

ELECTROLYTIC METHOXYLATION OF HALOGENOFURANS

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α -Halogenofurans are electrolytically methoxylated in two ways in the presence of sulfuric acid electrolyte, methoxyl groups either adding at the 2 and 5 positions in the furan ring or replacing a ring halogen atom. The following are methoxylated: 2-bromo-, 2-iodofuran, 5-chloro-, 5-bromo-, and 5-iodofurfural, ethyl 5-bromopyromucate. Derivatives of 2, 2, 5-trimethoxy-2, 5-dihydrofuran are prepared, giving on hydrolysis β -aldehyde- and β -ketoacrylic acids.

Total anode polarization graphs are obtained in order to study the electrolytic methoxylation reaction mechanism.

It is known that furan derivatives having negative substituents (COOH , COOC_2H_5 , $\text{CH}=\text{CHCOOC}_2\text{H}_5$, CHO^* , CO^*) in the furan ring cannot be methoxylated either with methanol and bromine, or electrochemically in the presence of ammonium bromide.

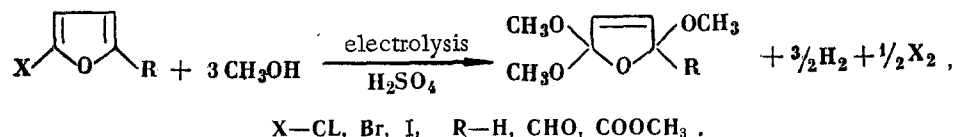
An unsuccessful attempt was made to methoxylate 2, 5-dibromofuran. Hence it was concluded that this reaction is inapplicable to halogenofurans, but, as will be shown below, this conclusion was wrong.

The results of research aimed at developing a preparative method of electrolytic methoxylation, and investigating some peculiarities in the course of the electrolysis are set out in this paper.

It was shown that methoxylation of halogenofurans succeeds if sulfuric acid is used as the electrolyte instead of ammonium bromide**. When halogenofurans are electrolyzed, elementary halogen separates at the anode, and a methoxyl group takes its place in the furan nucleus.

This can readily be confirmed by testing the electrolyte after electrolysis qualitatively for chlorine, bromine, or iodine.

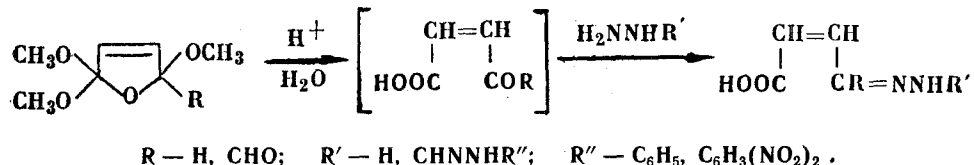
The final product, after three faradays have passed per 1 mole of starting halogenated furan, is the corresponding 2, 2, 5-trimethoxy-2, 5-dihydrofuran, formed according to the equation



It was possible to methoxylate 2-bromo- and 2-iodofuran, 5-chloro-, 5-bromo-, and 5-iodofurfural, and methyl 5-bromopyromucate by this method, the expected trimethoxydihydrofuran being formed in every case.

The bromo-compounds proved to be the most suitable halogenofurans for use as starting materials for preparative purposes, since the elementary iodine separating during electrolysis of iodine derivatives is difficult to remove when the electrolyte is worked up, while chlorofurans are more difficult to synthesize than the corresponding bromo-ones.

Hydrolysis of 2, 2, 5-trimethoxy-2, 5-dihydrofurans gives substituted β -formylacrylic acids, identified as their hydrazones.

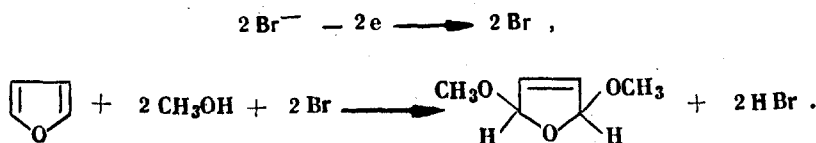


It is of interest that it was impossible to prepare a hydrazone from methyl 2, 2, 5-trimethoxy-2, 5-dihydrofuran carboxylate, though the ethyl ester gives one. This is mentioned in a paper [4] which came to our notice only after our own work in the field was finished [5].

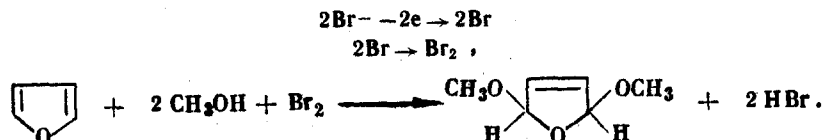
* Furfural and 2-acetylfuran methoxylate, but only after first undergoing conversion to the dimethylacetal [1, 2].

