

Electrolytic Methoxylation of Some  $\beta$ -Isopropylfurans

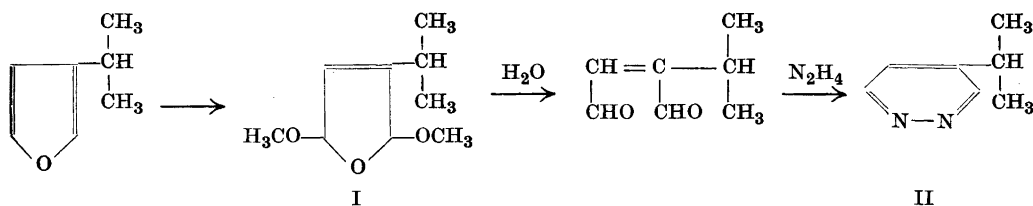
NIELS ELMING

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

The methoxylation of furans to 2,5-dialkoxy-2,5-dihydrofurans by the action of an oxidizing agent on a methanolic solution of the furan appears to be a very general reaction. So far furan<sup>1-2</sup>, silvan<sup>3</sup>, furfuryl alcohol<sup>3</sup>, furfuryl acetate<sup>3</sup>, furfuryl methyl ether<sup>4</sup>, furfural<sup>5</sup>, furfural dimethyl acetal<sup>3</sup>, furfural diacetate<sup>6</sup>, methyl 2-furoate<sup>7</sup> and 2,5-dimethylfuran<sup>8</sup> have been methoxylated. The oxidation is best carried out electrolytically in a methanolic solution of ammonium bromide or sulfuric acid.

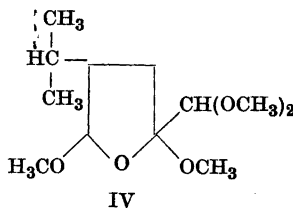
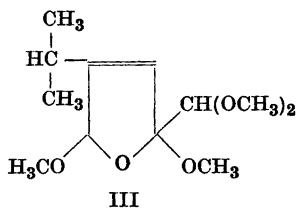
The electrolytic method of methoxylation has now been tried on three  $\beta$ -substituted furans, *viz.*  $\beta$ -isopropylfuran, 4-isopropyl-2-furaldehyde dimethyl acetal and methyl 4-isopropyl-2-furoate. All gave good yields of the corresponding dimethoxydihydrofurans, which are new compounds.

Hydrolysis of dimethoxy- $\beta$ -isopropylidihydrofuran and addition of an aqueous solution of dinitrophenylhydrazine to the hydrolysate gave a dinitrophenylhydrazone with the analytical values of a monohydrazone of isopropylmalealdehyde. The parent dihydrofuran must therefore be 2,5-dimethoxy-3-isopropyl-2,5-dihydrofuran I. In agreement herewith hydrolysis of dimethoxyisopropyl-dihydrofuran and addition of hydrazine gave a base with the formula  $C_7H_{10}N_2$ , which must be 4-isopropylpyridazine II.

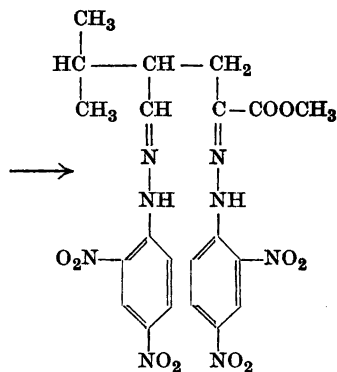
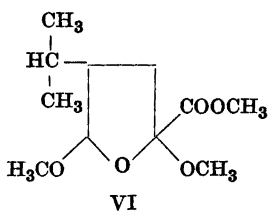
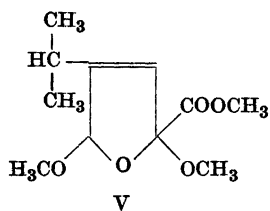


4-Isopropylpyridazine is also a new compound. It was characterized by a picrate and a methiodide. The yield of 4-isopropylpyridazine in the above synthesis was only 19 per cent.

Dimethoxy-4-isopropyl-dihydro-2-furaldehyde dimethyl acetal was hydrogenated catalytically to the corresponding tetrahydrofuran. The structure of these dimethoxy-compounds was not determined, but in view of what is known in general about the oxidation of furans the methoxy-groups in both compounds are probably in the 2,5-positions (formulas III and IV).



Methyl dimethoxy-4-isopropyl-dihydro-2-furoate was also hydrogenated to the corresponding tetrahydrofuran, which with dinitrophenylhydrazine in methanol formed a bis-dinitrophenylhydrazone with the formula  $C_{20}H_{19}O_9N_3$  ( $OCH_3$ ). This proves that the methoxy-groups in both compounds are in the 2,5-positions (formulas V and VI).



The above reactions bring the number of furans, which have been methoxylated to dihydrofurans, up to 13.

### EXPERIMENTAL

Microanalyses by F. Limborg, K. Glens and A. Grossmann

*2,5-Dimethoxy-3-isopropyl-2,5-dihydrofuran (I)*. A mixture of 22.0 g of  $\beta$ -isopropylfuran<sup>9</sup> (0.20 mole), 275 ml of methanol (technical product) and 5.0 g of ammonium bromide was electrolyzed and worked up in the usual way<sup>Cl. 3</sup>.

