ACTA CHEMICA SCANDINAVICA 9 (1955) 17—22

New Examples of Electrolytic Methoxylation of Furans

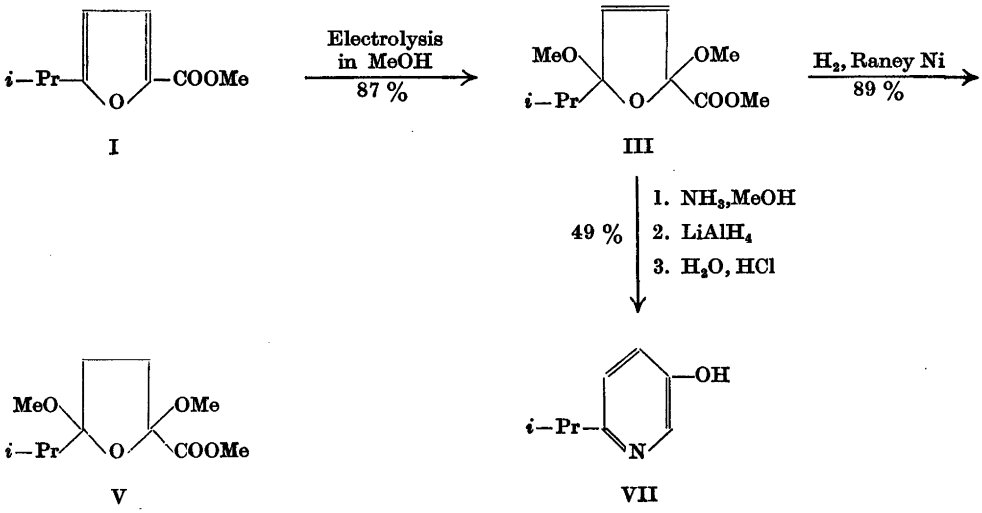
POUL NEDENSKOV, NIELS ELMING, JØRGEN TORMOD NIELSEN and NIELS CLAUSON-KAAS

Centrallaboratoriet, Sadolin & Holmblad A/S, Copenhagen, Denmark

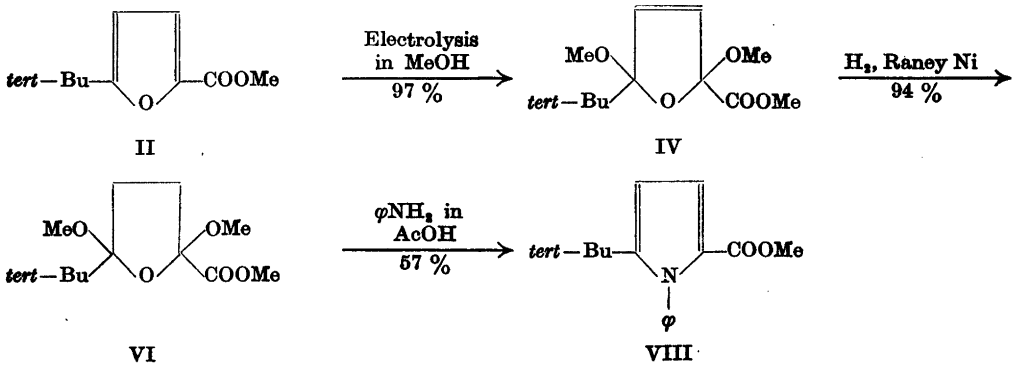
Four new 2,5-dimethoxy-2,5-dihydrofurans have been prepared by electrolytic methoxylation of the corresponding furans.

In connection with an investigation of certain furan compounds[1] four new dimethoxydihydrofurans have been prepared by the electrolytic methoxylation method[2,3]. In all 20 different furans have now been electrolytically methoxylated.

2-Carbomethoxy-5-*iso*propylfuran[4] (I) and 2-carbomethoxy-5-(*tert*butyl)-furan[4] (II) were electrolyzed in a sulfuric acid electrolyte[3]. Both dimethoxydihydrofurans (III and IV) were catalytically hydrogenated to the corresponding tetrahydrofurans (V and VI). The transformation of III into the 3-pyridinol VII[5] proves the structures of III and V. The structures of IV and VI were proved by transformation of VI into the pyrrole VIII (*cf.*[6]).

