University of Groningen

C3 Epimerization of Glucose, via Regioselective Oxidation and Reduction

Jumde, Varsha R.; Eisink, Niek N. H. M.; Witte, Martin D.; Minnaard, Adriaan J.

Published in:
Journal of Organic Chemistry

DOI:
[10.1021/acs.joc.6b02074](https://doi.org/10.1021/acs.joc.6b02074)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2016

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Jumde, V. R., Eisink, N. N. H. M., Witte, M. D., & Minnaard, A. J. (2016). C3 Epimerization of Glucose, via Regioselective Oxidation and Reduction. *Journal of Organic Chemistry*, 81(22), 11439-11443.
<https://doi.org/10.1021/acs.joc.6b02074>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

C3 Epimerization of Glucose, via Regioselective Oxidation and Reduction

Varsha R. Jumde, Niek N. H. M. Eisink, Martin D. Witte,* and Adriaan J. Minnaard*

Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 7, 9747 AG Groningen, The Netherlands

S Supporting Information

ABSTRACT: Palladium-catalyzed oxidation can single out the secondary hydroxyl group at C3 in glucose, circumventing the more readily accessible hydroxyl at C6 and the more reactive anomeric hydroxyl. Oxidation followed by reduction results in either allose or allitol, each a rare sugar that is important in biotechnology. Also, *N*-acetylglucosamine is selectively oxidized at C3. These results demonstrate that glucose and *N*-acetylglucosamine, the most readily available chiral building blocks, can be versatile substrates in homogeneous catalysis.

Glucose, an aldohexose, is arguably the most important monosaccharide because it is used in respiration to provide energy for cells. Of the 16 stereoisomeric aldohexoses, only D-glucose, D-mannose, and D-galactose (Figure 1) are readily available. The others, and in particular most L-sugars, are rare or do not occur as such in nature.¹ As a consequence, the properties of most of these rare aldohexoses have not been studied extensively, although these could be of importance in

Figure 1. Mutarotation in glucose and the most readily available monosaccharides.

chemical biology and pharmacy as mimics of the commonly occurring aldohexoses.

Some rare sugars have been obtained by selectively epimerizing asymmetric centers in other monosaccharides. This field, in which readily available hexoses are interconverted into the desired rare hexose, is largely the realm of enzyme catalysis, applying a highly versatile but limited set of transformations.² Important biotechnological processes are, for instance, the conversion of glucose into fructose and the conversion of fructose into psicose (Figure 1).³ The possible enzymatic interconversions of the hexoses have been beautifully represented in the so-called Izumoring (see the Supporting Information), a scheme that relates all aldohexoses, 2-ketohexoses, and hexitols.⁴ From this scenario, it becomes apparent that many of these hexoses are not readily accessible using the currently known enzymatic transformations.

Chemical interconversion of hexoses provides a viable alternative to these enzymatic transformations. On a lab scale, this has been performed for several hexoses using (multistep) synthetic procedures involving protection–deprotection strategies.⁵ Depending on the target sugar, this approach can be elegant and efficient, as shown by recent work of Fleet, Jenkinson, and Kanai.^{6–8} Surprisingly, however, homogeneous catalysis has refrained from this field entirely. This is rather surprising as several of the reactions used by enzymes to

Received: August 23, 2016

Published: October 18, 2016

interconvert hexoses, in particular oxidation and reduction, are studied intensively in transition metal catalysis and organo-catalysis.^{9–12}

With a focus on oxidation, the main challenge clearly is to single out a particular hydroxyl group, as the number of hydroxyl groups in carbohydrates closely equals the number of C–H bonds. The selective oxidation of the primary hydroxyl function in pyranoses and furanoses can often be achieved with reasonable selectivity by exploiting the limited steric hindrance compared to the secondary hydroxyl groups.^{13–15} The anomeric hydroxyl group on the other hand is readily oxidized selectively in the presence of both primary and secondary hydroxyl groups because of its lower pK_a value, like in the classic oxidation with bromine.¹⁶ This leaves the very similar secondary hydroxyl groups in the case of glucopyranosides.

