl derivative **3** (22%) and the 3′-eno derivative **4** (16%). The structure of **3** was ascertained on the basis of ^{1}H-n.m.r. (Table I) and mass-spectral data. In the n.m.r. spectrum of **3**, the resonance due to H-3′ at τ 4.77 was shifted 1.30 p.p.m. downfield, compared to the corresponding signal[10] for **1**, which indicated that position 3′ was acetylated. The resonance due to H-4′ was identified by spin decoupling experiments as a complex doublet of quartets at τ 7.68, which indicated that the methyl group was located at that position. This inference was supported further by the fact that the signal for H-4′ was shifted upfield by 1.58 p.p.m., as compared to the corresponding resonance for **2**. The large $J_{3',4'}$ value (10.3 Hz) indicated that the epoxide ring had been opened by the attack of methyl nucleophile at C-4′, to give **3** having the furanoid ring in the β-D-*fructo* configuration. A doublet at τ 8.82 ($J_{CH_3,4'}$ 6.56 Hz) was assigned to the methyl group. The coupling constants ($J_{1,2}$ 3.4, $J_{2,3}$ 10.8, $J_{3,4}$ 3.3, and $J_{4,5}$ 1.3 Hz) of **3** accorded with the α-D-*galacto* configuration and $^4C_1$ conformation for the hexopyranosyl ring. The mass spectrum of **3** contained intense peaks for ions at *m/z* 239 (9:6:1, a triplet) and 307 (3:1, doublet) due to ketofuranosyl and hexopyranosyl cations, respectively. In the ^{13}C-n.m.r. spectrum (Table II) of **3**, the resonance due to C-4′ was observed upfield at τ 39.9 as compared to those for 4,1′,6′-trichloro-4,1′,6′-trideoxy-*galacto*-sucrose penta-acetate (**6**, δ 75.0), sucrose octa-acetate[11] (δ 75.2), and the 3′,4′-epoxide **2** (δ 55.0). A β-effect (−3.0 p.p.m.) on C-3′ and C-5′ was also observed. The high-field resonance at δ 15.2 was attributed to Me-4′.

The structure of the 3′-eno compound **4** was also supported by its ^{1}H-n.m.r. and mass-spectral data. In the n.m.r. spectrum, a low-field doublet at τ 3.56 for H-3′ was split further (~1.4 Hz), presumably due to long-range coupling with H-5′. This allylic coupling was also observed in H-5′ which supported the presence of the 3′,4′-double bond in **4**. The coupling constants ($J_{1,2}$ 4.0, $J_{2,3}$ 10.7, $J_{3,4}$ 3.3, $J_{4,5}$ 1.5 Hz) accorded with the α-D-*galacto* configuration and $^4C_1$ conformation for the hexopyranosyl ring in **4**. The mass spectrum of **4** contained intense peaks for ions at *m/z* 223 (9:6:1, a triplet) and 307 (3:1, doublet) due to ketofuranosyl and hexopyranosyl cations, respectively.

EXPERIMENTAL

For general experimental details, see ref. 12.

*2,3,6-Tri-*O*-acetyl-4-chloro-4-deoxy-α-*D*-galactopyranosyl 3,4-anhydro-1,6-dichloro-1,6-dideoxy-β-*D*-lyxo-hexulofuranoside* (**2**). — A cooled (0°) solution of **1** (10 g, 25.2 mmol) in ethyl acetate was treated with DEAD (15.7 mL, 99.8 mmol) followed by TPP (26.2 g, 100 mmol). The mixture was kept below 5° for 0.5 h, then treated with methanol (15 mL), and concentrated to a syrup. Triphenylphosphine

oxide, which crystallised out on the addition of ether, was removed, the filtrate was concentrated, and the resulting syrup was treated with acetic anhydride (20 mL) and pyridine (100 mL) at ambient temperature for 4 h. The mixture was then concentrated and the residue was eluted from a short column of silica gel with ether–light petroleum (1:1) to give **2** (9.85 g, 80%), m.p. 133–134° (from ether–light petroleum), $[\alpha]_D$ +116° (*c* 1, chloroform). Mass spectrum [ions (a) corresponding to 3:1 doublet due to hexopyranosyl cation and (b) 9:6:1 triplet due to ketofuranosyl cation]: *m/z* 307 (a), 247 (a), 187 (a), 181 (b), 165 (b).

