Carbohydrate Research, 89 (1981) 159–162
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

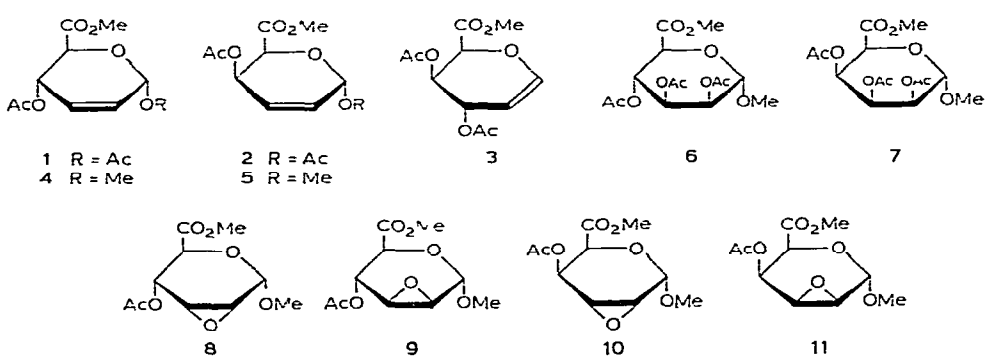
Note

A short synthesis of racemic uronic acids and 2,3-anhydrouronic acids*

RICHARD R SCHMIDT AND ROLF ANGERBAUER
Fakultat fur Chemie, Universitat Konstanz, Postfach 5560, 7750 Konstanz (Germany)
(Received March 18th, 1980, accepted for publication June 2nd, 1980)

The Diels–Alder reaction of *trans-trans*-1,3-butadienylene diacetate with activated carbonyl compounds yields 1-*O*-acetylpseudoglycals (hex-2-enopyranoses) which are intermediates for the stereospecific synthesis of *α-threo*-hex-2-enopyranosides[2,3] and for the regiospecific synthesis of 2,3-unsaturated nucleosides[4,5]. We now report on the application of this route for the synthesis of racemic mannuronic and taluronic acid and their 2,3-anhydro derivatives.

A good yield of a 1:1 mixture of the racemic 1-*O*-acetylpseudoglycal derivatives **1** and **2** was obtained by a Diels–Alder reaction of *trans-trans*-1,3-butadienylene diacetate with methyl glyoxylate. The glycal **3** was formed as a by-product. Compounds **2** and **3** are rearrangement products of the *cis*-cycloadduct having the *threo* configuration[3]. The components in the mixture **1–3** could be separated by chromatography, but this was unnecessary for further reactions[3]. The reaction of the mixture **1–3** with methanol, when catalysed by boron trifluoride, gave a quantitative yield of the α-glycosides **4** and **5**; therefore, **2** and **3** led exclusively to **5**. Compounds **4** and **5** were easily isolated by chromatography. The structures of **1–5** were assigned on the basis of ^{1}H-n.m.r. data and comparison with the corresponding butyl uronates[3].



1 R = Ac
4 R = Me

2 R = Ac
5 R = Me

3 6 7

8 9 10 11

(All the above products were racemic. The D forms are depicted for convenience.)

de novo Synthesis of Carbohydrates and Related Natural Products, Part 5[1]

TABLE I

^{1}H-N M R DATA[a] FOR **1–11**

	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*OAc*	*OCH$_3$*	*CO-CH$_3$*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
1	6 41	5 88	6 07	5 62	4 45	2 10 (6 H)	—	3 78	1 5	10	1 8	9
2	6 51	6 08	6 33	5 37	4 81	2 06 2 10	—	3 82	3	10	5	2 75
3	6 71	5 11	4 98	5 36	4 83	2 06 2 10	—	3 84	5 5	5 3 ($J_{2,1}$ 2)	1 4	1 5
4	5 02	5 85–6 05		5 46	4 39	2 08	3 48	3 78	[b]	[b]	1 8	9
5	5 06	5 98	6 15	5 26	4 74	2 01	3 45	3 78	2 5	10	4 75	3
6	4 82	5 23	5 27–5 44		4 31	1 99 2 03 2 12	3 45	3 76	2	[b]	[b]	9 5
7	4 94	5 04	5 31	5 60	4 62	1 98 2 06 2 10	3 44	3 75	1 5	3 5	3 5	2
8	5 01	3 53 (2 H)		5 31	4 33	2 10	3 48	3 74	2 5	[b]	1	9 5
9	5 01	3 10	3 25	5 20	4 18	2 10	3 50	3 75	0	3 5	0	9 5
10	5 13	3 47 (2 H)		5 50	4 57	2 10	3 48	3 75	2	[b]	1	1 5
11	5 07	3 13	3 68	5 22	4 53	2 10	3 48	3 75	0	3 5	5	3 5