The group of Waymouth has shown that certain palladium catalysts can effectively discriminate between primary and secondary hydroxyl groups, preferentially oxidizing the secondary hydroxyl group.^{17,18} On this basis, we demonstrated the highly regioselective oxidation of glucopyranosides, thereby expanding the selectivity to the differentiation among secondary hydroxyl groups.¹⁹ Oxidation takes place at the C3 position to provide the corresponding 3-keto sugars. The method was shown to be effective as well for the disaccharides maltose and cellobiose, and recently even for oligomaltoses up to the 7-mer.²⁰ Waymouth and co-workers recently revealed that 6-deoxyglycosides like L-rhamnopyranosides and L-fucopyranosides and pentoses like D-xylopyranosides and D-arabinopyranosides are selectively oxidized by these catalysts, as well.²¹ Invariably, glycosides have been used as substrates with the anomeric center as part of an acetal to avoid oxidation of the anomeric alcohol and to lock the equilibrium in one anomeric form. Glucose itself, being a so-called reducing sugar, consists of a mixture of the α - and β -anomers in aqueous solution, together with small amounts of furanoses and the inferred open form. In attempts to selectively oxidize glucose at a secondary hydroxyl position, one therefore has to cope not only with the reactive anomeric hydroxyl group (C1–OH) and the more accessible primary hydroxyl group (C6–OH) but also with a potentially complex equilibrium. However, we realized that the palladium-catalyzed selective oxidation of glucose would be worth pursuing as it would silence the common opinion that unprotected, reducing sugars are unsuitable substrates for homogeneous catalysis.

Recent studies by our group have revealed that the palladium catalyst chelates preferentially with vicinal bis-equatorial hydroxyl groups, preceding oxidation. This conclusion was reached on the basis of the observation that methyl glucoside oxidizes faster than methyl mannoside (C2–OH axial) and considerably faster than methyl galactoside (C4–OH axial).²² Glucose preferentially crystallizes as the α -anomer (C1–OH axial), and we reasoned that this readily available isomer would not have an inherent preference for oxidation at the anomeric position because it lacks a vicinal bis-equatorial diol at the C1–C2 bond. Equilibration (mutarotation) of α -glucose results in the formation of β -glucose, which does possess a vicinal bis-equatorial diol at the anomeric center and hence is likely to be oxidized to the corresponding gluconolactone (vide infra). To successfully oxidize glucose, it is therefore essential to suppress mutarotation during the oxidation reaction. This process is rapid in protic solvents, including water, and catalyzed by both acid and base.^{23,24} To our delight, α -glucose turned out to be stable in DMSO, not showing notable mutarotation at room

temperature over several hours.^{25,26} Apparently, the hydroxyl groups of the glucose itself are not sufficient to catalyze mutarotation to an appreciable extent, even at a glucose concentration of up to 1.5 M.

In that event, it turned out that α -glucose **2** is rapidly and with excellent selectivity oxidized at C3 with Waymouth's catalyst **1** and benzoquinone as a co-oxidant in DMSO. By NMR, no gluconolactone (the product resulting from oxidation at the anomeric center) could be detected. The reaction is exceptionally fast, reaching full conversion within 1 h with catalyst loadings as low as 0.5 mol % (Scheme 1).

Scheme 1. Regioselective Oxidation of α -Glucose and *N*-Acetyl- α -glucosamine^a

^aReaction conditions: [(neocuproine)PdOAc]₂OTf₂ (**1**) (0.5 mol %), benzoquinone (1.25 equiv), 1.5 M in DMSO, rt, 1 h.

Even a catalyst loading of 0.05 mol % resulted in 95% conversion after 1 h (see the Supporting Information). It is remarkable that the involved chelation control of the catalyst overrules both the better accessibility of the primary hydroxyl group and the enhanced reactivity of the anomeric hydroxyl group. Only prolonged reaction times at elevated temperatures induced further oxidation of the product at the anomeric center (vide infra). To determine whether α -glucose is unique in this reaction, we applied *N*-acetyl- α -D-glucosamine **3** in the same reaction and obtained the same highly selective oxidation at the C3 position.

