Supporting Information for

A General Method for Synthesizing Pyranoid Glycols. A New Route to Allal and Gulal Derivatives

Omar Boutureira, Miguel Angel Rodríguez, M. Isabel Matheu,
Yolanda Díaz*, Sergio Castellón*

Departament de Química Anàtica i Química Orgànica, Facultat de Química,
C/ Marcel·lí Domingo s/n, 43007 Tarragona, Spain.

Table of contents

1. General Procedure for synthesizing glycals	3
2. Synthesis of 6	3
3. Synthesis of 14	4
4. Synthesis of 15	4
5. Synthesis of 17	5
6. Synthesis of 18	6
7. Synthesis of 19	6
8. Synthesis of 22	7
9. ¹ H NMR of 5	8
10. ¹³ C NMR of 5	9
11. ¹ H NMR of 6	10
12. ¹³ C NMR of 6	11
13. ¹ H NMR of 7	12
14. ¹³ C NMR of 7	13
15. ¹ H NMR of 8	14
16. ¹³ C NMR of 8	15
17. ¹ H NMR of 10	16
18. ¹³ C NMR of 10	17
19. ¹ H NMR of 11	18
20. ¹ H NMR of 12	19
21. ¹ H NMR of 14	20
22. ¹³ C NMR of 14	21
23. ¹ H NMR of 15	22
24. ¹³ C NMR of 15	23
25. ¹ H NMR of 17	24
26. ¹³ C NMR of 17	25
27. ¹ H NMR of 18	26
28. ¹³ C NMR of 18	27
29. ¹ H NMR of 19	28
30. ¹³ C NMR of 19	29
31. References	30

General Procedure for synthesizing glycals from 2-deoxy-2-iodo-1-thio-glycosides

The 2-deoxy-2-iodo-pyranoside derivative (1 mmol) and NaOAc (1.4 mmol) were dissolved in a mixture of THF (1.7 mL) and acetic acid (63 μ L) and cooled to 0 $^{\circ}$ C. Zn/Cu couple (661 mg) was then added and the reaction was allowed to reach room temperature. The mixture was then diluted with dichloromethane and washed with a saturated solution of NaHCO₃. The combined aqueous layer was extracted with dichloromethane, and the combination of organic layers was dried with MgSO₄ and concentrated. The residue was purified by chromatographic techniques.

3,4,6-tri-*O*-benzyl-D-allal (3,4,6-tri-*O*-benzyl-D-ribo-hex-1-enitol) (**6**).¹

The title compound was prepared following the general procedure above starting from phenyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-1-thio- α -D-*allo*-pyranoside (**5**) (α : β 1:9) (75 mg, 0.11 mmol) in a mixture of 0.2 mL THF, 10 μ L acetic acid, NaOAc (13 mg, 0.16 mmol) and 72.7 mg Zn/Cu couple. The reaction was monitored by TLC (EtOAc/hexane 1:3) and was allowed to reach room temperature over a period of 6 h. The crude product was purified by radial chromatography (from hexane to EtOAc/hexane 1:3) to afford the product **6** (48 mg, 100%) as a yellowish syrup.

R_f (EtOAc/hexane 1:3): 0.43.

Anal. Calcd for C₂₇H₂₈O₄: 77.86% C, 6.78% H. Found: 77.70% C, 6.70% H.

RMN ¹H (CDCl₃, 400 MHz) δ in ppm: 7.36-7.25 (15H, m, Ar), 6.47 (1H, d, J_{1,2}= 6 Hz, H-1), 4.90 (1H, dd, J_{1,2}=J_{2,3}= 6 Hz, H-2), 4.72 (1H, d, J_{AB}=12 Hz, CH₂Ph), 4.64 (1H, d, J_{AB}=11.6 Hz, CH₂Ph), 4.63 (1H, d, J_{AB}=12 Hz, CH₂Ph), 4.60 (1H, d, J_{AB}=11.6 Hz, CH₂Ph), 4.59 (1H, d, J_{AB}=11.6 Hz, CH₂Ph), 4.47 (1H, d, J_{AB}=11.6 Hz, CH₂Ph), 4.31 (1H, app. t (full paper), J_{4,5}= 10.4 Hz, H-5), 3.96 (1H, dd, J_{2,3}= 5.2 Hz, J_{3,4}= 3.6 Hz, H-3), 3.85 (2H, m, H-6a,b), 3.79 (1H, dd, J_{4,5}= 10.4 Hz, J_{3,4}= 3.6 Hz, H-4).