** Electrolytic methoxylation of furan derivatives using sulfuric acid as electrolyte was first applied to methoxylation of a pyromucic ester, which, as referred to above, is not methylated using ammonium bromide.

Hitherto the mechanism of electrolytic methoxylation of furans has not been specially studied. Meanwhile, by analogy with known examples of the mechanism of addition of halogen to organic depolarizers [6], the reaction of electrolytic methoxylation can be considered from two different viewpoints. One approach to the problem is to assume that the bromine anion first donates an electron to the anode, and then undergoes direct reaction with the furan and methanol, according to the equations

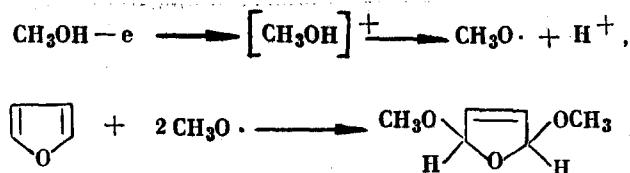


The other case is where the bromine formed at the anode reacts essentially as molecular bromine



If the reaction is described by the first equations, a fall in anode potential is to be expected when furan is added to the solution of methanol and ammonium bromide. In the second case the addition of furan should not cause any decrease in anode potential.

A third alternative reaction mechanism is also conceivable. This is that a methoxyl radical is originally formed at the anode and then reacts further with the furan according to the equations



Here the anode potential should also be lowered by adding furan. Still, this mechanism is improbable with an ammonium bromide solution, but is realized if the electrolyte is a solution of sulfuric acid in methanol.

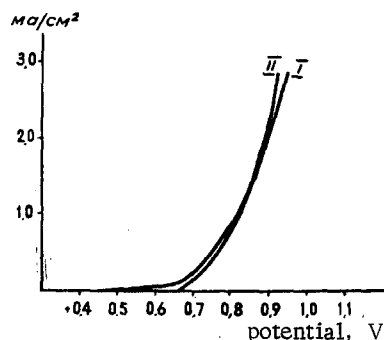


Fig. 1. Relationship between current density and anode potential in methanol solution: I - ammonium bromide, II - ammonium bromide and furan.

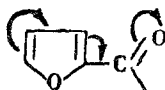
We prepared total polarization graphs for anodic methoxylation both for furan derivatives and for α -halogenofurans, to ascertain which of the above schemes for the electrolytic methoxylation is correct, and to ascertain the role of the furan. The polarization curves measured were obtained at constant voltage under electrolysis conditions close to these used for preparative purposes, the electrodes being of graphite, and the anode and cathode field identical.

Figs. 1-5 show the polarization curves found.

Fig. 1 shows the polarization curves for the electrolysis of a methanol solution of ammonium bromide before and after adding furan, which does not lead to any displacement of the polarization graph. The same is found in the electrolysis of methylfuran and furfural.

On the other hand, addition of furan, furfural, or methyl pyromucate to a methanol plus sulfuric acid electrolyte shifts the polarization curve towards lower potentials (Fig. 2), i. e., as if the anode were depolarized. Here it appears that the degree of depolarization depends on the nature of the functional group in the furan nucleus. Furan and furfural themselves have the greatest depolarizing effects, the pyromucic ester the least.

Hence, the first step in the electrolytic methoxylation of furans in the presence of ammonium bromide is evidently formation, by electrolysis, of atomic bromine, which then recombines to give Br_2 . Methoxylation is through a bromine molecule Br_2 , as the process no longer takes place at the surface of the electrode, but in the bulk of the electrolyte. The following can be adduced in support of this view: furan derivatives containing electronegative substituent groups are not methoxylated, e. g., in the case of the ester of pyromucic acid, where attack at the carbon atom at position 5 in the furan ring by the bromine cation Br^+ [7] is hampered by the positive charge on the carbon atom, or else



they undergo methoxylation only after acetylation of the carbonyl group, e. g., in the case of furfural.