To confirm our hypothesis that oxidation of α -glucose is selective because of the axial hydroxyl group at the anomeric center, we also studied the oxidation of β -glucose **6**, which can be obtained by crystallization of glucose from pyridine.²⁷ Because the anomeric hydroxyl group is now in an equatorial position, we predicted oxidation at this center. In the palladium-catalyzed oxidation reaction, we indeed observed a mixture of products, likely formed by oxidation at either C3 or C1. In an attempt to drive the reaction to the doubly oxidized product, the reaction mixture was heated to 40 °C for a prolonged time (~12 h). Although one product was indeed formed, it turned out not to be the expected ketolactone! In addition, prolonged reaction times and elevated temperatures in the oxidation of both α -glucose and gluconolactone, in the presence of excess benzoquinone, led selectively to the same compound (see the Supporting Information). Initially, extensive NMR studies did not provide a conclusive answer, until we realized that glucose is available in its all-¹³C-labeled form. Upon oxidation of glucose-¹³C₆, the ¹H and ¹³C NMR spectra in combination with two-dimensional NMR techniques led unambiguously to compound **11**. Apparently, ketolactone **7** is formed but rapidly tautomerizes to the corresponding enediol **8**, which in turn is rapidly oxidized to diketolactone **9**. This intermediate subsequently undergoes intramolecular lactol formation followed by α -ketol rearrangement leading to **11** (Scheme 2). None of the intermediate stages could be observed by NMR. Although **11** as such has not been described in the literature, products of this α -ketol rearrangement in pyranoses

Scheme 2. Oxidation of β -D-Glucose Leads to Rearranged Bislactone 11^a

^aReaction conditions: [(neocuproine)PdOAc]₂OTf₂ (1) (2.5 mol %), benzoquinone (3 equiv), 0.3 M in DMSO, 40 °C, 18 h.

have been reported and the skeleton is present in the antibiotic ashimycin A.^{28–31}

To study the implications of this regioselective oxidation of α -D-glucose on the interconversion of hexoses, we aimed to reduce 3-ketoglucose with sodium borohydride to D-allose. Noteworthy is the fact that the synthesis of this rare sugar currently takes several steps.² Treatment of aqueous solutions of the parent carbohydrate glucose with sodium borohydride is used to produce glucitol (sorbitol), as the minute amount of the open form, the aldehyde, is rapidly reduced.³² In the reduction of α -D-3-ketoglucose to D-allose, the reduction of the open form has to be effectively suppressed as both the starting material 3-ketoglucose and the product allose are vulnerable to the reduction of the open form. In addition, the axial hydroxyl group at the anomeric center is required to induce the desired stereoselectivity in the reduction of the keto group by hampering the approach of the borohydride from the bottom face. Any mutarotation to the β -anomer would eradicate this stereoselectivity. We were pleased to see that treatment of the crude 3-ketoglucose in DMSO with an aqueous solution of sodium borohydride at 0 °C cleanly effected the reduction. The resulting 3:2 mixture of allose and glucose could be effectively separated by chelation chromatography on a calcium-loaded ion exchange resin affording pure D-allose in 54% yield from glucose over just two steps.^{33–36} The ratio of allose to glucose was somewhat disappointing as we had shown that this reduction performed on 3-keto α -methyl glucoside produces α -methyl alloside with high selectivity.¹⁹ Variation of the reducing agent (see Scheme 3 and the Supporting Information) showed that the bulky LS-selectride produces D-allose in high selectivity, though at the expense of a more complicated workup and purification.