RMN ¹³C (CDCl₃, 100.6 MHz) δ in ppm: 146.9 (C-1), 138.8-138.1 (C, Ar), 128.6-127.8 (CH, Ar), 98.3 (C-2), 74.0 (C-4), 73.8 (CH₂Ph), 73.2 (C-5), 71.5, 70.5 (2CH₂Ph), 69.0 (C-6), 65.5 (C-3).

3,4,6-tri-*O*-benzyl-D-gulal (3,4,6-tri-*O*-benzyl-D-xylo-hex-1-enitol) (14).

The title compound was prepared following the general procedure starting from the phenyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-1-thio- α -D-*gulo*-pyranoside (**7**) (α : β 10:1) (159 mg, 0.24 mmol) in a mixture of 0.4 mL THF, 20 μ L acetic acid, NaOAc (28 mg, 0.34 mmol) and 161 mg Zn/Cu couple for 1 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). The crude product was purified by radial chromatography (EtOAc/hexane 1:4) to afford the product **14** (50 mg, 92%) as a colorless syrup.

R_f (EtOAc/hexane 1:3): 0.46.

$[\alpha]_D^{25} = 64.3$ (CH_2Cl_2 , $c = 2$)

Anal. Calcd for $\text{C}_{27}\text{H}_{28}\text{O}_4$: 77.86% C, 6.78% H. Found: 77.80% C, 6.74% H

RMN ^1H (CDCl_3 , 400 MHz) δ in ppm: 7.36-7.21 (10H, m, Ar), 6.36 (1H, ddd, $J_{1,2} = 6.4$ Hz, $J_{1,3a} = 1.6$ Hz, $J_{1,3b} = 2.4$ Hz, H-1), 4.63 (1H, ddd, $J_{2,1} = 6.4$ Hz., $J_{2,3a} = 5.2$ Hz., $J_{2,3b} = 2.6$ Hz., H-2), 4.62-4.50 (4H, m, $J_{AB} = 9.0$ Hz., $J_{AB'} = 12.0$ Hz., 4 CH_2Ph), 3.90 (1H, ddd, $J_{5,4} = 8.0$ Hz., $J_{5,6a} = J_{5,6b} = 4.0$ Hz., H-5), 3.79 (1H, m, H-4, H-6a, H-6b), 2.38 (1H, dddd, $J_{3a,3b} = 16.4$ Hz., $J_{3a,2} = 5.2$ Hz., $J_{3a,4} = 6.0$ Hz., $J_{3a,1} = 1.6$ Hz., H-3a), 2.08 (1H, dddd, $J_{3b,3a} = 16.4$ Hz., $J_{3b,2} = 2.6$ Hz., $J_{3b,4} = 8.4$ Hz., $J_{3b,1} = 2.4$ Hz., H-3b) .

RMN ^{13}C (CDCl_3 , 100.6 MHz) δ in ppm: 143.3 (C-1), 138.4-127.8 ($\text{C}_{\text{aromatic}}$), 97.8 (C-2), 76.9 (C-5), 73.7, 71.3 (2 CH_2Ph), 70.7 (C-4), 69.2 (C-6), 26.7 (C-3).

6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-D-galactal

(6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-D-lyxo-hex-1-enitol) (15).²

The title compound was prepared following the general procedure above starting from **8** (α : β 40:1) (200 mg, 0.30 mmol) in a mixture of 0.5 mL THF, 24 μ L acetic acid, NaOAc (36 mg, 0.42 mmol) and 200 mg Zn/Cu couple for 1 h. The reaction was monitored by TLC (CH_2Cl_2). The crude product was purified by radial chromatography (from hexane to EtOAc/hexane 1:3) to afford the expected product **15** (110 mg, 86%) as a colorless syrup.

