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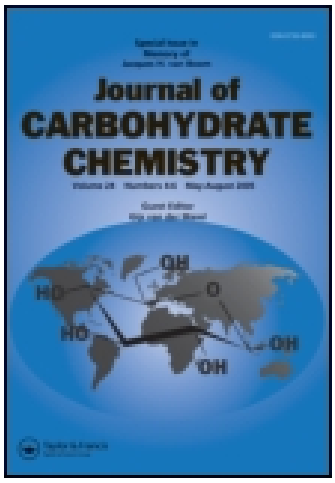

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Preparation of Sugar Derivatives Using the Amalgam Process

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Published online: 15 Aug 2006.

To cite this article: Carl Heinz Hamann & Thorsten Röpke (2005) Preparation of Sugar Derivatives Using the Amalgam Process, Journal of Carbohydrate Chemistry, 24:1, 13-17, DOI: 10.1081/CAR-200049405

To link to this article: http://dx.doi.org/10.1081/CAR-200049405

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Journal of Carbohydrate Chemistry, 24:13–17, 2005
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ISSN: 0732-8303 print
DOI: 10.1081/CAR-200049405

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Preparation of Sugar Derivatives Using the Amalgam Process

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Methyl α-D-glucopyranoside dissolved in *N,N*-dimethylformamide was benzylated with benzylbromide using sodium amalgam and grains of an electrocatalyst for the generation of intermediate sugar anions. The obtained substitution pattern is comparable to the pattern generated using a platinum electrode at $-2\,\mathrm{V}\,\mathrm{Ag}/\mathrm{Ag}^+$ for the generation of the anions.

Keywords Sugar derivatives, Sugar anions, Amalgam process

INTRODUCTION

In preceding papers we have examined the *O*-alkylation, especially benzylation, of carbohydrates using electrochemical processes and semiempirical calculations.[1–5] The electrochemical processes require the use of electrochemical cells, reference electrodes and potentiostats to apply a potential of $-2\,\mathrm{V}$ $\mathrm{Ag}/\mathrm{Ag}^+$ at the platinum working electrode. In this way the sugar anions could be produced that are needed, for instance, for the reaction with benzylbromide.

In the present paper we describe how *O*-alkylation can be carried out electrochemically without the mentioned special equipment.

Sodium amalgam is used as an electron donor. The electrons are transferred via an electrocatalyst to the species under consideration. This principle is widely used in electrochemical engineering, for instance, for the production of alkali metal alkoxides.[6,7]

Received July 12, 2004; accepted December 1, 2004.
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According to this principle, sugar anions are produced in our case.

$$NaHg_x + ROH \xrightarrow{\text{electrocatalyst}} RO^-Na^+ + \frac{1}{2}H_2 + xHg$$

EXPERIMENTAL

Experiments were carried out at 24°C in a conventional beaker with a volume of 200 cm^3. Two hundred grams of sodium amalgam ($NaHg_X$) containing 0.24 wt. % sodium was brought into contact with 20 g catalyst grains (ca. 10 mm diameter; see end of experimental section). Next, 7.77 g of methyl α-D-glucopyranoside (Fluka) was dissolved in 100 mL *N,N*-dimethylformamide (Riedel-de Haën), with a remaining water concentration of 450 ppm. This solution was added while the reaction mixture was continuously stirred. The resulting increase of the conductivity (formation of anions and cations in the solution) was measured with a conductivity meter (Radiometer CDM 83). The reaction ended after 10 min. This was indicated by reading a constant final conductivity amounting to 240 μScm^{-1}.

In a further experiment under the same conditions the conductivity increase during the reaction of $NaHg_x$ with water traces in the solvent without methyl α-D-glucopyranoside led to a final conductivity of 21 μScm^{-1}.

The *N,N*-dimethylformamide containing the dissolved reaction products was decanted from mercury and catalyst. Benzylbromide (Fluka) was added in 1.1 mol equivalents (3.9 g) as scavenger. The addition was calculated from the amount of electrons (20.9 mmol), which resulted from the complete decomposition of sodium amalgam. The end of the reaction was reached after approximately 3 hr of stirring at room temperature. In this time the pH value decreased constantly from pH 9 to 7. After removing of the solvent, the resulting product mixture was acetylated for easier separation and identification. The product mixture was dissolved in 160 mL pyridine (Fluka) and 80 mL acetic anhydride (Riedel-de Haën). After 1 hr of stirring at room temperature the mixture was hydrolyzed with ice water followed by extraction with four times 40 mL dichlormethane (Merck). The combined organic phases were washed with deionized water, with saturated sodium hydrogencarbonate (Sigma-Aldrich) solution, and afterwards with deionized water. After drying over sodium sulphate (Sigma-Aldrich) for 24 hr and removal of dichlormethane, a product mixture (syrup) of 13.9 g was obtained. Five grams were further separated by chromatography on a silicagel column (KG 60, 450 mm × 50 mm) with a mixture of n-hexane and ethyl acetate (1:1, both Fluka) as eluent.