With these results in hand, a two-step, one-pot conversion of glucose to allitol was envisioned. Allitol and galactitol (dulcitol), being meso compounds, play a central role in Izumoring as the bridges between D- and L-hexoses. Currently, allitol is produced by a combination of enzymatic transformations (Figure 2).^{37,38} The envisioned chemical method for interconverting glucose to allitol not only would be a drastic shortcut in the Izumoring scheme but also would demonstrate that homogeneous catalysis is complementary to the existing biotechnological methods and can be used to fill blank spots in the Izumoring. Treatment of the crude 3-ketoglucose with

Scheme 3. Selective Reduction of 3-Ketoglucose to Allose and Allitol^a

^aReaction conditions: (A) NaBH₄ (0.75 equiv), DMSO/H₂O (1:1), 0 °C; (B) LS-selectride (3 equiv), DMSO/THF (2:1), 0 °C; (C) NaBH₄ (6 equiv), DMSO/H₂O (1:1), rt, 12 h.

Figure 2. Chemical conversion of D-glucose to D-allose and allitol, complementary to the current enzymatic conversions.

aqueous sodium borohydride at room temperature led smoothly to a mixture of allitol and glucitol (3:2) (Scheme 3) from which allitol was readily purified by calcium chelation chromatography. This synthesis of allitol from glucose in a two-step, one-pot sequence is more efficient than the current enzymatic route. Furthermore, with LS-selectride as the reducing agent, up to 90% selectivity for allitol would be obtained.

Apart from the conversion into platform chemicals, the field of transition metal catalysis has kept its distance from unprotected carbohydrates as substrates for selective transformations. We show that in addition to biotechnology, homogeneous catalysis can make an important contribution to the selective conversion and interconversion of unprotected carbohydrates. This is demonstrated in the palladium-catalyzed regioselective oxidation of glucose and *N*-acetylglucosamine. Chelation control overrules in this case both steric hindrance and the reactivity of the anomeric hydroxyl group. Subsequent reduction under controlled conditions leads directly to either

allose or allitol. This strategy provides grounds for not only the straightforward synthesis of rare sugars but also their potential applications in chemical biology.

EXPERIMENTAL SECTION

General Information. All solvents used for reaction, extraction, filtration, and chromatography were of commercial grade and used without further purification. [(Neocuproine)PdOAc]₂OTf₂ was prepared according to the literature procedure.³⁹ TLC was performed on silica gel TLC plates, and visualization was achieved by staining with anisaldehyde reagent [a mixture of acetic acid (300 mL), H₂SO₄ (6 mL), and anisaldehyde (3 mL)] or potassium permanganate stain [a mixture of KMnO₄ (3 g), K₂CO₃ (10 g), and water (300 mL)]. ¹H, ¹³C, APT, COSY, HMBC, and HMQC NMR were performed at 400 or 100 MHz using D₂O or DMSO-*d*₆ as the solvent. Chemical shift values are reported in parts per million with the solvent resonance as the internal standard (DMSO-*d*₆, δ 2.50 for ¹H and δ 39.5 for ¹³C; D₂O, δ 4.80 for ¹H). Data are reported as follows: chemical shifts (δ), multiplicity (s, singlet; d, doublet; dd, double doublet; ddd, double doublet doublet; t, triplet; appt, apparent triplet; q, quartet; m, multiplet), coupling constants *J* (hertz), and integration.

Exchange of the Resin with Ca²⁺. Dowex 50WX8 (200–400 mesh) resin in the H⁺ or Na⁺ form was exchanged with the Ca²⁺ form by stirring the resin with 4 M aqueous CaCl₂ (3 mL per gram of resin) for at least 3 h. The aqueous layer was decanted, and the resin was washed with water and decanted once more. This washing step was repeated until there was a negative result for chlorides in the aqueous layer with AgNO₃ (1 M).

General Procedure for the Ion Exchange Column. Dowex 50WX8 (200–400 mesh) in the Ca²⁺ form was loaded into a thin and long cylindrical glass column (column diameter of 3.2 cm, filled to 24 cm). The crude material was loaded in 1–2 mL of water on top of the column and eluted with water. The effluent was fractionated every 1.5–2.0 mL with a FRAC-100 fraction collector maintaining the flow rate between 0.6 and 0.8 mL/min.