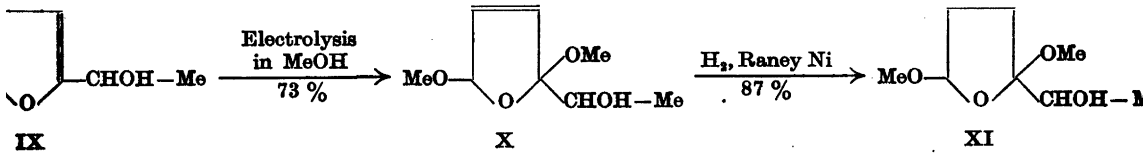


I III V VII

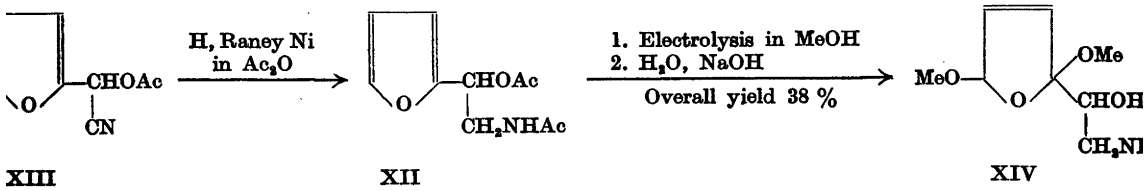


The Zeisel methoxy determination of 1-phenyl-2-carbomethoxy-5-(*tert*-butyl)-pyrrole (VIII) gave consistently 16—17 % of "methoxy" instead of the calculated 12.1 %. We believe that the unexpectedly high values come from the splitting off of methyl groups as methyl iodide from the *tert*-butyl group. Huang and Morsingh[7] have reported another instance in which certain dimethylalkylaryl methanes behaved similarly.

2-(α-Hydroxyethyl)-furan[8] (IX) was electrolyzed in an ammonium bromide electrolyte[2] and the resulting dimethoxydihydrofuran X catalytically hydrogenated to the tetrahydrofuran XI.



2-(α-Acetoxy-β-acetamidoethyl)-furan (XII), prepared by catalytic hydrogenation of furfural cyanohydrin acetate[9] (XIII) in acetic anhydride, was also electrolyzed in an ammonium bromide electrolyte. The reaction product was not isolated pure, but hydrolyzed with sodium hydroxide to 2,5-dimethoxy-2-(α-hydroxy-β-aminoethyl)-2,5-dihydrofuran (XIV), which was obtained pure by distillation.



We consider that it now may be regarded as an established fact that alkoxylation of furans always takes place at the α-carbons. The structures of the new compounds X, XI and XIV are therefore proved by the syntheses.

EXPERIMENTAL

Microanalyses by E. Boss, K. Glens and W. Egger

2,5-Dimethoxy-2-carbomethoxy-5-isopropyl-2,5-dihydrofuran (III). 2-Carbomethoxy-5-*iso*propylfuran (I)[4] (10.5 g, b.p.$_{14}$ 106–107°, n_D^{25} 1.4834) was mixed with anhydrous methanol (45 ml) and concentrated sulfuric acid (0.375 g, 0.0038 mole) and the solution electrolyzed in the small cell described previously[10] (temperature of cooling-bath −20°).

Time hr	Current amp	Potential across the cell during electrolysis volt	Ampere hours (per cent of theoretical amount)
1.0	0.9	8.0	0.82 (25 %)
3.0	0.8	7.9	2.40 (72 %)
5.0	0.7	7.8	3.62 (108 %)
5.9	0.6	7.7	4.20 (125 %)

After electrolysis the yellow liquid was poured into a solution of sodium methoxide (from 175 mg of sodium (0.0076 mole)) in methanol (7 ml) and the methanol evaporated in a vacuum. Anhydrous ether (50 ml) was added to the oily, light-brown residue, a precipitate of sodium sulfate removed by filtration and the filtrate distilled in a vacuum.

Fraction (g)		B.p.$_{0.1}$ °C	n_D^{25}	OCH_3 Calc. 40.4 %
1	(1.8)	71	1.4500	37.8
2	(7.4)	71	1.4497	40.1
3	(3.3)	70–75	1.4502	41.0

The yield (all fractions) was 12.5 g (87 %, current efficiency 70 %) of III (colorless liquid). A portion of fraction 2 was also analyzed for carbon and hydrogen.

$C_8H_9O_2(OCH_3)_3$ (230.3) Calc. C 57.4 H 7.9
Found » 57.6 » 8.1

2,5-Dimethoxy-2-carbomethoxy-5-isopropyl-tetrahydrofuran (V). III (3.45 g) and anhydrous methanol (15 ml) were shaken (20 hr) with Raney nickel (0.5 g) under hydrogen (100 atm). The product was isolated by distillation. The yield was 3.10 g (89 %) of V (colorless liquid, b.p.$_{0.1}$ 66–67°, n_D^{25} 1.4426).

