

**The Alkoxylation of Furans With a Negative α -Substituent;
Preparation of 2,5-Dimethoxy-2,5-dihydro-2-furoic Acid
Methyl Ester and 2,5-Dimethoxytetrahydro-2-furoic Acid
Methyl Ester**

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The oxidation of furans to stable 2,5-disubstituted 2,5-dihydrofurans is a useful reaction since the dihydrofurans may serve as intermediates in the preparation of various types of compounds, which are otherwise difficult of accession. Several methods for the oxidation of furans to 2,5-dihydrofurans are known, Meinels method of methoxylation with halogens in methanol being by far the most convenient¹⁻³. This method is, however, not generally applicable as furans with a negative α -substituent can usually not be methoxylated in this way. Of 2-furoic acid, ethyl 2-furoate, ethyl 2-furylacrylate, furfural and 2-acetylfuran only furfural is methoxylated by bromine in methanol under the usual reaction conditions^{1,3}. Besides furfural, the only other furan with a negative substituent, which has been methoxylated, is methyl 2-furoate (Jones²). Chlorine in boiling methanol was used for the methoxylation. But the yield of dimethoxydihydro-2-furoic acid methyl ester was only 12 per cent and the product, of which no analyses were reported, can not have been very pure since it boiled from 120° to 140° at 20 mm.

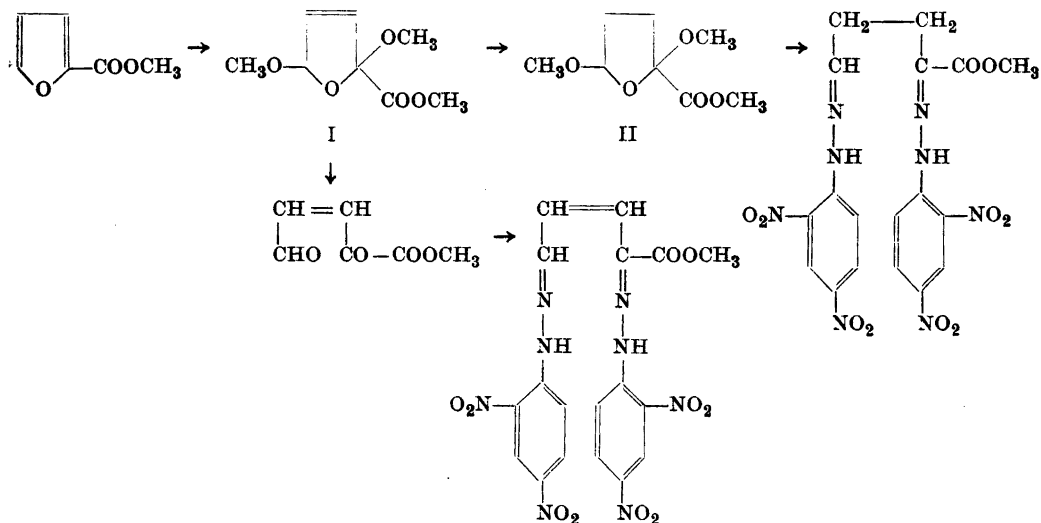
We have now found that a 68 per cent yield of analytically pure dimethoxydihydro-2-furoic acid methyl ester is obtained by electrolyzing a mixture of methyl furoate, methanol and sulfuric acid in the cell described previously for the methoxylation of furan⁴. It is possible that this new form of the alkoxylation method may also be used for the alkoxylation of other furans with a negative substituent*.

* Patent pending.

Dimethoxydihydrofuroic acid methyl ester was hydrogenated catalytically to dimethoxytetrahydrofuroic acid methyl ester, which is a new compound. Dimethoxytetrahydrofuroic acid methyl ester formed, with dinitrophenylhydrazine in methanol, a bis-dinitrophenylhydrazone with the formula $C_{17}H_{13}O_9N_8(OCH_3)$. This proves, that the methoxy groups in both dimethoxy compounds are in the 2,5-positions (formulas I and II).

The product obtained by treatment of methyl 2-furoate with chlorine in methanol gave, as reported by Jones², after hydrolysis and reaction with dinitrophenylhydrazine, a bis-dinitrophenylhydrazone with the formula $C_{18}H_{14}O_{10}N_8$. Jones' product must therefore also have the methoxy groups in the 2,5-positions.

The reactions starting from methyl 2-furoate so far carried out are shown below.



The structure of dialkoxydihydrofurans has, as a rule, been proved by identification of the compounds formed by hydrolysis^{Cf. 5}. Hydrogenation of the dialkoxydihydrofurans to dialkoxytetrahydrofurans and subsequent hydrolysis or alcoholysis, as described above, can likewise be used as a proof of structure, and it may now and then be easier to obtain, from the dialkoxytetrahydrofuran, a high yield of a derivative, which crystallizes well and melts sharply.

