*Carbohydrate Research*, 225 (1992) 151–153
Elsevier Science Publishers B.V., Amsterdam



# Note

## Synthesis of 1,6-anhydro-2,3-dideoxy-β-D-*erythro*- and -*threo*-hex-2-enopyranose from 3,4-di-*O*-substituted glycals by a facile intramolecular Ferrier reaction*

Hari Babu Mereyala†, Kanamarlapudi C. Venkataramanaiah, and V. Sukanya Dalvoy‡
*Indian Institute of Chemical Technology, Hyderabad 500 007 (India)*

(Received March 15th, 1991; accepted July 19th, 1991)

The 1,6-anhydro-2,3-dideoxy-β-D-*erythro*-/-*threo*-hex-2-enopyranoses **7–12** are valuable synthons for the preparation of structurally diverse natural products[1–4], because (*a*) the rigid [3.2.1]bicyclic framework facilitates highly stereo- and regio-selective reactions[2c], (*b*) each contains a reactive double bond and allylic hydroxyl group, (*c*) the locked conformation facilitates the generation of stereo centres which are opposite in configuration to those generated from compounds with conventional $^4C_1$ conformations, and (*d*) the internal acetal reduces the number of protecting groups that are required. Compounds **7–12** have been prepared by low-yielding, multi-step procedures starting from 1,6-anhydrogalactopyranose[4c,4d].

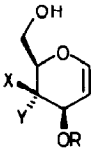
We now report on a new, general, and efficient route to the 1,6-anhydro-2,3-dideoxy-β-D-*erythro*- (**7–9**) and -β-D-*threo*-hex-2-enopyranoses (**10–12**) from the easily accessible 3,4-di-*O*-substituted glycals **1–6**, which involves a novel "intramolecular" Ferrier reaction[5,6].

Thus, 3,4-di-*O*-acetyl- (**1**), 3,4-di-*O*-benzoyl- (**2**), and 3,4-di-*O*-benzyl-D-glucal (**3**) were each reacted in dry dichloromethane at 0° with a catalytic amount of boron trifluoride etherate to give 4-*O*-acetyl-1,6-anhydro-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (**7**), 1,6-anhydro-4-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (**8**), and 1,6-anhydro-4-*O*-benzyl-β-D-*erythro*-hex-2-enopyranose (**9**), respectively, in yields of 85–90%. Likewise, 3,4-di-*O*-acetyl- (**4**), 3,4-di-*O*-benzoyl- (**5**), and 3,4-di-*O*-benzyl-D-galactal (**6**) gave 4-*O*-acetyl-1,6-anhydro-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**10**), 1,6-anhydro-4-*O*-benzoyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**11**), and 1,6-anhydro-4-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**12**), respectively, in yields of 80–86%.

Compounds **7–12** were characterised by comparison of the $^1$H-n.m.r. data with those[4c] of 1,6-anhydro-2,3-dideoxy-β-DL-*erythro*- and -β-DL-*threo*-hex-2-enopyranose.

*IICT Communication No. 2797.
† To whom correspondence, should be addressed
‡ National Chemical Laboratory, Poona 411 008, India

0008-6215/92/$ 05.00 



| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1 | X = H, | Y = OR, | R = Ac | 7 | X = H, | Y = OAc | |
| 2 | X = H, | Y = OR, | R = Bz | 8 | X = H, | Y = OBz | |
| 3 | X = H, | Y = OR, | R = Bn | 9 | X = H, | Y = OBn | |
| 4 | X = OR, | Y = H, | R = Ac | 10 | X = OAc, | Y = H | |
| 5 | X = OR, | Y = H, | R = Bz | 11 | X = OBz, | Y = H | |
| 6 | X = OR, | Y = H, | R = Bn | 12 | X = OBn, | Y = H | |

The signal for C-1 at $\delta \sim 95.0$ in the $^{13}C$-n.m.r. spectra of **7–12** further confirmed the presence of the 1,6-anhydropyranose ring. There was no evidence for the formation of products resulting from intermolecular Ferrier reaction or allylic rearrangement.

## EXPERIMENTAL

*General methods.* — N.m.r. spectra ($^1H$, 90 and 300 MHz; $^{13}C$, 22.63 MHz) were recorded for solutions in $CDCl_3$ (internal $Me_4Si$) with Bruker WH-90-FT and Varian MSL-300 spectrometers. Optical rotations were measured on a JASCO DIP-181 polarimeter on 1% solutions in $CHCl_3$. Silica gel (60–120 mesh, Acme) was used for column chromatography, together with 4:1 hexane–ethyl acetate. T.l.c. was performed on Silica Gel G (Acme) with detection by charring with $H_2SO_4$.