For Separation of Glucose and Allose. Glucose elutes first, followed by allose. Fractions were collected roughly on the basis of the intensity of the spots on the TLC sample stained with anisaldehyde.

For Separation of Sorbitol and Allitol. Allitol elutes first followed by sorbitol. TLC separation is visible between allitol and sorbitol (20% H₂O/acetonitrile as TLC eluents).

3-Keto-α-D-glucose (4). To a mixture of α-D-glucose 2 (35 mg, 0.19 mmol, 1 equiv) and benzoquinone (60 mg, 0.58 mmol, 3 equiv) in DMSO-*d*₆ (650 μL, 0.3 M) was added [(2,9-dimethyl-1,10-phenanthroline)-Pd(μ-OAc)]₂(OTf)₂ (5 mg, 45 μmol, 2.5 mol %). The reaction mixture was left at rt for 30 min. The product was left crude and characterized by NMR: ¹H NMR (400 MHz, DMSO-*d*₆) δ 5.30 (d, *J* = 4.1 Hz, 1H), 4.21 (dd, *J* = 4.2, 1.5 Hz, 1H), 4.06 (dd, *J* = 9.7, 1.6 Hz, 1H), 3.74 (ddd, *J* = 9.6, 4.7, 1.9 Hz, 1H), 3.68 (dd, *J* = 11.8, 2.0 Hz, 1H), 3.61 (dd, *J* = 11.9, 4.7 Hz, 1H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 207.2, 95.3, 75.3, 75.1, 72.2, 61.0.

Characterization matches the literature.⁴⁰

D-Allose (12) from 3-Keto-α-D-glucose (4). To a mixture of α-D-glucose 2 (120 mg, 0.67 mmol, 1 equiv) and benzoquinone (90 mg, 0.83 mmol, 1.25 equiv) in DMSO (450 μL, 1.5 M) was added [(2,9-dimethyl-1,10-phenanthroline)-Pd(μ-OAc)]₂(OTf)₂ (3.5 mg, 3.33 μmol, 0.5 mol %). The reaction mixture was stirred at rt for 1.5 h. Upon complete conversion (monitored by TLC in a 20% H₂O/acetonitrile solvent or ¹H NMR), the reaction mixture was directly used for the successive reduction step. The reaction mixture was diluted with water (2:1 DMSO/H₂O solvent). A cold solution of NaBH₄ (19 mg, 0.5 mmol, 0.75 equiv) in water (225 μL) was added dropwise to the reaction mixture at 0 °C and the solution stirred for 1.5 h. When the reaction showed complete conversion as indicated by TLC, methanol and acetone (1:1, 2 mL) were added to quench the reaction. The reaction mixture was concentrated in vacuo, and the remaining DMSO was diluted with dichloromethane to the point of precipitation. To this suspension was added activated carbon (1 g); the solution was filtered, and the charcoal was washed multiple times with

dichloromethane until TLC indicated complete elution of the DMSO. Upon complete elution of DMSO, the charcoal was dried with a stream of air, and water was added to elute off the products. Concentration in vacuo resulted in a mixture of 12 and 2. The mixture was further purified on an ion exchange column [Dowex DVB WX8 Ca²⁺ (180 g of dry resin)] and resulted in pure allose (65 mg, 0.36 mmol, 54%): ¹H NMR (400 MHz, D₂O) (assignment of the major configuration, β-D-allose) δ 4.89 (d, *J* = 8.2 Hz, 1H), 4.17 (t, *J* = 3.0 Hz, 1H), 3.89 (dd, *J* = 12.1, 2.0 Hz, 1H), 3.83–3.76 (m, 1H), 3.70 (dd, *J* = 12.0, 5.9 Hz, 1H), 3.64 (dd, *J* = 10.0, 2.9 Hz, 1H), 3.42 (dd, *J* = 8.3, 3.0 Hz, 1H); ¹³C NMR (101 MHz, D₂O) (assignment of the major configuration, β-D-allose) δ 94.2, 74.4, 72.0, 71.9, 67.5, 61.9.