$C_8H_{11}O_2(OCH_3)_3$ (232.3) Calc. C 56.9 H 8.7 OCH_3 40.1
Found » 56.8 » 8.6 » 39.5

2-Carbomethoxy-5-(tert-butyl)-furan (II). This compound was prepared from methyl furoate (30.3 g, 0.24 mole), *tert*-butyl chloride (22.2 g, 0.24 mole) and aluminum chloride (48 g, 0.36 mole) after the directions of Gilman and Calloway[4]. From the final solution carbon disulfide and ether were removed by distillation through a Vigreux column and the residue distilled through a 5 cm column packed with Dixon gauze rings.

The yield was 37.6 g (86 %) of II (b.p.$_{11-12}$ 110—113°, n_D^{25} 1.4789); previously found[4] b.p.$_{15}$ 110—114° and n_D^{25} 1.4792. On standing the product crystallized (m.p. 27—28° (Hershberg apparatus, corr.)).

2,5-Dimethoxy-2-carbomethoxy-5-(tert-butyl)-2,5-dihydrofuran (IV). II (9.2 g) was electrolytically methoxylated as described above for the preparation of III. The yield was 12.0 g (97 %, current efficiency 78 %) of IV (colorless liquid, b.p.$_{0.2-0.3}$ 67—71°, n_D^{25} 1.4502).

$C_9H_{11}O_2(OCH_3)_3$ (244.3)	Calc.	C 59.0	H 8.3	OCH_3 38.1
	Found	» 59.1	» 8.3	» 37.6

2,5-Dimethoxy-2-carbomethoxy-5-(tert-butyl)-tetrahydrofuran (VI). IV (3.7 g) was hydrogenated and the reaction product isolated as described above for the preparation of V.

Fraction (g)	B.p.$_{0.1}$ °C	n_D^{25}	OCH_3 Calc. 37.8 %
1 (0.96)	70—74	1.4479	37.0
2 (2.55)	69—74	1.4473	37.4

The yield (both fractions) was 3.51 g (94 %) of VI (colorless liquid). A portion of fraction 2 was also analyzed for carbon and hydrogen.

$C_9H_{13}O_2(OCH_3)_3$ (246.3)	Calc.	C 58.5	H 9.0
	Found	» 58.7	» 8.9

1-Phenyl-2-carbomethoxy-5-(tert-butyl)-pyrrole (VIII). VI (2.46 g, 0.01 mole) was dissolved in a mixture of aniline (0.93 g, 0.01 mole) and glacial acetic acid (2.4 ml) and the solution heated under reflux for 5 minutes. The acetic acid and the methyl acetate formed by the reaction were removed by distillation in a vacuum. The yellow, crystalline residue was crystallized from ethanol-water, yielding 2.10 g (82 %) of VIII (slightly yellow crystals, m.p. 64—68°). Crystallization from ether-petroleum ether gave 1.46 g (57 %) of white crystals, m.p. 72°. Further crystallization did not change the m.p.

$C_{15}H_{16}ON(OCH_3)$ (257.3)	Calc.	C 74.7	H 7.4	N 5.4	OCH_3 12.1
	Found	» 74.7	» 7.8	» 5.0	"OCH_3" 16.9

The product gave a positive Ehrlich reaction after boiling with 15 % sulfuric acid for 2 minutes.

2,5-Dimethoxy-2-(α-hydroxyethyl)-2,5-dihydrofuran (X). 2-(α-Hydroxyethyl)-furan (IX)[8] (44.8 g, 0.40 mole) was electrolytically methoxylated and the reaction mixture worked up as described previously for the preparation of dimethoxydihydrofurfuryl alcohol[11].

Fraction (g)	B.p.$_{11-10}$ °C	n_D^{25}	OCH_3 Calc. 35.6 %
1 (7.0)	62—104	1.4641	17.0
2 (8.7)	104—107	1.4540	35.8
3 (42.0)	107	1.4542	35.6
4 (1.0)	107—108	1.4549	38.2
Residue (3)			

All fractions showed a negative Beilstein test for halogens. The yield (fractions 2 and 3) was 50.7 g (73 %, current efficiency 86 %) of X (colorless liquid). A portion of fraction 3 was also analyzed for carbon and hydrogen.

$C_6H_8O_2(OCH_3)_2$ (174.2)	Calc.	C	55.2	H	8.1
	Found	»	55.4	»	8.0

2,5-Dimethoxy-2-(α-hydroxyethyl)-tetrahydrofuran (XI). X (3.50 g) and anhydrous methanol (15 ml) were shaken (3 hr) with Raney nickel (0.50 g) under hydrogen (100 atm) and the reaction product isolated by distillation.

Fraction (g)	B.p.$_{15-16}$ °C	n_D^{25}	OCH_3 Calc. 35.2 %
1 (0.37)	102—104	1.4439	33.9
2 (2.06)	105—106	1.4456	34.8
3 (0.64)	107—108	1.4464	34.7

The yield (all fractions) was 3.07 g (87 %) of XI (colorless liquid). A portion of fraction 2 was also analyzed for carbon and hydrogen.