*General procedure for intramolecular Ferrier reactions.* — Boron trifluoride etherate (1 mmol) was added to a solution of the substrate (**1–6**, 10 mmol) in dry dichloromethane (35 mL) at 0° and the mixture was allowed to reach room temperature. After completion of the reaction (usually 1 h), solid anhydrous $K_2CO_3$ (1 g) was added, the mixture was stirred for 30 min, diluted with more dichloromethane (200 mL), washed with water, and dried ($Na_2SO_4$), and the solvent was evaporated. The residue was washed through a bed of silica gel (40 g) with 4:1 hexane–ethyl acetate to yield **7–12** (80–90%).

4-*O*-Acetyl-1,6-anhydro-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (**7**), isolated as a syrup (85%), had $[\alpha]_D$ +190°. N.m.r. data: $^1H$, $\delta$ 3.45 (dd, 1 H, $J_{6exo,6endo}$ 8.0, $J_{5,6endo}$ 1.6 Hz, H-6*endo*), 3.92 (dd, 1 H, $J_{5,6exo}$ 6.5 Hz, H-6*exo*), 4.65–4.9 (m, 2 H, H-4,5), 5.5 (dd, 1 H, $J_{1,2}$ 3.4, $J_{1,3}$ 0.8 Hz, H-1), 5.71 (dddd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 4.5, $J_{3,5}$ 1.7 Hz, H-3), 6.15 (ddd, 1 H, $J_{2,4}$ 0.9 Hz, H-2); $^{13}C$, $\delta$ 20.6 (q, $OCOCH_3$), 63.2 (t, C-6), 67.9, 73.4 (2 d, C-4,5), 95.2 (d, C-1), 122.8, 128.5 (2 d, C-2,3), and 173.7 (s, $OCOCH_3$).

Anal. Calc. for $C_8H_{10}O_4$: C, 65.20; H, 5.89. Found: C, 56.14; H, 5.81.

4-*O*-Acetyl-1,6-anhydro-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**10**), isolated as a syrup (81%), had $[\alpha]_D$ −13.5°. N.m.r. data: $^1H$, $\delta$ 2.05 (s, 3 H, OAc), 3.82 (ddd, 1 H, $J_{6exo,6endo}$ 7.8, $J_{5,6exo}$ 6.4, $J_{4,6exo}$ 1.3 Hz, H-6*exo*), 4.1 (ddd, 1 H, $J_{5,6endo}$ 1.6, $J_{1,6endo}$ 0.5 Hz, H-6*endo*), 4.64 (dddd, $J_{3,4}$ 1.3, $J_{4,5}$ 4.7 Hz, H-5), 5.48–6.0 (m, 4 H, H-1,2,3,4); $^{13}C$, $\delta$ 64.1 (t, C-6), 68.7, 79.5 (2 d, C-4,5), 95.3 (d, C-1), 127.1, 128.7 (2 d, C-2,3), and 174.1 (s, $OCOCH_3$).

*Anal.* Found: C, 56.11; H, 5.79.

1,6-Anhydro-4-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (**8**), isolated as a syrup (84%), had $[\alpha]_D$ +150°. N.m.r. data: $^1$H (300 MHz): $\delta$ 3.55 (dd, 1 H, $J_{6exo,6endo}$ 8.0, $J_{5,6endo}$ 1.9 Hz, H-6*endo*), 3.95 (dd, 1 H, $J_{5,6exo}$ 6.5 Hz, H-6*exo*), 4.79 (dddd, 1 H, $J_{4,5}$ 1.1, $J_{3,5}$ 1.8 Hz, H-5), 4.97 (ddd, 1 H, $J_{3,4}$ 4.3, $J_{2,4}$ 1.0 Hz, H-4), 5.57 (dd, 1 H, $J_{1,2}$ 3.5, $J_{1,3}$ 0.6 Hz, H-1), 5.85 (dddd, 1 H, $J_{2,3}$ 9.6 Hz, H-3), 6.18 (ddd, 1 H, H-2), 7.35–8.1 (m, 5 H, Ph); $^{13}$C, $\delta$ 62.7 (t, C-6), 68.0, 73.8 (2 d, C-4,5), 95.0 (d, C-1), 122.1, 127.7, 129.4, 132.3, 132.8 (C-2,3 and aromatic), and 165.5 (s, O*C*OPh).

*Anal.* Calc. for $C_{13}H_{12}O_4$: C, 66.99; H, 5.19. Found: C, 66.86; H, 5.11.

1,6-Anhydro-4-*O*-benzoyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**11**), isolated as a syrup (82%), had $[\alpha]_D$ −8.2°. N.m.r. data: $^1$H, $\delta$ 3.91 (ddd, 1 H, $J_{6exo,6endo}$ 7.8, $J_{5,6exo}$ 6.4, $J_{4,6exo}$ 1.4 Hz, H-6*exo*), 4.2 (ddd, 1 H, $J_{5,6endo}$ 1.5, $J_{1,6}$ 0.5 Hz, H-6*endo*), 4.75 (dddd, 1 H, $J_{3,4}$ 1.3, $J_{4,5}$ 4.6 Hz, H-5), 5.45 (dd, 1 H, $J_{1,2}$ 3.1, $J_{1,3}$ 0.8 Hz, H-1), 5.7–5.90 (m, 3 H, H-2,3,4), 7.35–8.15 (m, 5 H, Ph); $^{13}$C, $\delta$ 64.9 (t, C-6), 69.1, 78.7 (2 d, C-4,5), 95.1 (d, C-1), 127.3, 128.5 (2 d, C-2,3), and 165.2 (s, O*C*OPh).