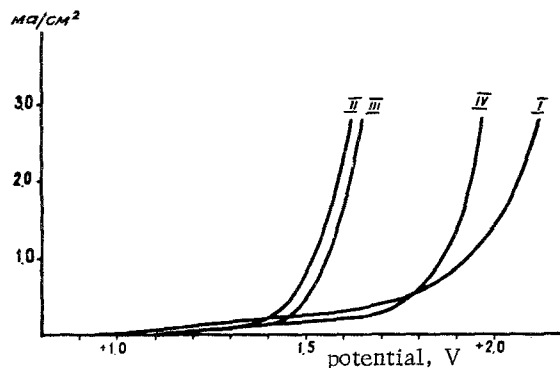


Fig. 2. Relationship between current density and anode potential in methanol solution: I - conc. H_2SO_4 . II - conc. H_2SO_4 and furan. III - conc. H_2SO_4 and furfural. IV - conc. H_2SO_4 and methyl pyromucate.

polarization curve in the above cases, two regions of current growth appear when methoxylating 5-bromo- and 5-chlorofurfural. The first wave is most markedly shown with 5-bromofurfural, and least with 5-chlorofurfural. Two degrees of polarization were not observed with furfural and 5-iodofurfural. Further, introduction of a chlorine atom into the furfural ring caused a general increase in reaction potential as compared with the bromo- and iodo- derivatives, or non-halogenated furfural.

Another quite interesting observation was made during preparative electrolytic methoxylation of α -bromofuran derivatives, viz., during removal of halogen in its replacement by the methoxyl group, the electrical conductivity of the reaction solution changes considerably. Fig. 6 shows the drop in potential with time when methoxylating 2-bromofuran, 5-bromofurfural, and methyl 5-bromopyromucate.

It is evident that the potential drops most rapidly when methoxylating bromofuran, and most slowly when methoxylating the bromopyromucic ester. This indicates that replacement of the halogen by a methoxyl group, and hence breaking of a C-Br bond, takes place most quickly with bromofuran, more slowly with bromofurfural, and slowest of all with the bromopyromucic ester.

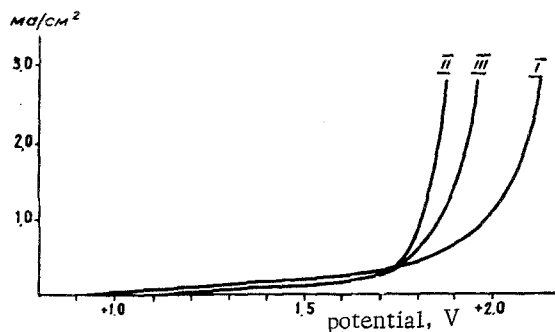


Fig. 4. Relationship between current density and anode potential in methanol solution: I - conc. H_2SO_4 . II - conc. H_2SO_4 and methyl 5-bromopyromucate. III - conc. H_2SO_4 and methyl pyromucate.

Obviously in the case of sulfuric acid the methoxylating agents are absorbed methoxyl radicals, forming at the anode. However, it is not excluded that the furan acts as a direct depolarizer, due to transfer of electrons from the α carbon atoms of the furan ring, which have electron clouds of higher density. The resultant furyl radicals then participate in the methoxylation reaction.

Halogenofurans have an even greater capacity for lowering the anode potential than the furan derivatives so far considered. Fig. 3 gives polarization curves obtained with solutions of 2-bromofuran and 2-iodofuran. Evidently 2-bromofuran methoxylates at a much lower potential, and 2-iodofuran at a much higher one, though still at a lower potential than furan. Introduction of bromine at position 5 in the furan ring of methyl pyromucate also lowers the reaction potential (Fig. 4).

A somewhat different picture is found when methoxylating an α -halogenofurfural (Fig. 5). If only one wave appears in the

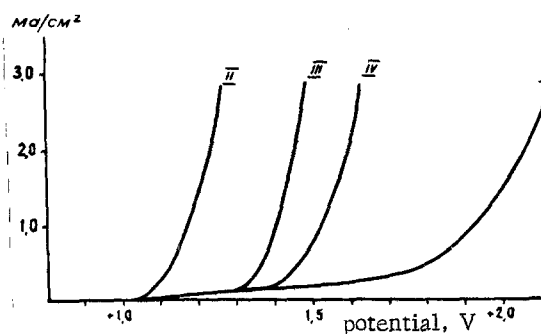


Fig. 3. Relationship between current density and anode potential in methanol solution: I - conc. H_2SO_4 . II - conc. H_2SO_4 and 2-bromofuran. III - conc. H_2SO_4 and 2-iodofuran. IV - conc. H_2SO_4 and furan.

This contradicts the usual view regarding nucleophilic halogen substitution [8], but is in good agreement with the view which the present authors previously advanced that replacement of halogen by the methoxyl group is a radical reaction.