$C_6H_{10}O_2(OCH_3)_2$ (176.2)	Calc.	C	54.5	H	9.2
	Found	»	54.7	»	9.2

Hydrogenation for 20 hours did not change the yield or the quality of the reaction product.

Furfural cyanohydrin acetate (XIII). This compound was prepared from furfural (96 g) after the directions of Lukeš, Kastner, Gut and Herben[9]. The yield was 122 g (74 %) (b.p.$_{0.1}$ 67—68°, n_D^{25} 1.4683); previously found[9] b.p.$_{10}$ 115°. Two crystallizations from ether gave white crystals, m. p. 27—29°.

$C_6H_4O_2N(COCH_3)$ (165.1)	Calc.	C	58.2	H	4.3	N	8.5	$COCH_3$ 26.1
	Found	»	58.0	»	4.4	»	8.0	» 25.3

2,5-Dimethoxy-2-(α-hydroxy-β-aminoethyl)-2,5-dihydrofuran (XIV). XIII (33.0 g, 0.20 mole) and acetic anhydride (200 ml) were shaken (2 hr) with Raney nickel (4.0 g) under hydrogen (100 atm, 50—58°). After filtration the solvent was evaporated in a vacuum, finally under 0.1 mm at 55—60°. The residue was dissolved in methanol (250 ml), ammonium bromide (5.0 g) was added and the mixture electrolyzed with the set-up described previously[2] for the electrolytic methoxylation of furan.

Time hr	Current amp	Potential across the cell during electrolysis volt	Ampere hours (per cent of theoretical amount		Temperature in the cell °C
0.1	3.0	4.9	0.3	(3 %)	—13
0.5	2.9	4.8	1.5	(14 %)	—13
1.0	2.7	4.7	2.9	(27 %)	—14
3.5	2.3	5.3	9.2	(86 %)	—14
4.8	1.9	5.6	11.8	(110 %)	—14

After electrolysis the liquid was poured into a solution of sodium methoxide (from 5.8 g of sodium in methanol (70 ml)) and the methanol and the ammonia evaporated in a vacuum. Sodium hydroxide (3 *N*, 200 ml) was added, the mixture heated under reflux (20 hr), continuously extracted with ether and the etheral solution distilled. The yield was 14.5 g (38 % based upon furfural cyanohydrin acetate) of XIV (colorless liquid, b.p.$_{0.1}$ 91–93°, n_D^{25} 1.4836).

$C_4H_4O_2N(OCH_3)_3$ (189.2)	Calc.	C	50.8	H	8.0	N	7.4	OCH_3 32.8
	Found	»	50.9	»	8.2	»	7.6	» 32.3

In a separate experiment 2-(α-acetoxy-β-acetamidoethyl)-furan (XII) was isolated pure by crystallization from ether (white crystals, m. p. 64–67°).

$C_4H_7O_2N(COCH_3)_2$ (211.2)	Calc.	C	56.9	H	6.2	N	6.6	$COCH_3$ 40.8
	Found	»	56.8	»	6.1	»	6.5	» 39.8

REFERENCES

1. Clauson-Kaas, N., Elming, N. and Tyle, Z. *Acta Chem. Scand.* **9** (1955) 1.
2. Clauson-Kaas, N., Limborg, F. and Glens, K. *Acta Chem. Scand.* **6** (1952) 531.
3. *Cf.* Clauson-Kaas, N. and Limborg, F. *Acta Chem. Scand.* **6** (1952) 551.
4. Gilman, H. and Calloway, N. O. *J. Am. Chem. Soc.* **55** (1933) 4197.
5. Clauson-Kaas, N. and Nedenskov, P. *Acta Chem. Scand.* **9** (1955) 14.
6. Elming, N. and Clauson-Kaas, N. *Acta Chem. Scand.* **6** (1952) 867.
7. Huang, R. L. and Morsingh, F. *Anal. Chem.* **24** (1952) 1359.
8. Ushakov, M. I. and Kucherov, V. F. *Zhur. Obshchei Khim.* **14** (1944) 1080; *Chem. Abstracts* **40** (1946) 7185.
9. Lukeš, R., Kastner, F., Gut, J. and Herben, J. *Collection Czechoslov. Chem. Communs.* **12** (1947) 647.
10. Limborg, F. and Clauson-Kaas, N. *Acta Chem. Scand.* **7** (1953) 234.
11. Clauson-Kaas, N., Limborg, F. and Dietrich, P. *Acta Chem. Scand.* **6** (1952) 545.

Received November 24, 1953.