3,4-*O*-isopropylidene-D-arabinal (3,4-*O*-isopropylidene-D-*erythro*-pent-1-enitol) (18).⁴

The title compound was prepared following the general procedure above starting from **11** ($\alpha:\beta$ 12:1) (55 mg, 0.14 mmol) in a mixture of 240 μ L THF, 11 μ L acetic acid, NaOAc (16 mg, 0.20 mmol) and 93 mg Zn/Cu couple for 1.5 h. The reaction was monitored by TLC (CH_2Cl_2). The crude product was purified by flash chromatography (CH_2Cl_2) to afford the product **18** (200 mg, 91%) as a colorless syrup.

R_f (CH_2Cl_2): 0.33.

Anal. Calcd for $\text{C}_8\text{H}_{12}\text{O}_3$: 70.58% C, 5.88% H. Found: 70.32% C, 5.74% H

RMN ^1H (CDCl_3 , 400 MHz) δ in ppm: 6.52 (1H, d, $J_{1,2} = 9$ Hz, H-1), 5.13 (1H, m, H-2), 4.51 (1H, m, H-3), 4.20 (1H, m, H-4), 4.05 (1H, m, H-5a), 3.65 (1H, m, H-5b), 1.51, 1.39, (6H, s, 2 CH_3).

RMN ^{13}C (CDCl_3 , 100.6 MHz) δ in ppm: 146.9 (C-1), 108.9 (C_{ketal}), 99.2 (C-2), 69.6 (C-3), 66.8 (C-4), 64.3 (C-5), 27.9, 25.5 (2 CH_3).

4,6-di-*O*-benzyl-3-deoxy-D-allal (4,6-di-*O*-benzyl-D-*erythro*-pent-1-enitol) (19).⁵

The title compound was prepared following the general procedure above starting from an equimolar mixture of **12** (130 mg, 0.24 mmol) in a mixture of 0.5 mL THF, 20 μ L acetic acid, NaOAc (27 mg, 0.33 mmol) and 160 mg Zn/Cu couple. The reaction was monitored by TLC (EtOAc/hexane 1:3) and was allowed to reach 15 $^\circ\text{C}$ over a period of 4 h. The crude product was purified by radial chromatography (EtOAc/hexane 1:4) to afford the expected product **19** (50 mg, 71%) as a colorless syrup.

R_f (EtOAc/hexane 1:3): 0.40.

Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_3$: 77.42% C, 7.10% H. Found: 77.20% C, 7.01% H

RMN ^1H (CDCl_3 , 400 MHz) δ in ppm: 7.35-7.23 (15H, m, Ar), 6.61 (1H, d, $J_{1,2}$ = 6.0 Hz, H-1), 4.95 (1H, ddd, $J_{1,2}$ = 6.0 Hz., $J_{2,3}$ = 5.2 Hz., $J_{2,4}$ = 1.8 Hz., H-2), 4.59-4.27 (6H, m, J_{AB} = 12.0 Hz., $J_{AB'}$ = 8.6 Hz. $J_{AB''}$ = 12.6 Hz., 6CH₂Ph), 4.16 (1H, ddd, $J_{4,5}$ = 1.6 Hz., $J_{5,6a}$ = 6.4 Hz., $J_{5,6b}$ = 5.6 Hz., H-5), 3.76 (1H, dd, $J_{6a,5}$ = 6.4 Hz., $J_{6a,b}$ = 10.0 Hz., H-6a), 3.74 (1H, d, $J_{2,3}$ = 5.2 Hz, H-3), 3.66 (1H, d, $J_{4,5}$ = 1.6 Hz, H-4), 3.58 (1H, dd, $J_{5,6b}$ = 5.6 Hz., $J_{6a,b}$ = 10.0 Hz., H-6b).