The individual dialkoxydihydrofurans and the dialkoxytetrahydrofurans are usually spoken of, as if they were pure compounds, but it should be remembered, that they may be mixtures of the *cis* and the *trans* isomers, as is probably

the case with electrolytically prepared 2,5-dimethoxy-2,5-dihydrofuran ⁴. They may furthermore, as mentioned by Clauson-Kaas and Limborg ⁶, contain small amounts of structural isomers, *e. g.* 2,3-dialkoxy-2,3-dihydrofurans, which have escaped notice during the structure determination.

EXPERIMENTAL

Microanalyses in part by Kirsten Glens

2,5-Dimethoxy-2,5-dihydro-2-furoic acid methyl ester (I). A mixture of 63.0 g of methyl 2-furoate (0.50 mole), 230 ml of methanol (5.7 moles) and 1.00 ml of concentrated sulfuric acid (0.019 mole) (note 1) is electrolyzed with the set-up used previously for the methoxylation of furan⁴.

Hours	Current (ampere)	Potential across the cell during electrolysis (volt)	Temperature in the cell	Ampere hours (per cent of theoretical amount)
0.5	2.3	6.4	- 13°	1.1 (4 %)
3.3	2.0	6.6	- 13°	7.2 (27 %)
9.1	1.6	7.0	- 15°	17.9 (67 %)
20.1	1.1	7.1	- 17°	32.0 (119 %)
	1.1	7.1	- 17°	33.5 (125 %)

After electrolysis the light-brown liquid in the cell is poured into a solution of sodium methoxide (0.95 g of sodium (0.041 mole) in 15 ml of methanol) and the methanol evaporated in vacuum from a water-bath. The oily dark-brown residue is precipitated with 200 ml of ether and the precipitate removed by centrifugation and washed with ether. The ether is then distilled from a water-bath and the residue distilled further in vacuum through a 5 cm column packed with glass helices.

Fraction (g)	B.p.13-14	n_D^{25}	OCH ₃ Calc. 49.4
1 (2.8)	72-119°	1.4549	
2 (20.7)	119-121°	1.4476	48.0
3 (43.0)	121	1.4476	49.2
residue (14)			

Yield (fractions 2-3) 63.7 g of dimethoxydihydrofuroic acid methyl ester = 68 %; current efficiency 54 %. Fraction 2 was also analyzed for carbon and hydrogen.

$C_5H_3O_2(OCH_3)_3$ (188.2) Calc. C 51.1 H 6.4
Found » 51.0 » 6.4

2,5-Dimethoxytetrahydro-2-furoic acid methyl ester (II). 63.1 g of dimethoxydihydrofuroic acid methyl ester (b.p.₁₈ = 127-131°, n_D^{25} = 1.4474) and 100 ml of anhydrous methanol are shaken with 2.0 g of Raney nickel under 100 atmospheres of hydrogen for 5 hours. After filtration the methanol is evaporated in vacuum from a water-bath and the residue distilled further in vacuum.

Fraction (g)	B.p. ₁₃	n_D^{25}	OCH ₃ Calc. 48.9 %
1 (5.2)	100-102°	1.4348	47.8
2 (20.2)	102-105°	1.4347	47.8
3 (27.5)	105-108°	1.4348	48.6
4 (5.1)	108-113°	1.4353	49.3
5 (3.7)	113-136°	1.4361	49.8
residue (1)			

Yield (fractions 1-4) 58.0 g of dimethoxytetrahydrofuroic acid methyl ester = 91 %. Fraction 3 was also analyzed for carbon and hydrogen.

$C_5H_5O_2(OCH_3)_3$ (190.2) Calc. C 50.5 H 7.4
Found » 50.7 » 7.3

Bis-dinitrophenylhydrazone of methyl α,δ -dioxo-n-valerate. 188 mg of dimethoxytetrahydrofuroic acid methyl ester in 4 ml of methanol was added to a solution of 500 mg of dinitrophenylhydrazine in 7 ml of methanol and 1 ml of concentrated sulfuric acid. The yellow hydrazone, which crystallized almost immediately, was filtered off after one hour and washed thoroughly with methanol; yield 364 mg of bis-dinitrophenylhydrazone = 73 %; m.p. (Hershberg apparatus, corr.) 246-248° (destruction). 50 mg was crystallized from nitromethane; yield 38 mg; m.p. 256-258°. Recrystallization gave 31 mg; m.p. 253-255°. This product was dried (sulfuric acid, 0.01 mm, 80°, 16 hours) and analyzed.

$C_{17}H_{13}O_9N_8(OCH_3)$ (504.4) Calc. C 42.9 H 3.2 N 22.2 OCH₃ 6.2
Found » 42.8 » 3.3 » 21.7 » 6.2

Note 1. All materials were technical products.

SUMMARY

2,5-Dimethoxy-2,5-dihydro-2-furoic acid methyl ester has been prepared by electrolytic methoxylation of methyl 2-furoate. Catalytic hydrogenation gave 2,5-dimethoxytetrahydro-2-furoic acid methyl ester, which is a new compound.

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