*Anal.* Found: C, 66.83; H, 5.08.

1,6-Anhydro-4-*O*-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (**9**), isolated as a syrup (80%), had $[\alpha]_D$ +149°. N.m.r. data: $^1$H, $\delta$ 3.35 (dd, 1 H, $J_{6exo,6endo}$ 8.0, $J_{5,6endo}$ 1.7 Hz, H-6*endo*), 3.45 (ddd, 1 H, $J_{3,4}$ 4.3, $J_{4,5}$ 1.1, $J_{2,4}$ 1.0 Hz, H-4), 3.83 (dd, 1 H, $J_{5,6exo}$ 6.3 Hz, H-6*exo*), 4.2–4.8 (m, 3 H, H-5 and OC$H_2$Ph), 5.54 (dd, 1 H, $J_{1,2}$ 3.5, $J_{1,3}$ 0.9 Hz, H-1), 5.75 (dddd, 1 H, $J_{2,3}$ 9.5, $J_{3,5}$ 1.7 Hz, H-3), 6.12 (ddd, 1 H, H-2), 7.2–7.4 (m, 5 H, Ph); $^{13}$C, $\delta$ 62.8 (t, C-6), 70.3, 72.8, 73.9 (2 d, t, C-4,5 and O*C*$H_2$Ph), 95.1 (d, C-1), 122.0–130.0 (C-2,3 and aromatic).

*Anal.* Calc. for $C_{13}H_{14}O_3$: C, 71.32; H, 6.45. Found: C, 71.25; H, 6.36.

1,6-Anhydro-4-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (**12**), isolated as a syrup (82%), had $[\alpha]_D$ −9.5°. N.m.r. data: $^1$H, $\delta$ 3.87 (ddd, 1 H, $J_{6exo,6endo}$ 7.9, $J_{5,6exo}$ 6.3, $J_{4,6exo}$ 1.4 Hz, H-6*exo*), 4.15 (ddd, 1 H, $J_{5,6endo}$ 1.6, $J_{1,6endo}$ 0.5 Hz, H-6*endo*), 4.25–4.65 (m, 4 H, H-4,5, and OC$H_2$Ph), 5.38 (dd, 1 H, $J_{1,2}$ 3.1, $J_{1,3}$ 0.7 Hz, H-1), 5.65 (ddd, 1 H, $J_{2,3}$ 9.9, $J_{3,4}$ 2.0 Hz, H-3), 5.86 (ddd, 1 H, $J_{2,4}$ 1.4 Hz, H-2), 7.2–7.4 (m, 5 H, Ph); $^{13}$C, $\delta$ 64.5 (t, C-6), 69.5, 73.9, 78.2 (t, 2 d, C-4,5 and O*C*$H_2$Ph), 95.0 (d, C-1), 127.2, 128.6 (2 d, C-2,3), and 121.0–132.0 (aromatic).

*Anal.* Found: C, 71.21; H, 6.34.

## REFERENCES


1 M. Cerny and J. Stanek, *Adv. Carbohydr. Chem. Biochem.*, 34 (1977) 23–177.

2 (a) H. Paulsen, B. Schroder, H. Bottcher, and R. Hohlweg, *Chem. Ber.*, 114 (1981) 322–332; M. Georges, D. Mackay, and B. Fraser-Reid, *J. Am. Chem. Soc.*, 106 (1984) 731–734; (c) P. J. Hodges and G. Proctor, *Tetrahedron Lett.*, 26 (1985) 4111–4114.

3 L. Magdzinski and B. Fraser-Reid, *Can. J. Chem.*, 66 (1988) 2819–2825.

4 (a) M. Georges and B. Fraser-Reid, *Carbohydr. Res.*, 127 (1984) 162–164; (b) M. V. Rao and M. Nagarajan, *ibid.*, 162 (1987) 141–144; (c) K. Ranganayakulu, U. P. Singh, T. P. Murray, and R. K. Brown, *Can. J. Chem.*, 52 (1974) 988–992; (d) P. Koll, T. Schultek, and R. W. Rennecke, *Chem. Ber.*, 109 (1976) 337–344.

5 R. J. Ferrier and N. Prasad, *J. Chem. Soc. C*, (1969) 570–575.

6 H. B. Mereyala and K. C. Venkataramanaiah, *J. Chem. Res. (S)*, (1991) 197.