EXPERIMENTAL

Electrolytic methoxylation method. The electrolytic cell used for preparing the 2, 2, 5-trimethoxy-2, 5-dihydrofurans consisted of a glass test tube-shaped cylinder 16 cm high, 2.5 cm diameter, and holding 150 ml. The lid was used to fix in the cell, two graphite electrodes 8 mm in diameter. The immersed electrode length was 135 cm, and the apparent surface area 33.75 cm^2 . A stirrer and a thermometer were put between the electrodes. The cell was immersed in a thermostat containing butanol, solid carbon dioxide being added as a coolant. The electrolysis was carried out at a current density of approx.

2, 2, 5-Trimethoxy-2, 5-dihydrofuran. 130 ml absolute methanol, 0.8 ml conc. H₂SO₄, and 5.9 g (0.04 ml) 2-bromofuran are placed in the electrolyzer. The electrolyte is cooled to -15°, and the current switched on. When 3.2 amp hr have passed, electrolysis is stopped, and the electrolyte neutralized to pH 7-8 with sodium methoxide. The methanol is distilled off, and 50 ml dry ether added to the residue. The precipitate of sodium sulfate formed is filtered off and the ether distilled off on a water bath. The residue is distilled, to give 6.4 g of light green liquid boiling 190-200° (750 mm); n_D²⁰ 1.4390. Redistillation using a rod and disc column gives 2, 2, 5-trimethoxy-2, 5-dihydrofuran as a colorless liquid, immiscible with water but soluble in most ordinary organic solvents, boiling 82-85° (12 mm); n_D²⁰ 1.4360; d₄²⁰ 1.081. Yield 4.6 g (72%). Found: C 52.22; H 7.43%. MRD 38.74. Calculated for C₇H₁₂O₄: C 52.49; H 7.55%. MRD 38.43.

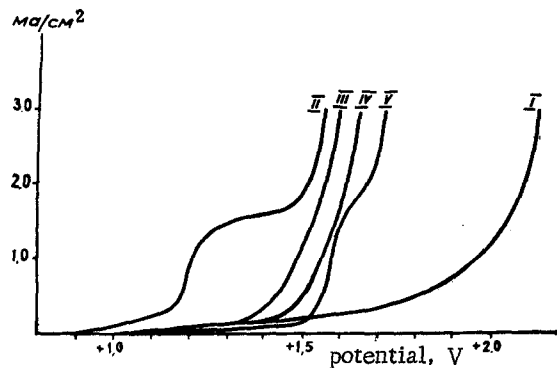


Fig. 5. Current density relationship in methanol solution: I - conc. H₂SO₄. II - conc. H₂SO₄ and 5-bromofurfural. III - conc. H₂SO₄ and 5-iodofurfural. IV - conc. H₂SO₄ and furfural. V - conc. H₂SO₄ and 5-chlorofurfural.

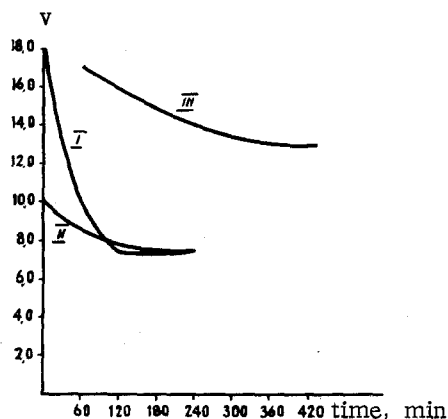


Fig. 6. Relationship between potential and time of electrolysis: I - 2-bromofuran, II - 5-bromofurfural, III - methyl 5-bromopyromucate.

2, 2, 5-trimethoxy-2, 5-dihydrofurfural dimethylacetal. 130 ml absolute methanol, 2 ml conc. H₂SO₄, and 7.0 g (0.04 mole) 5-bromofurfural are placed in the electrolyzer, cooled to -10°, and the current switched on. After 4 amp hr have passed, the electrolysis is stopped, and the electrolyte neutralized to pH 7-8 by means of sodium methoxide. The methanol is distilled off, and 50 ml ether added to the residue. The resultant ppt is filtered off, the ether distilled off on a water bath, and the residue vacuum-distilled. Yield 6.5 g of a lemon-yellow oil, boiling 85-100° (1-2 mm). After repeated fractionation it boils at 90-92° (1-2 mm); n_D²⁰ 1.4510; d₄²⁰ 1.140; Found: C 49.95; H 7.51%. MRD 55.32. Calculated for C₁₀H₁₈O₆: C 51.27; H 7.75%. MRD 55.57.