RMN ^{13}C (CDCl_3 , 100.6 MHz) δ in ppm: 146.9 (C-1), 138.5-127.9 ($\text{C}_{\text{aromatic}}$), 98.7 (C-2), 73.6 (CH₂Ph), 73.0 (C-5), 72.7 (C-4), 72.4, 70.0 (2CH₂Ph), 69.1 (C-6), 67.3 (C-3).

Phenyl 4,6-di-O-benzyl-2,3-dideoxy-1-thio- α/β -D-ribo-pyranoside (22**).**

The title compound was prepared following the general procedure above starting from an equimolar mixture of **21** (40 mg, 0.08 mmol) in a mixture of 0.5 mL THF, 7 μL acetic acid, NaOAc (9.6 mg, 0.12 mmol) and 53 mg Zn/Cu couple for 1.5 h. The reaction was monitored by TLC (EtOAc/hexane 1:4). The crude product was purified by radial chromatography (EtOAc/hexane 1:5) to afford the product **22** (31 mg, 88%) as a 1:1 α/β anomeric mixture as a colorless syrup.

Anal. Calcd for $\text{C}_{26}\text{H}_{26}\text{O}_3\text{S}$: 74.26% C, 6.67% H, 7.62% S. Found: 74.42% C, 6.75% H, 7.75% S.

RMN ^1H (CDCl_3 , 400 MHz) δ in ppm: 7.61-7.22 (15H, m, Ar), 4.71 (1H, d, $J_{1,2a}$ = 10.4 Hz, H-1), 4.61-4.40 (4H, m, J_{AB} = 11.6 Hz., $J_{AB'}$ = 12.0 Hz., 4CH₂Ph), 3.80-3.68 (4H, m, H-2a, H-2b, H-6a, H-6b), 3.58 (1H, ddd, $J_{5,4}$ = 9.6 Hz., $J_{5,6a}$ = 2.0 Hz., $J_{5,6b}$ = 4.8 Hz., H-5), 3.47 (1H, ddd, $J_{4,5}$ = 9.6 Hz., $J_{4,3a}$ = 4.4 Hz., $J_{4,3b}$ = 10.4 Hz., H-4), 2.88 (1H, ddd, $J_{3a,3b}$ = 12.4 Hz., $J_{3a,2a}$ = 4.8 Hz., $J_{3a,4}$ = 4.4 Hz., H-3a), 2.03 (1H, ddd, $J_{3b,3a}$ = 12.4 Hz., $J_{3b,4}$ = 10.4 Hz., $J_{3b,2a}$ = 11.2 Hz., H-3b).

RMN ^{13}C (CDCl_3 , 100.6 MHz) δ in ppm: 133.4-127.8 ($\text{C}_{\text{aromatic}}$), 89.5 (C-1), 82.0 (C-5), 73.6 (C-4), 72.7, 71.7 (2CH₂Ph), 69.3 (C-6), 45.7 (C-2), 41.9 (C-3).

7 α / β

References

- ¹ a) Tamarez, M.M.; Franck, R.W.; Geer, A. *Tetrahedron* **2003**, *59*, 4249-4259. b) Dios, A.; Franck, R.W.; Capossi, G.; Menichetti, S.; Nativi, C. *Org. Lett.* **1999**, *1*, 111-113. C. Grenwal, G.; Franck, R.W. *J. Org. Chem.* **1992**, *57*, 2084.
- ² Broddefalk, J.; Bergquist, K-E.; Kihlberg, J. *Tetrahedron*, **1998**, *54*, 12047-12050.
- ³ Wardrop, D.J.; Zhang, W. *Tetrahedron Lett.* **2002**, *43*, 5389-5391.
- ⁴ Cook, M.J.; Fletcher, M.J.E.; Gray, D.; Lovell, P.J.; Gallagher, T. *Tetrahedron* **2004**, *60*, 5085-5092.
- ⁵ a) Gopal Reddy, B.; Vankar, Y.D. *Tetrahedron Lett.* **2003**, *44*, 4765-4767. b) Fraser-Reid, B.; Radatus, B. *J. Am. Chem. Soc.* **1970**, *92*, 6661-6663.