Characterization matches the literature.⁴¹

Allitol (13) from 3-Keto-α-D-glucose (4). To a mixture of α-D-glucose 2 (120 mg, 0.666 mmol, 1 equiv) and benzoquinone (90 mg, 0.833 mmol, 1.25 equiv) in DMSO (450 μL, 1.5 M) was added [(2,9-dimethyl-1,10-phenanthroline)-Pd(μ-OAc)]₂(OTf)₂ (3.5 mg, 3.33 μmol, 0.5 mol %). The reaction mixture was stirred at rt for 1.5 h. Upon complete conversion (monitored by TLC, 20% H₂O/ACN, or ¹H NMR), the reaction mixture was directly used for the successive reduction step. To this end, the reaction mixture was diluted with water (2:1 DMSO/H₂O solvent). A cold solution of NaBH₄ (150 mg, 4 mmol, 6 equiv) in water (1 mL) was added dropwise to the reaction mixture at 0 °C and stirred for 18 h. When the reaction showed complete conversion as indicated by TLC, methanol and acetone (1:1, 2 mL) were added to quench the reaction. The reaction mixture was concentrated in vacuo. The residue in DMSO was diluted with dichloromethane to the point of precipitation. To this suspension was added activated carbon (1 g); the solution was filtered, and the charcoal was washed multiple times with dichloromethane until TLC (20% H₂O/ACN) indicated complete elution of the DMSO. Upon complete elution of DMSO, the charcoal was dried with a stream of air, and water was added to elute the product. Concentration in vacuo resulted in a mixture of 13 and 14. The mixture was separated on an ion exchange column [Dowex DVB WX8 Ca²⁺ (180 g of dry resin)] and resulted in pure allitol 13 (76 mg, 0.419 mmol, 62%) (contains ~40% DMSO by NMR integration, isolated yield corrected for the presence of DMSO): ¹H NMR (400 MHz, D₂O) δ 3.92–3.84 (m, 2H), 3.82–3.73 (m, 4H), 3.69–3.58 (m, 2H); ¹³C NMR (101 MHz, D₂O) δ 73.0, 72.8, 63.0.

Characterization matches the literature.⁴²

Oxidation of D-Glucose-¹³C₆. To a mixture of D-glucose-¹³C₆ (34 mg, 0.18 mmol, 1 equiv) and benzoquinone (58 mg, 0.54 mmol, 3 equiv) in DMSO-*d*₆ (600 μL, 0.3 M) was added [(2,9-dimethyl-1,10-phenanthroline)-Pd(μ-OAc)]₂(OTf)₂ (4.7 mg, 45 μmol, 2.5 mol %). The reaction mixture was left at 40 °C for 4 h. The product was left crude, and the structure was elucidated by NMR: ¹H NMR (400 MHz, DMSO-*d*₆) (decoupled for ¹³C) δ 4.97 (d, *J* = 5.2 Hz, 1H, H5), 4.66–4.58 (m, 2H, H6a + H4), 4.44 (d, *J* = 12.2 Hz, 1H, H6b); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.2 (dd, *J* = 55.0, 1.6 Hz, C1), 166.2 (d, *J* = 51.4 Hz, C3), 79.9 (ddd, *J* = 54.9, 51.5, 36.5 Hz, C2), 78.9 (appt, *J* = 35.0 Hz, C5), 71.6 (appt, *J* = 35.9 Hz, C4), 70.2 (d, *J* = 35.0 Hz, C6); HRMS (ESI) calcd for C₆H₇O₆ [M + H]⁺ *m/z* 175.024, found *m/z* 175.024.

