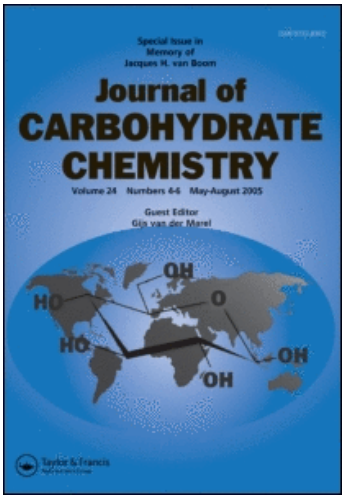

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthesis of Isomeric Benzyl 6-Deoxy-α-L-talo- and α-L-Gulopyranosides

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To cite this Article Banaszek, Anna(1994) 'Synthesis of Isomeric Benzyl 6-Deoxy-α-L-talo- and α-L-Gulopyranosides', Journal of Carbohydrate Chemistry, 13: 2, 285 — 291
To link to this Article: DOI: 10.1080/07328309408009193
URL: http://dx.doi.org/10.1080/07328309408009193

J. CARBOHYDRATE CHEMISTRY, 13(2), 285-291 (1994)

SYNTHESIS OF ISOMERIC BENZYL 6-DEOXY-α-L-TALO- AND α-L-GULOPYRANOSIDES

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Received April 2, 1993 - Final Form October 20, 1993

ABSTRACT

Synthesis of benzyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-talopyranoside (**6**) and its α-L-*gulo* isomer **7** was performed by a five-step sequence starting from L-rhamnal **1**. The L-*talo* isomer was proved to be identical with the component of *O*-antigenic polysaccharide of the *genus Rhizobium.*

INTRODUCTION

6-Deoxy-L-talose was reported to be present in some bacterial lipopolysaccharides (LPS).[1] Very recent studies on the LPS discovered that 6-deoxy-L-talose is a unique carbohydrate component of *O*-specific antigen of highly pathogenic bacteria: *Pseudomonas mallei,*[2] *Actinobacillus actinomycetemcomitans,*[3] and *Mycobacterium xenopi.*[4] In all cases the L-*talo* configuration was ascribed to the novel serotype-specific

polysaccharide component by comparison of its NMR data with those of other 6-deoxy-hexopyranoses. The structural elucidation of the carbohydrate moiety of the complex carbohydrate, based on NMR spectroscopy analysis is, however, very uncertain, despite the reliable methods used, *i.e.* 2D homonuclear shift-correlated (COSY) and one-step relayed-coherence-transfer shift-correlated (COSYRCT) spectroscopy supported by selective irradiation.[2-4] It has been demonstrated[4] in the case of a mycobacterial antigenic glycopeptidolipid, GPL X-1, whose oligosaccharide part was composed of three 6-deoxypyranoses (L-rhamnose, D-quinovose, and L-talose) that the assignment of these proton resonances to individual monosaccharide units was impossible, due to the complexity of the H-3, H-4 and H-5 regions.

The NMR analysis of the complex carbohydrates could be facilitated by direct comparison of their spectra with those of the authentic samples.

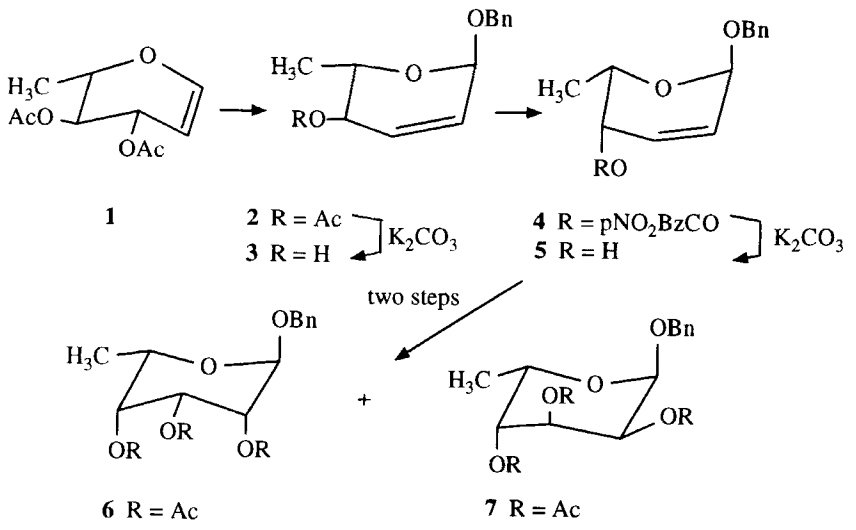
The present paper describes a new synthesis of the rare isomeric benzyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-talo- and α-L-gulopyranosides (**6** and **7**, respectively), not commercially available. Both synthetic sugars were used for comparative analysis, in the unambigous elucidation of the structure of three 6-deoxypyranoses which are the components of two *O*-antigenic polysaccharides of the *genus Rhizobium*.[5]