[a]80 MHz, $CDCl_3$ (internal Me_4Si) δ scale [b]Not determined

Treatment[6] of **4** with hydrogen peroxide in *tert*-butyl alcohol with osmium tetroxide as catalyst effected *cis*-hydroxylation from the less-hindered side[7] and, after acetylation, only the mannuronic acid derivative **6** was obtained Because of steric hindrance, *cis*-hydroxylation of **5** proceeded much more slowly than that of **4** and, after acetylation, the taluronic acid derivative **7** was the only product The structures of **6** and **7** were assigned on the basis of ^{1}H-n m r data (see Table I), which accorded with those for the corresponding *tert*-butyl uronates synthesised *via* a different route[8]

The reaction of **4** with 50% hydrogen peroxide and benzonitrile gave 48% of a 3 2 mixture of the epoxides **8** and **9** Likewise **5** afforded 59% of a 1 3 mixture of the epoxides **10** and **11** AcO-4 was lost during the epoxidation, and re-acetylation was necessary for ^{1}H-n m r assignments The relative configurations of the epoxides **8–11** were assigned on the basis of *J* values (See Table I) and a comparison of the ^{1}H-n m r data with those of other 2,3-anhydrohexoses[9,10] The preferred formation of **8** and **11** is due to the influence of HO-4 in the intermediates[9,11]

EXPERIMENTAL

General — Melting points are uncorrected ^{1}H-N m r spectra were recorded

for solutions in $CDCl_3$ (internal Me_4Si) with a Bruker CW-80 spectrometer. *trans-trans*-1,3-Butadienylene diacetate was prepared from cyclo-octatetraene[12]. Methyl glyoxylate (containing ~2% of acetic acid), obtained by oxidative cleavage of methyl tartrate according to the procedure used for butyl glyoxylate[13], had b.p. 35–38°/12 mmHg.

*Methyl 1,4-di-O-acetyl-2,3-dideoxy-α-*DL-erythro- (**1**) *and* -threo-*hex-2-enopyranuronate* (**2**), *and methyl 3,4-di-O-acetyl-*DL-*xylo-hex-1-enopyranuronate* (**3**). — A solution of *trans-trans*-1,3-butadienylene diacetate (6.8 g, 40 mmol), methyl glyoxylate (5.3 g, 70 mmol), and hydroquinone (20 mg) in benzene (10 ml) was kept at 125° for 60 h in an autoclave. The mixture was then concentrated and the residue was eluted from silica gel with ethyl acetate–benzene–light petroleum (b.p. 40–60°) (1:2:2) to give, first, **3** (1.1 g, 11%) as a slightly yellow oil, R_F 0.49.

Anal. Calc. for $C_{11}H_{14}O_7$: C, 51.16; H, 5.47. Found: C, 50.99; H, 5.38.

Eluted second was **1** (2.65 g, 25%) as a colourless oil, R_F 0.45.

Anal. Found: C, 51.25; H, 5.49.

Eluted third was **2** (2.42 g, 26%) as a colourless oil, R_F 0.30.

Anal. Found: C, 51.01; H, 5.49.

See Table I for ^{1}H-n.m.r. data.

*Methyl (methyl 4-O-acetyl-2,3-dideoxy-α-*DL-erythro- *and* -threo-*hex-2-enopyranosid)uronate* (**4** *and* **5**). — To a solution of the foregoing mixture **1**–**3** (5.2 g, 20 mmol) in methanol (15 ml) and anhydrous acetonitrile (500 ml) was added boron trifluoride etherate (5 ml) at 0–5°. After 3 h, the mixture was neutralised with saturated aqueous sodium hydrogencarbonate (40 ml) and extracted with chloroform (3 × 500 ml), and the combined extracts were dried (Na_2SO_4) and concentrated. The residue was eluted from silica gel with ethyl acetate–benzene–light petroleum (b.p. 40–60°) (1:2:2) to give, first, **4** (1.9 g, 41%) as a colourless oil, R_F 0.47.

Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.26; H, 6.20.

Eluted second was **5** (2.6 g, 56%) as a colourless oil, R_F 0.33.

Anal. Found: C, 52.15; H, 5.99.

See Table I for ^{1}H-n.m.r. data.