Electrolysis was effected at -10°, current 1 a, other conditions as follows:

Time, min	Voltage, V	Current, amp hr
--	10.0	--
30	9.0	0.5
60	8.5	1
120	7.8	2
180	7.5	3
240	7.5	4

Electrolysis was carried out at -15°, current 0.9 a, the other variables being as follows:

Time, min	Voltage, v	Current, amp hr
--	17	--
30	14	0.45
60	10	0.9
90	8.5	1.35
120	7.5	1.8
180	7.5	2.7
213	7.5	3.2

Hydrolysis of 2, 2, 5-trimethoxy-2, 5-dihydrofuran and identification of cis-β-formylacrylic acid. 0.21 g 2, 2, 5-trimethoxy-2, 5-dihydrofuran are heated for a few seconds with 2 ml 0.1 N sulfuric acid. 0.5 ml of freshly-distilled phenylhydrazine in 2 ml acetic acid and 5 ml water are then added to the solution. After 15 min the yellow ppt is filtered off, washed with water, and dried. Yield 0.2 g (80%), mp 146-148°. After recrystallizing from acetone-petrol ether it melts at 153-153.5° (ref. [9] gives 150°). Found: C 63.71; H 5.77; N 14.29%. Calculated for C₁₀H₁₀N₂O₂: C 63.16; H 5.32; N 14.74%.

2, 4-Dinitrophenylhydrazone of the hydrolysis product of 2, 2, 5-trimethoxy-2, 5-dihydrofurfural is prepared by the known method [10] from 0.25 g of 2, 2, 5-trimethoxy-2, 5-dihydrofurfural dimethylacetal. Yield 0.41 g (74%) of dihydrazone melting at 211-212° (from nitromethane). Found: C 41.81; H 2.47; N 22.94%. Calculated for $C_{17}H_{12}N_8O_{10}$: C 41.30; H 2.62; N 22.57%.

Methyl 2, 2, 5-trimethoxy-2, 5-dihydropyromucate. 130 ml absolute methanol, 2 ml conc. H_2SO_4 , and 8.2 g (0.04 mole) of methyl 5-bromopyromucate are placed in the electrolyzer, cooled to -5° , and the current turned on. Electrolysis is stopped after 12 amp hr have passed, and the electrolyte is neutralized to pH 7-8 by means of sodium methoxide. The solvent is distilled off, and 50 ml dry ether added to the residue. The precipitate is filtered off, the ether distilled off on a water bath, and the residue vacuum-distilled. Yield 6 g of a yellow oil boiling 110-135°/11 mm, which is repeatedly fractionated. Boils 131-134°(11mm), n_D^{20} 1.4520, d_4^{20} 1.1540. Yield 3.5 g (40.5%). Found: C 49.01; H 5.99%; MR_D 51.08. Calculated for $C_9H_{14}O_6$: C 49.54; H 6.47; MR_D 51.05.

Electrolysis was effected at -5° , current 1 a, other conditions as follows:

Time, min	Voltage, V	Current amp hr
--	17	--
60	17	1
120	16	2
180	15	3
240	14.5	4
300	13	5
720	13	12

Method of obtaining polarization curves. The electrolytic cell for determining polarization curves was a small 50 ml beaker with a gas-tight lid to which two graphite electrodes and an electrolytic switch were secured. The nominal anode area was the same as that of the cathode, and with immersion in the electrolyte to a depth of 4 cm, was 10.5 cm². A magnetic stirrer stirred the electrolyte under investigation in the beaker, its speed being determined with a stopwatch. A calomel electrode, made up using a saturated solution of potassium chloride in methanol, was used as a reference electrode. The intermediate beaker and electrolytic switch contained the same liquid. Cell, intermediate beaker, and calomel electrode were immersed in a thermostatted bath. The latter contained butanol, was precooled with dry ice and kept the temperature of the system constant between -7° to -6.5° while the curve was being measured. An ABO-5M1 universal ammeter was used to measure the circuit current. The anode potential was measured with the cathode voltmeter A4-M2, within 1 min of applying the voltage. The electrolyte was prepared using distilled absolute methanol, the concentration being that used in the electrolytic preparation. 16.0 g ammonium bromide (A.R.) or 14 ml conc. H_2SO_4 (C.P.) were dissolved in 1 l methanol. The compounds investigated, viz., bromo- and iodofuran, chloro-, bromo-, and iodofurfural, and methyl bromopyromucate were synthesized by known methods, and their constants were those given in the literature. Before each experiment the electrolytic cell and electrodes were twice washed with methanol and once with electrolysis solution. For all measurements 50 ml electrolyte were charged to the cell, and the polarization curve of the base electrolyte determined. Then 0.010 mole of the compound to be investigated was added, and the polarization curve redetermined. As it was present in excess, constant concentration was secured over the entire time of determination of the polarization curve. The potential variation on repeating polarization curves (reproducibility) did not exceed ± 0.2 v.

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