RESULTS AND DISCUSSION

Benzyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-talopyranoside (**6**) and its α-L-*gulo* isomer **7** were synthesized according to the sequence depicted in scheme 1.

Ferrier rearrangement[6] of the 1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol **1**[7] into the benzyl glycoside of L-*erythro* configuration **2** was performed in a 75% yield when tin(IV) chloride was used as a catalyst. The reaction of **1** with benzyl alcohol was carried out in dichloromethane at -60° → -35 °C during 0.5 h, and the α and β-anomers formed were separated by column chromatography (α : β ≈ 93 : 7).

It is worth noting that other catalysts, like $BF_3 \cdot OEt_2$, $TiCl_4$, *p*-toluenesulfonic acid or $ZnBr_2$, gave a mixture of products from which the desired glycoside **2** was isolated by distillation *in vacuo* in a 35-50% yield. The polymerized residue sludge was not identified.



SCHEME 1

Deacetylation of **2** using anhydrous potassium carbonate in methanol led to **3**. In the Mitsunobu reaction[8] with triphenylphosphine, diethylazodicarboxylate and *p*-nitrobenzoic acid, the α-anomer (**3**) smoothly underwent S_N2-type substitution with inversion of configuration to afford benzyl 2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α-L-*threo*-hex-2-enopyranoside (**4**, 90%). Debenzoylation of ester **4** under the conditions described for **2** gave **5** (76%). The structure of both isomeric, unsaturated sugars **2** and **4** was established on the basis of ^1H NMR spectral data, *i.e.*, the broad triplet of H-1 at 4.9 ppm and allylic coupling constant $J_{1,2}$ = 1.3 Hz, as well as $J_{3,4}$ = 3.3 Hz and $J_{4,5}$ = 9.2 Hz. These data confirmed the α-L-erythro configuration of **2**, whereas $J_{3,4}$ = 5.5 Hz and $J_{2,4}$ = Hz were characteristic of the α-L-threo configuration of **4**. The comparable patterns have been described for similar compounds of D-configuration.[10] Exhaustive *cis*-hydroxylation of the allylic alcohol **5** with osmium tetroxide in pyridine, followed by acetylation resulted in the formation of two isomeric sugars **6** and **7**, which were separated by column chromatography in a 70% yield (ratio **6** : **7** ≈ 2 : 1).

The configuration of the isomeric 6-deoxypyranosides **6** and **7** was determined univocally from their spectral data. Thus, the ^1H NMR spectrum of **6** showed the coupling constant values $J_{1,2}$ = 1.1 Hz and $J_{3,4}$ = 3.7 Hz, which corresponded to the *talo*

isomer (equatorial-equatorial and axial-equatorial proton arrangements, respectively). In contrast, the ^{1}H NMR spectrum of isomer **7** showed $J_{1,2}$ = 4.0 and $J_{3,4}$ = 0.7 Hz, corresponding to the *gulo* configuration (equatorial-axial and equatorial-equatorial proton disposition, respectively). All other protons of **6** and **7** had the orientation described for the substrate **4**.

The selectivity of hydroxylation of **5** is apparently governed by the *trans* disposition of the substituents at C-1 and C-4.[11] The present results are comparable with those of *cis*-hydroxylation of racemic methyl 2,3,6-trideoxy-α-*threo*-hexopyranoside.[12]

6-Deoxy sugars **6** and **7**, readily accessible by the here described route, were used in the structural studies of two LPS isolated from *Rhizobium leguminosarum bv. trifolii* strains 24.1 and the nodulating exo-mutant AR20.[5]

By way of direct comparison of three 6-deoxy sugars isolated from LPS with the authentic samples using gas-liquid chromatography (GLC), combined gas-liquid chromatography-mass spectrometry (GLC-MS) and ^{1}H NMR spectroscopy, two major components were identified as L-rhamnose and 6-deoxy-L-talose, and the third minor component as 6-deoxy-L-gulose.[5]

EXPERIMENTAL

^{1}H NMR spectra were recorded in $CDCl_3$ or in a C_6D_6 solution with a Bruker 500 MHz or a Varian 200 MHz spectrometer (TMS = 0 ppm). Optical rotations were measured with a Perkin-Elmer 141 spectropolarimeter. Melting points are uncorrected. Column chromatography was performed on silica gel (Merck, 230-400 mesh), and TLC on plates coated with silica gel GF_{254} (Merck). PE = petroleum ether.

Benzyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (**2**). To L-rhamnal **1**[7] (10.6 g, 49.5 mmol) and benzyl alcohol (5.9 g, 54.5 mmol) dissolved in dry dichloromethane (100 mL), dropwise was added a solution of $SnCl_4$ (3 mL, 24.7 mmol in 47 mL of dry CH_2Cl_2) at -60 °C under argon. The mixture was stirred for 0.5 h at -60 °C, whereupon the temperature was allowed to rise to -35 °C. The solution was then neutralized with Et_3N (3.2 mL, 27.1 mmol), diluted with dichloromethane, and poured into an ice-cooled saturated solution of $NaHCO_3$. The organic layer was washed with

brine, dried over $MgSO_4$, and concentrated to dryness. The residual oil was purified by flash chromatography (PE-EtOAc, 95 : 5) to yield 9.7 g (75%) of compound **2** as a colourless oil; $[\alpha]_D^{20}$ -118.8° (*c* 2.45, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.19 (d, 3H, 6-CH_3), 2.10 (s, 3H, Ac), 4.00 (dq, 1H, H-5), 4.60, 4.80 (2x1H, ABq of CH_2Ph), 5.05-5.08 (m, 2H, H-1, H-4), 5.81 (ddd, 1H, H-2), 5.86 (bd, 1H, H-3), 7.28-7.36 (m, 5H, arom.), $J_{1,2}$ = 1.1, $J_{2,3}$ = 10.6, $J_{4,5}$ = 2.9, $J_{5,6}$ = 6.2 Hz. ^1H NMR (C_6D_6) δ 1.16 (d, 3H, 6-CH_3), 1.62 (s, 3H, Ac), 4.13 (dq, 1H, H-5), 4.40, 4.67 (2x1H, ABq of CH_2Ph, J = 12.1 Hz), 4.90 (bt, 1H, H-1), 5.25 (ddd, 1H, H-4), 5.59 (ddd, 1H, H-3), 5.78 (dt, 1H, H-2), 7.24-7.32 (m, 5H, arom.), $J_{1,2}$ = 1.3, $J_{2,3}$ = 10.2, $J_{2,4}$ = 1.8, $J_{3,4}$ = 3.3, $J_{4,5}$ = 9.2, $J_{5,6}$ = 6.2 Hz.[13]

Anal. Calcd for $C_{15}H_{18}O_4$ (262.31): C, 68.69; H, 6.92. Found: C, 68.67; H, 7.08.

Benzyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (3). To a stirred solution of **2** (9.71 g, 37.06 mmol) in dry methanol (70 mL), anhyd K_2CO_3 (1.68 g, 55.6 mmol) was added. After 2 h of stirring at room temperature the mixture was filtered through Celite, and was concentrated to dryness. Purification of the residue by flash chromatography (PE - acetone, 95 : 5) yielded 7.95 g (77%) of **3**; colourless oil, $[\alpha]_D^{20}$ -41.6° (*c* 2.63, $CHCl_3$); ^1H NMR (C_6D_6) δ 1.28 (d, 3H, 6-CH_3), 2.06 (bs, 1H, OH), 3.74 (dq, 1H, H-5), 3.82 (dq, 1H, H-4), 4.58, 4.77 (2x1H, AB of CH_2Ph, J = 11.9 Hz), 5.02 (bt, 1H, H-1), 5.74 (ddd, 1H, H-3), 5.91 (dt, 1H, H-2), 7.25 (m, 5H, arom.), $J_{1,2}$ = 1.2, $J_{2,3}$ = 10.1, $J_{2,4}$ = 1.5, $J_{3,4}$ = 3.35, $J_{4,5}$ =8.9, $J_{5,6}$ = 6.2 Hz.