*Methyl (methyl 2,3,4-tri-O-acetyl-α-*DL-*mannopyranosid)uronate* (**6**). — To a solution of **4** (230 mg, 1 mmol) in 6% hydrogen peroxide in *tert*-butyl alcohol (7.2 ml) was added 10% osmium tetroxide in *tert*-butyl alcohol[6] (1.25 ml). After the disappearance of **4**, excess of hydrogen peroxide was decomposed with a catalytic amount of manganese dioxide. The reaction mixture was concentrated to dryness, and the residue was acetylated with acetic anhydride–pyridine (5 ml, 1:1) at room temperature. The product was eluted from silica gel with chloroform–ether (9:1), to give **6** (180 mg, 52%) as a colourless oil.

Anal. Calc. for $C_{14}H_{20}O_{10}$: C, 48.28; H, 5.79. Found: C, 48.27; H, 5.67.

See Table I for ^{1}H-n.m.r. data.

*Methyl (methyl 2,3,4-tri-O-acetyl-α-*DL-*talopyranosid)uronate* (**7**). — Using the method described above, **5** (230 mg, 1 mmol) was converted into **7** (170 mg, 49%), m.p. 129° (from cyclohexane).

Anal Calc for $C_{14}H_{20}O_{10}$ C, 48 28. H 5 79 Found C, 48 25, H, 5 68

See Table I for ^{1}H-n m r data

*Methyl (methyl 4-O-acetyl-2 3-anhydro-α-*DL*-allo- and -manno-pyranosid)uronate* (**8** *and* **9**) — To a solution of **4** (691 mg. 3 mmol) in methanol (10 ml) were added sodium hydrogencarbonate (1 g). benzonitrile (2 5 ml), and 50% hydrogen peroxide (2 5 ml) at room temperature After the disappearance of **4** (1–3 days), excess of hydrogen peroxide was decomposed with a catalytic amount of manganese dioxide The mixture was filtered and concentrated, and the residue was acetylated with acetic anhydride–pyridine (10 ml. 1 1) at room temperature Elution of the product from silica gel with benzene–acetone (19 1) gave. first, **9** (130 mg, 18%) as a colourless oil R_F 0 28

Anal Calc for $C_{10}H_{14}O_7$. C, 48 78, H, 5 73 Found C, 48 88, H, 5 85

Eluted second was **8** (220 mg, 30%) as a colourless oil R_F 0 20

Anal Found C. 48 82 H, 5 72

See Table I for ^{1}H-n m r data

*Methyl (methyl 4-O-acetyl-2,3-anhydro-γ-*DL*-gulo- and -talo-pyranosid)uronate* (**10** *and* **11**) — Using the method described above **5** (691 mg, 3 mmol) was converted into **10** (100 mg. 14%), isolated, first by chromatography as a colourless oil, R_F 0 30

Anal Calc for $C_{10}H_{14}O_7$ C, 48 78 H, 5 73 Found C 48 94 H, 5 85

Eluted second was **11** (330 mg, 45%) m p 125° (from cyclohexane), R_F 0 24

Anal Found C, 49 14, H, 5 74

See Table I for ^{1}H-n m r data

ACKNOWLEDGMENTS

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie We thank BASF AG, Ludwigshafen, for a generous gift of cyclo-octatetraene

REFERENCES

1 Part 4 R R Schmidt and R Scheibe *Justus Liebigs Ann Chem*, (1980) 1307–1320
2 R R Schmidt and R Angerbauer, *Angew Chem Int Ed Engl* 16 (1977) 783–784
3 R Angerbauer and R R Schmidt, *Carbohydr Res*, 89 (1981) 193–201
4 S Y Tam and B Fraser-Reid *Can J Chem* 55 (1977) 3996–4001
5 R R Schmidt and R Angerbauer *Carbohydr Res*, 72 (1979) 272–275
6 N A Milas J H Trepagnier, J T Nolan and M I Iliopoulos, *J Am Chem Soc*, 81 (1959) 4730–4733
7 O Achmatowicz and B Szechner *Rocz Chem*, 49 (1975) 1715–1724
8 J Mieczkowski and A Zamojski, *Carbohydr Res* 55 (1977) 177–192
9 O Achmatowicz and B Szechner *Carbohydr Res* 50 (1976) 12–33
10 M Chmielewski, J Mieczkowski W Priebe A Zamojski, and H Adamowicz *Tetrahedron*, 34 (1978) 3325–3330
11 J Thiem and J Schwentner, *Tetrahedron Lett* (1978) 459–462
12 R M Carlson and R K Hill, *Org Synth* 50 (1970) 24–27
13 F J Wolf and J Weijard *Org Synth*, *Coll Vol IV*, (1963) 124–126
14 S D Yablonovskaya, N M Sekhtman, N D Antonova, S V Bogatkov, S M Jakin, and N S Zefirow. *Zh Org Khim* 6 (1970) 871–877