Anal. Calc. for $C_{18}H_{23}Cl_3O_{10}$: C, 42.7; H, 4.5; Cl, 21.1. Found: C, 43.0; H, 4.6; Cl, 20.8.

Reaction of **2** *with lithium dimethylcuprate.* — To a stirred suspension of cuprous iodide (10.6 g, 160 mmol) in anhydrous ether (60 mL) under nitrogen at 0° was added methyl-lithium–lithium bromide complex (1.5M in ether, ~54 mL) until the bright-yellow colour disappeared. A solution of **2** (7 g, 14 mmol) in dry ether (100 mL) was then added, and the suspension was stirred for 6 h, then diluted with aqueous ammonium chloride, washed sequentially with aqueous ammonium chloride, aqueous sodium hydrogencarbonate, and brine, dried (Na_2SO_4), and concentrated. The resulting syrup was treated with acetic anhydride (12 mL) and pyridine (50 mL) at ambient temperature for 8 h. T.l.c. (ether–light petroleum, 4:1) then revealed two products. The mixture was concentrated and the residue was eluted from a column of silica gel with ether–light petroleum (1:1) to give 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 4-*O*-acetyl-1,6-dichloro-1,3,6-trideoxy-β-D-*glycero*-hex-3-enofuranoside (**4**; 1.2 g, 16%), $[\alpha]_D$ +36° (*c* 1, chloroform). Mass spectrum [ions (a) correspond to 3:1 doublet due to hexopyranosyl cation and (b) 9:6:1 triplet due to ketofuranosyl cation]: *m/z* 307 (a), 247 (a), 223 (b).

Anal. Calc. for $C_{20}H_{24}Cl_3O_{11}$: C, 43.9; H, 4.4; Cl, 19.2. Found: C, 44.1; H, 4.3; Cl, 19.0.

Eluted second was 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,6-dichloro-1,4,6-trideoxy-4-*C*-methyl-β-D-fructofuranoside (**3**; 1.7 g, 22%), $[\alpha]_D$ +55° (*c* 0.9, chloroform), m.p. 98–100° (from ether–light petroleum). Mass spectrum [ions (a) correspond to 3:1 doublet due to hexopyranosyl cation and (b) 9:6:1 triplet due to ketofuranosyl cation]: *m/z* 307 (a), 239 (b), 179 (b).

Anal. Calc. for $C_{21}H_{29}Cl_3O_{11}$: C, 44.7; H, 5.1; Cl, 18.9. Found: C, 44.9; H, 5.2; Cl, 18.8.

ACKNOWLEDGMENT

We thank Professor R. C. Righelato (Director, Tate & Lyle Group Research and Development) for his interest and support.

REFERENCES

1 R. KHAN AND G. PATEL, *Carbohydr. Res.*, 162 (1987) 209–215.
2 T. D. INCH AND G. J. LEWIS, *Carbohydr. Res.*, 15 (1970) 1–10.
3 S. R. JENKINS AND E. WALTON, *Carbohydr. Res.*, 26 (1973) 71–75.
4 A. YAMASHITA AND A. ROSONSKY, *J. Org. Chem.*, 41 (1976) 3422–3425.
5 D. R. HICKS, R. AMROSE, AND B. FRASER-REID, *Tetrahedron Lett.*, (1973) 2507–2508.
6 S. HANESSIAN, P. DEXTRAZE, AND R. MASSE, *Carbohydr. Res.*, 26 (1973) 264–267.
7 B. E. DAVISON AND R. D. GUTHRIE, *J. Chem. Soc., Perkin Trans. 1*, (1972) 658–662.
8 K. OMURA, A. K. SHARMA, AND D. SWENN, *J. Org. Chem.*, 41 (1976) 957–962.
9 J. S. BRIMACOMBE, J. G. H. BRYAN, A. HUSEIN, M. STACEY, AND M. S. TOLLEY, *Carbohydr. Res.*, 2 (1966) 251–260.
10 G. PATEL, Ph.D. Thesis, London University, 1984.
11 H. LINDSETH, Ph.D. Thesis, London University, 1980.
12 R. KHAN, M. R. JENNER, AND H. LINDSETH, *Carbohydr. Res.*, 65 (1978) 99–108.