Anal. Calcd for $C_{13}H_{16}O_3 \cdot (CH_3)_2CO$ (278.34): C, 69.04; H, 7.97. Found: C, 69.23; H, 7.79.

Benzyl 2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α-L-*threo*-hex-2-enopyranoside (4). A mixture of compound **3** (5.5 g, 20.4 mmol), triphenylphosphine (10.75 g, 41 mmol), *p*-nitrobenzoic acid (6.85 g, 41 mmol) and diethylazodicarboxylate (6.4 mL, 41 mmol) in 100 mL of dry THF was stirred for 2 h at room temperature. Then the mixture was concentrated *in vacuo*, the residue was dissolved in dichloromethane, washed with water and saturated $NaHCO_3$, dried over $MgSO_4$ and concentrated to dryness. The residue was purified by flash chromatography (PE - acetone, 95 : 5) to give 6.75 g (92%) of **4**; mp 112-113 °C; $[\alpha]_D^{20}$ +240.8° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.26 (d, 3H, 6-CH_3), 4.39 (dq, 1H, H-5), 4.66, 4.80 (2x1H, AB of CH_2Ph, J = 11.9 Hz), 5.17 (dd, 1H, H-4), 5.19 (bd, 1H, H-1), 6.11 (ddd, 1H, H-2), 6.20 (ddd, 1H, H-3), 7.40-8.25 (m, 9H, arom.), $J_{1,2}$ = 3.1, $J_{1,3}$ = 0.9, $J_{2,3}$ = 9.9, $J_{2,4}$ = 0.6, $J_{3,4}$ = 5.5, $J_{4,5}$ = 2.4, $J_{5,6}$ = 6.5 Hz.

Anal. Calcd for $C_{20}H_{19}NO_6$ (369.37): C, 65.03; H, 5.18; N, 3.79. Found: C, 65.26; H, 4.99; N, 3.91.

Benzyl 2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranoside (**5**). Compound **4** (7 g, 19 mmol) dissolved in a mixture of 200 mL of dry methanol and 200 mL of dichloromethane was treated with anhyd K_2CO_3 (4 g, 28.5 mmol) and the mixture was stirred at room temperature. After 2 h of standing the mixture was filtered through Celite, concentrated to dryness, whereupon the residue was purified by flash chromatography (PE - acetone, 9 : 1) to afford 4 g (76%) of **5**; mp 60-61 °C; $[\alpha]_D^{20}$ +102.6° (*c* 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.27 (d, 3H, 6-CH_3), 1.60 (d, 1H, OH), 3.59 (ddd, 1H, H-4), 4.16 (dq, 1H, H-5), 4.60, 4.77 (2x1H, AB of CH_2Ph, J = 11.9 Hz), 5.05 (bd, 1H, H-1), 5.89 (ddd, 1H, H-2), 6.18 (ddd, 1H, H-3), 7.25-7.37 (m, 5H, arom.), $J_{1,2}$ = 3.1, $J_{1,3}$ = 0.9, $J_{2,3}$ = 9.9, $J_{2,4}$ = 0.5, $J_{3,4}$ = 5.6, $J_{4,5}$ = 2.2, $J_{5,6}$ = 6.6, $J_{4,OH}$ = 10.3 Hz.

Anal. Calcd for $C_{13}H_{16}O_3 \cdot (CH_3)_2CO$ (278.34): C, 69.04; H, 7.97. Found: C, 69.38; H, 7.89.

Benzyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-*talo*- and **α-L-*gulo*-pyranosides** (**6** and **7**, respectively). To a solution of **5** (0.139 g, 0.5 mmol) in 2 mL of pyridine OsO_4 (0.14 g, 0.55 mmol) of was added. After stirring at room temperature for 3 days the reaction mixture was treated with 0.58 g of $NaHSO_3$, 4 mL of pyridine, and 4 mL of H_2O for decomposition of the osmium complexes. Stirring was continued for 2 more days. Then water was added and the mixture was extracted with dichloromethane. The organic layer was washed with brine, dried, and concentrated to dryness. The residue was then acetylated using acetic anhydride in pyridine. Usual work-up gave a syrup composed of two products (TLC hexane - ethyl ether, 1: 1) which was chromatographed on a silica gel column. Elution with hexane - ethyl ether (3:1) afforded pure **7** (43 mg, 23%) as the first fraction, and then the *talo* isomer **6** (89 mg, 47%) as the second fraction.

