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ELECTROLYTIC METHANOLYSIS OF ACYLATED AMINO SUGARS

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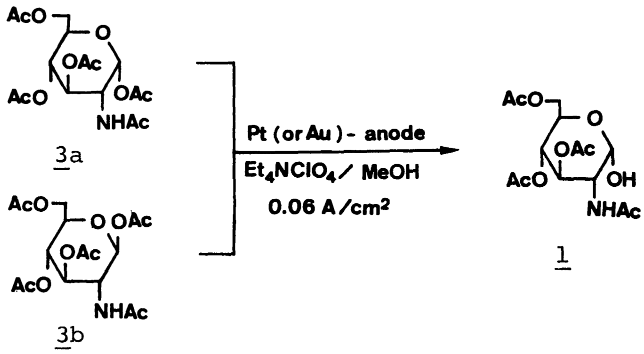
Electrolysis of 2-acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-α- or β-D-glucose in methanol gives specifically 1-deacetylated product, 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucose, while methyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucoside is deacetylated to yield 2-acetamido-6-O-acetyl-2-deoxy- and 2-acetamido-2-deoxy-α-D-glucosides.

It is known that the compounds having an amide group are easily oxidized at the α-carbon of nitrogen atom by anodic oxidation.1) However, during the electrolysis of the methanolic solution of hexosamine polyacetates in the hope of obtaining 2-methoxy derivatives, we have found that site-specific methanolysis of O-acyl moiety took place and the α-carbon of acylamino group was not oxidized at all. This electrolytic methanolysis gives a convenient and efficient method for the synthesis of 2-acetamido-3,4,6-tri-O-acetyl- and 2-benzamido-3,4,6-tri-O-benzoyl-2-deoxy-α-D-glucopyranoses [(1)2) and (2)3)].



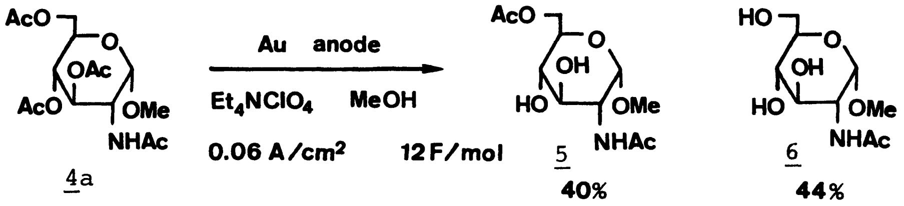
Substrate	Anode	F/mol	Yield (%)
3a	Pt	4	81
3b	Pt	6	76
3a	Au	2	98

Scheme 1

2-Acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-α- or β-D-glucopyranose [(3a) or (3b)]4) was electrolyzed in absolute MeOH in the presence of Et_4NClO_4 in a non-divided cell by the aid of gold or platinum electrodes, giving only 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranose (1) in a good to excellent yield (Scheme 1). It should be noted that further supply of electricity caused no additional reaction. Electrolysis by means of graphite electrodes proceeded at lower efficiency (36% from 3b). The structure of 1 1) was established by acetylation to give 3a and by diazomethane treatment to give 4a.

In the electrolysis of 3a in MeCN (Et_4NClO_4 as electrolyte) and in AcOH (NaOAc or Et_4NOTs as electrolyte), neither solvolysis nor oxidation occurred and the substrate was recovered unchanged.

The application of the electrolysis to methyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranoside (4a) using a gold anode contrasted oddly with that in the case of 3a or 3b. At the 3- and 4-positions concurrently, and then at the 6-position 3a was deacetylated and 5 (mp 141-143°C) and 6 5) were obtained. No product methanolyzed at either 3- or 4-position separately, however, was detected even at the early stage of electrolysis (Scheme 2).



Scheme 2

On the other hand, the conversion in the electrolysis of the β-isomer (4b) was low (<50%) even after supply of 20 F/mol of electricity. The use of platinum anode instead of gold was far less efficient in this case. These facts suggest that the reacting sites and the reactivity vary markedly with substrates.6)

For comparison, the electrolysis was applied to penta-O-acetyl-α-D-glucopyranose having no acylamino group. Although the 1-deacetylated product was the main product at the early stage, prolonged reaction resulted in the formation of a mixture of mono- and polydeacetylated products.

In the electrolysis of two model compounds, 2-acetamidoethyl acetate and trans-

2-acetamidocyclohexyl acetate, neither deacetylation nor oxidation at the α-carbon of nitrogen atom occurred. This fact indicates that the compounds having an acetoxyl group at the β-position of acylamino group are not susceptible to anodic oxidation probably owing to the electronic effect.

To uncover the mechanism of this substrate-dependent and site-specific reaction, following three experiments were carried out.

1) Electrolysis of 3a in a divided cell showed that the electrolysis proceeded at the anodic site.7)

2) Cyclic voltammograms of 3a, 3b, 4a, 4b and α-D-glucose pentaacetate exhibited no remarkable peak of oxidation as the blank solution (Et_4NClO_4 in MeOH) did. This fact assures that the electrolysis is a secondary reaction having no direct electron-transfer between the substrate and the anode.

3) The electrolysis of 2-benzamido-1,3,4,6-tetra-O-benzoyl-α-D-glucopyranose gave the 1-debenzoylated product (2)3) in 90% yield and nearly stoichiometric formation of methyl benzoate was observed.

Although, from the above experiments, this electrolytic methanolysis8) is reminiscent of an acid-catalyzed transesterification, the difference is evident from the following acid-catalyzed methanolyses of 3a and 4a (p-TsOH as catalyst in absolute MeOH at room temperature). The methanolysis of 3a took place first at the 1-position, but with the elapse of time further reaction occurred at other positions before full conversion of the 1-position. In the case of 4a, the methanolysis took place at the acetoxyl groups of various positions.

A reasonable mechanism for this electrolytic methanolysis of acylamino sugars can be envisioned from the whole experimental results. The adsorption mode9) of the substrate to the anode surface is important because the substrate-depending feature in the reaction site and the reactivity in the electrolytic methanolysis (heterogeneous reaction) is different from that in the acid-catalyzed transesterification (homogeneous reaction). However, the appearance of the substrate dependency and the site specificity further needs a short-lived mediator10) which effects the methanolysis of the adsorbed substrate and not of the substrate in the bulk, since there is no direct electron-transfer between the substrate and the anode from the experiments of cyclic voltammetry. We assume as the mediator a strong acid $^{+}CH_2OH$ (pK_a below -8)11) which is formed inevitably in the process from MeOH to formaldehyde.

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References and Notes

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6) Methyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-galactopyranoside was deacetylated step by step giving diverse products and the selectivity was poor.

7) Cell separation makes strongly acidic in anode cell and strongly alkaline in cathode cell. To avoid acid- or base-catalyzed methanolysis, the product was examined only at early stage of the electrolysis (0.1 F).

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9) For the importance of adsorption phenomena, see G. Cauquis, in ref. 8, p. 64.

10) R. Dietz, in ref. 8, p. 822.

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