The catalyst grains used consisted of coal coated with molybdenum carbide, prepared according to Hamann and Schmittinger.[7] For laboratory purposes it may be more convenient to use platinum-activated carbon.

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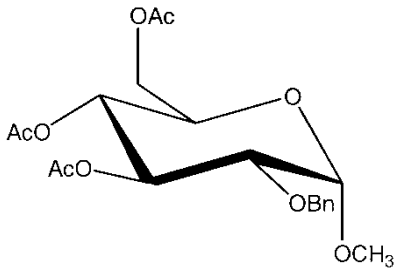
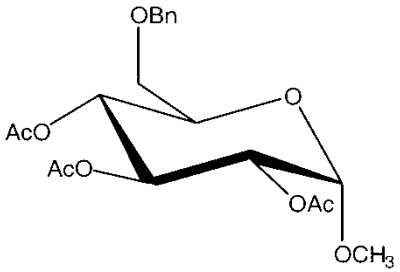
Table 1: Spectroscopic Identified Compounds.

Compound	Methyl 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-α-D-glucopyranoside	Methyl 2,3,4-tri-*O*-acetyl-6-*O*-benzyl-α-D-glucopyranoside
		
Yield (g)	2.5 (69%)	1.1 (31%)
η^a (%)	29.2	12.9
^{1}H-NMR data^b ($CDCl_3$)	δ = 2.00, 2.02, 2.08 (3 s, 9 H, 3 CH_3CO); 3.40 (s, 3 H, OCH_3); 3.65 (dd, H2, $^3J_{1,2}$3.3 Hz, $^3J_{2,3}$10 Hz); 3.93 (ddd, H5, $^3J_{4,5}$10 Hz, $^3J_{5,6}$2.5 Hz, $^3J_{5,6'}$4.3 Hz); 4.03 (dd, H6, $^2J_{6,6'}$12.5 Hz); 4.24 (dd, H6′); 4.58 (d, $PhCH_a$, $^2J_{Ha,Hb}$12 Hz); 4.63 (d, $PhCH_b$); 4.68 (d, H1); 4.94 (t, H4, $^3J_{3,4}$10 Hz); 5.42 (t, H3); 7.20–7.40 ppm (m, 5 H, Ph).	δ = 1.92, 2.01, 2.07 (3 s, 9 H, 3 CH_3CO.); 3.40 (s, 3 H, OCH_3); 3.51 (dd, H6′, $^3J_{5,6'}$ = 3 Hz, $^2J_{6,6'}$ = 11 Hz); 3.55 (dd, H6, $^3J_{5,6}$ = 3.5 Hz); 3.91 (ddd, H5, $^3J_{4,5}$ = 10 Hz, $^3J_{5,6}$ = 3.5 Hz); 4.48 (d, $PhCH_a$, $^2J_{Ha,Hb}$ = 12 Hz); 4.57 (d, $PhCH_b$); 4.88 (dd, H2, $^3J_{1,2}$ = 3.5 Hz, $^3J_{2,3}$ = 10 Hz); 4.96 (d, H1); 5.1 (t, H4, $^3J_{3,4}$ = 10 Hz); 5.44 (t, H3); 7.20–7.40 ppm (m, 5 H, Ph).

[a] The Faradaic efficiencies have been calculated in respect to the maximal amount of available electrons (20.9 mmol, see experimental section).
[b] Chemical shift δ (ppm), coupling constant J (Hz).

RESULTS

After separation two monobenzylated compounds could be determined by ^{1}H-NMR spectroscopy (Bruker AM 300 MHz, using TMS as internal standard). Table 1 shows the identified compounds and ^{1}H-NMR data,[8–11] their yields, and Faradaic efficiencies η. No further compounds could be identified.

DISCUSSION

From Table 1 follows a yield ratio of 69:31 concerning the 2-*O*- and 6-*O*-compounds. This value must be compared to the ratio generated by use of a platinum electrode at -2 V Ag/Ag$^+$. A 2-*O*- to 6-*O*- compound ratio of 43:13 was found, the rest of 44% consisting of other substitution products, for example, disubstituted species in the percent range. Taking the byproducts into consideration, the two yield ratios are quite comparable. This adds evidence that the mechanism discussed in Refs.[1–5] is also valid in case of amalgam as reducing agent.

CONCLUSION

It was shown that methyl α-D-glucopyranoside undergoes benzylation if brought into contact with sodium amalgam and a suitable electrocatalyst followed by the addition of benzylbromide. The reaction mechanism is considered to follow the path described in Refs.[1–5] It may be assumed that other nonreducing sugars such as methyl α-D-mannopyranoside, D-glucal, or sucrose (see Refs.[1–3]) could behave similarly.

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