Oxidation of N-Acetyl-α-D-glucosamine (3). To a mixture of N-acetyl-α-D-glucosamine (40 mg, 0.18 mmol, 1 equiv) and benzoquinone (58 mg, 0.54 mmol, 3 equiv) in DMSO-*d*₆ (600 μL, 0.3 M) was added [(2,9-dimethyl-1,10-phenanthroline)-Pd(μ-OAc)]₂(OTf)₂ (4.7 mg, 45 μmol, 2.5 mol %). The reaction mixture was left at rt for 1.5 h. The crude product was characterized by NMR: ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (d, *J* = 8.2 Hz, 1H), 5.34 (d, *J* = 4.0 Hz, 1H), 4.69 (ddd, *J* = 8.2, 4.0, 1.3 Hz, 1H), 4.15 (dd, *J* = 9.7, 1.3 Hz, 1H), 3.82 (ddd, *J* = 9.6, 4.7, 2.0 Hz, 1H), 3.70 (dd, *J* = 11.9, 2.1 Hz, 1H), 3.64 (dd, *J* = 11.9, 4.7 Hz, 1H), 1.92 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 204.0, 169.8, 93.8, 75.3, 72.5, 61.0, 59.5, 22.4.

Characterization matches the literature.⁴³

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02074.

Associated analytical data (^1H NMR, ^{13}C NMR, and APT spectra for all compounds) (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: a.j.minnaard@rug.nl.

*E-mail: m.d.witte@rug.nl.

Author Contributions

V.R.J. and N.N.H.M.E. contributed equally to this work.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from The Netherlands Organization for Scientific Research (NWO-CW, Grants 714.014.004 and 718.016.001) is acknowledged. P. van der Meulen is acknowledged for NMR assistance.

■ REFERENCES

- (1) de Leder Kremer, R. M.; Gallo-Rodriguez, C. *Adv. Carbohydr. Chem. Biochem.* **2004**, 59, 9.
- (2) Li, Z.; Gao, Y.; Nakanishi, H.; Gao, X.; Cai, L. *Beilstein J. Org. Chem.* **2013**, 9, 2434.
- (3) Lim, Y. R.; Oh, D. K. *Appl. Microbiol. Biotechnol.* **2011**, 91, 229.
- (4) Izumori, K. *J. Biotechnol.* **2006**, 124, 717.
- (5) Miljkovic, M. Relative Reactivity of Hydroxyl Groups in Monosaccharides. In *Carbohydrates: Synthesis, Mechanisms and Stereo-electronic Effects*; Springer-Verlag: New York, 2009; p 113.
- (6) Martinez, R. F.; Liu, Z.; Glawar, A. F. G.; Yoshihara, A.; Izumori, K.; Fleet, G. W. J.; Jenkinson, S. F. *Angew. Chem., Int. Ed.* **2014**, 53, 1160.
- (7) Liu, Z.; Yoshihara, A.; Wormald, M. R.; Jenkinson, S. F.; Gibson, V.; Izumori, K.; Fleet, G. W. *J. Org. Lett.* **2014**, 16, 5663.
- (8) Wei, X.-F.; Shimizu, Y.; Kanai, M. *ACS Cent. Sci.* **2016**, 2, 21.
- (9) Tsuda, Y.; Liu, H.-M. *Chem. Pharm. Bull.* **1992**, 40, 1975.
- (10) Liu, H.-M.; Sato, Y.; Tsuda, Y. *Chem. Pharm. Bull.* **1993**, 41, 491.
- (11) Liu, H.-M.; Tsuda, Y. *Chem. Pharm. Bull.* **1996**, 44, 80.
- (12) Liu, H.; Tsuda, Y. *Chem. Pharm. Bull.* **1996**, 44, 88.
- (13) Trincado, M.; Kühlein, K.; Grützmacher, H. *Chem. - Eur. J.* **2011**, 17, 11905.
- (14) de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Tetrahedron* **1995**, 51, 8023.
- (15) Gassama, A.; Hoffmann, N. *Adv. Synth. Catal.* **2008**, 350, 35.
- (16) Gunasundari, T.; Chandrasekaran, S. *J. Org. Chem.* **2010**, 75, 6685.
- (17) Painter, R. M.; Pearson, D. M.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2010**, 49, 9456.
- (18) Chung, K.; Banik, S. M.; De Crisci, A. G.; Pearson, D. M.; Blake, T. R.; Olsson, J. V.; Ingram, A. J.; Zare, R. N.; Waymouth, R. M. *J. Am. Chem. Soc.* **2013**, 135, 7593.
- (19) Jäger, M.; Hartmann, M.; de Vries, J. G.; Minnaard, A. J. *Angew. Chem., Int. Ed.* **2013**, 52, 7809.
- (20) Eisink, N. N. H. M.; Lohse, J.; Witte, M. D.; Minnaard, A. J. *Org. Biomol. Chem.* **2016**, 14, 4859.
- (21) Chung, K.; Waymouth, R. M. *ACS Catal.* **2016**, 6, 4653.
- (22) Unpublished results.
- (23) Giuliano, J. J.; Hill, D. G. *J. Am. Chem. Soc.* **1946**, 68, 2359.
- (24) Lin, C.-E.; Yu, C.-J.; Chen, C.-L.; Chou, L.-D.; Chou, C. *J. Phys. Chem. A* **2010**, 114, 1665.
- (25) Ballash, N. M.; Robertson, E. B. *Can. J. Chem.* **1973**, 51, 556.