Characterization data of **6** : $[\alpha]_D^{20}$ -90.1° (*c* 1.0, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 1.19 (d, 3H, 6-CH_3), 1.99 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.16 (s, 3H, Ac), 4.16 (dq, 1H, H-5), 4.63 (q, 2H, AB of CH_2Ph, J = 11.9 Hz), 4.92 (d, 1H, H-1), 5.11-5.17 (m, 2H, H-2, H-4), 5.32 (t, 1H, H-3), 7.3-7.4 (m, 5H, arom.), $J_{1,2}$ = 1.1, $J_{2,3}$ = 3.7, $J_{3,4}$ = 3.7, $J_{4,5}$ = 1.1, $J_{5,6}$ = 6.6 Hz.

Anal. Calcd for $C_{19}H_{24}O_8$ (380.15): C, 59.98; H, 6.36; Found: C, 59.79; H, 6.77.

Characterization data of **7**: $[\alpha]_D^{20}$ -112.0° (*c* 0.7, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 1.07 (d, 3H, 6-CH_3), 2.05 (s, 3H, Ac), 2.12 (s, 3H, Ac), 2.16 (s, 3H, Ac), 4.40

(dq, 1H, H-5); 4.68 (q, 2H, AB of CH_2Ph, J = 12.4 Hz), 4.91 (dd, 1H, H-4), 5.00 (d, 1H, H-1), 5.16 (td, 1H, H-2), 5.25 (t, 1H, H-3), 7.3-7.4 (m, 5H, arom.), $J_{1,2}$ = 4.0, $J_{2,3}$ = 3.8, $J_{3,4}$ = 0.7, $J_{4,5}$ = 1.7, $J_{5,6}$ = 6.6 Hz.

Anal. Calcd for $C_{19}H_{24}O_8$ (380.15): C, 59.98; H, 6.36. Found: C, 59.63; H, 6.62.

REFERENCES AND NOTES

1. A. Markowitz, *Bacterial Proc.*, 193 (1961); *J. Biol. Chem.*, **237**, 1767 (1962); B. Lindberg in *Adv. Carbohydr. Chem. Biochem.*, **49**, 279 (1990).

2. Y. A. Knirel, N. A. Paramonov, A. S. Shashkov, N. K. Kochetkov, R. G. Yarullin, S. M.Farber, and V. I. Efremenko, *Carbohydr. Res.*, **233**, 185 (1992).

3. N. Shibuya, K. Amano, J.-I. Azuma, T. Nishihara, Y. Kitamura, T. Noguchi, and T. Koga, *J. Biol. Chem.*, **266**, 16318 (1991).

4. M. Riviére and G. Puzo, *J. Chim. Phys.*, **89**, 199 (1992).

5. R. Russa, T. Urbanik-Sypniewska, A. Banaszek. A. Zamojski, and H. Mayer, presented at *VIIth Eur. Carbohydr. Symp.*, Cracow, Poland, August 22-27, 1993.

6. R. J. Ferrier and N. Prasad, *Chem. Commun.*, **476** (1968).

7. G. Catelani and E. Mastrorilli, *J. Chem. Soc. Perkin Trans. I.*, 2717 (1983); R. Csuk, A. Fürstner, H. Stork, and H. Weidmann, *J. Carbohydr. Chem.*, **7**, 773 (1988).

8. O. Mitsunobu, *Synthesis*, 1 (1981).

9. G. Grynkiewicz and H. Burzyńska, *Tetrahedron*, **32**, 2109 (1976).

10. I. Dyorg, J. Weigand, and J. Thiem, *Liebigs Ann. Chem.*, 577 (1986).

11. A. Zamojski, A. Banaszek, and G. Grynkiewicz, *Adv. Carbohydr. Chem. Biochem.*, **40**, 1 (1982).

12. O. Achmatowicz, Jr., and B. Szechner, *Rocz. Chem.*, **49**, 1715 (1975).

13. Signals due to the β-L-*erythro* **2** (~7%) visible in ^{1}H NMR spectrum of **2** ($CDCl_3$) δ 1.36 (d, 3H, 6-CH_3), 3.91 (dq, 1H, H-5), 4.61, 4.86 (2x1H, ABq of CH_2Ph), 5.22 (m, 2H, H-1, H-4), 5.94 (m, H-2, H-3); $J_{1,2}$ = 0.8 Hz.