- (26) Signorella, S.; Lafarga, R.; Daier, V.; Sala, L. F. *Carbohydr. Res.* **2000**, 324, 127.
- (27) Behrend, R. *Justus Liebigs Ann. Chem.* **1907**, 353, 106.
- (28) Ericsson, B.; Lindgren, B. O.; Theander, O.; Petersson, G. *Carbohydr. Res.* **1972**, 23, 323.
- (29) Theander, O.; Dahlqvist, A.; Möller, J.; Detoni, S. *Acta Chem. Scand.* **1958**, 12, 1887.
- (30) Vuorinen, T. *Carbohydr. Res.* **1985**, 141, 307.
- (31) Tohma, S.; Kondo, H.; Yokotsuka, J.; Iwamoto, J.; Matsuhashi, G.; Ito, T.; Seto, H. *J. Antibiot.* **1989**, 42, 1205.
- (32) Garrett, E. C.; Serianni, A. S. *Carbohydr. Res.* **1990**, 208, 23.
- (33) Verhaar, L. A. T.; Kuster, B. F. M. *J. Chromatogr. A* **1981**, 210, 279.
- (34) Hicks, K. B.; Sondey, S. M.; Doner, L. W. *Carbohydr. Res.* **1987**, 168, 33.
- (35) Wilhelm, A. M.; Riba, J. P. *J. Chromatogr. A* **1989**, 484, 211.
- (36) Beveridge, R. J.; Davis, M.; Morris, J. L.; Hoogenraad, N. J. *Carbohydr. Res.* **1982**, 101, 348.
- (37) Takeshita, K.; Ishida, Y.; Takada, G.; Izumori, K. *J. Biosci. Bioeng.* **2000**, 90, 545.
- (38) Zhu, Y.; Li, H.; Liu, P.; Yang, J.; Zhang, X.; Sun, Y. *J. Ind. Microbiol. Biotechnol.* **2015**, 42, 661.
- (39) Conley, N. R.; Labios, L. A.; Pearson, D. M.; McCrory, C. C. L.; Waymouth, R. M. *Organometallics* **2007**, 26, 5447.
- (40) Lichtenthaler, F. W.; Nishiyama, S.; Weimer, T. *Liebigs Ann. Chem.* **1989**, 1989, 1163.
- (41) Hopley, P.; Howarth, O.; Ibbett, R. N. *Magn. Reson. Chem.* **1996**, 34, 755.
- (42) Robinson, T. V.; Taylor, D. K.; Tiekink, E. R. T. *J. Org. Chem.* **2006**, 71, 7236.
- (43) Wong, C.-H.; Ichikawa, Y.; Krach, T.; Gautheron-Le Narvor, C.; Dumas, D. P.; Look, G. C. *J. Am. Chem. Soc.* **1991**, 113, 8137.