Hours	Current (ampere)	Potential across the cell during electrolysis (volt)	Temperature in the cell °C	Ampere hours (per cent of theoretical amount)
0.1	2.0	3.4	- 13	0.3 (3 %)
1.2	1.8	3.5	- 16	2.4 (22 %)
3.5	1.7	3.6	- 17	6.5 (60 %)
5.2	1.5	3.6	- 17	9.3 (86 %)
5.8	1.3	3.8	- 16	10.2 (95 %)

Fraction (g)	B. p. <sub>15</sub>	$n_D^{25}$	OCH <sub>3</sub> Calc. 36.0 %
1 (4.5)	83-84°	1.4385	35.7
2 (3.0)	84-86°	1.4387	35.7
3 (14.2)	84-86°	1.4388	35.9
4 (3.1)	85-86°	1.4388	35.9

All fractions were colourless. Yield (fractions 1-4) 24.8 g of dimethoxy-isopropyl-dihydrofuran = 72 %; current efficiency 76 %. Fraction 3 was further analyzed for carbon and hydrogen.

$C_7H_{10}O(OCH_3)_2$  (172.2) Calc. C 62.8 H 9.4  
 Found » 62.6 » 9.4

43 mg of dimethoxy-isopropyl-dihydrofuran was boiled with 2 ml of *N*/10 sulfuric acid for one minute. After cooling 50 ml of an 0.2 % solution of dinitrophenylhydrazine in 2 *N* hydrochloric acid was added, the mixture shaken vigorously and left standing for 1.5 hours with occasional shaking. The orange-red hydrazone was isolated in the usual way. Yield 50 mg of crude isopropylmalealdehyde dinitrophenylhydrazone = 65 %. Yield after crystallization from absolute ethanol 25 mg; m. p. 175-177° (Hershberg apparatus corr.). The product was dried (sulfuric acid, 0.05 mm, 20°, 20 hours) and analyzed.

$C_{13}H_{14}O_5N_4$  (306.3) Calc. C 51.0 H 4.6 N 18.3 OCH<sub>3</sub> 0  
 Found » 50.7 » 4.8 » 18.1

In another experiment the crude product was recrystallized twice from absolute ethanol; m. p. 178–180°.

Found C 51.0 H 4.9 N 18.1 OCH<sub>3</sub> 0.2

*4-Isopropylpyridazine (II)*. 12.0 g of 2,5-dimethoxy-3-isopropyl-2,5-dihydrofuran (0.07 mole) was stirred at room temperature with 168 ml of *N*/10 sulfuric acid. After stirring for 10 minutes the mixture became homogeneous, but 5–10 minutes later it again became turbid. 100 ml of methanol was added whereby the mixture became almost clear. After cooling to 0° a solution of 10.5 g of 50 % hydrazine hydrate (0.105 mole) in 28 ml of water was added during 15–30 seconds whereby the temperature rose to 7°. The mixture was left standing overnight and was then refluxed for 30 minutes. After cooling 27 ml of 4.8 *N* sulfuric acid was added, the methanol evaporated in vacuum and 5.2 g of sodium hydroxide in 10 ml of water added. The resulting solution was extracted continuously with ether, until no more high-boiling products could be extracted. From the ethereal extract 3.62 g of a pale-yellow liquid was isolated by distillation; b. p.<sub>15</sub> = 122–150°;  $n_D^{25}$  = 1.5011. 2.56 g of this product was added to 500 ml of a 1 % aqueous solution of picric acid at 50° and the mixture left standing for 2 hours at room temperature with occasional shaking. The resulting picrate of 4-isopropylpyridazine was filtered off and washed with water; yield 3.76 g = 22 % proportionate to dimethoxy-isopropyl-dihydrofuran; m. p. 92–95°.

C<sub>13</sub>H<sub>13</sub>O<sub>7</sub>N<sub>5</sub> (351.3) Calc. C 44.5 H 3.7 N 19.9  
Found » 44.7 » 4.1

Another sample of isopropylpyridazine picrate from another experiment was crystallized twice from ethanol; m. p. 95–97°.

Found C 44.9 H 3.9 N 19.8

The free isopropylpyridazine (C<sub>7</sub>H<sub>10</sub>N<sub>2</sub> (122.2)) was prepared from 3.74 g of the picrate in the usual way and purified by distillation.

Fraction (g)	B. p. <sub>14</sub>	$n_D^{25}$	C Calc. 68.8 %	H Calc. 8.3 %	N Calc. 22.9 %
1 (0.13)	121°	1.5015	68.7	8.2	22.6
2 (0.98)	121°	1.5025	68.8	8.5	23.2

Yield 1.11 g of isopropylpyridazine = 85 % proportionate to the picrate (19 % proportionate to dimethoxy-isopropyl-dihydrofuran).

The methiodide of 4-isopropylpyridazine was also prepared and crystallized twice from absolute ethanol-ether; m. p. 156–158°.

C<sub>8</sub>H<sub>13</sub>N<sub>2</sub>I (264.1) Calc. C 36.4 H 5.0 N 10.6 I 48.1  
Found » 36.5 » 4.4 » 10.8 » 48.0

*Dimethoxy-4-isopropyl-dihydro-2-furaldehyde dimethyl acetal*. 14.7 g of 4-isopropyl-2-furaldehyde dimethyl acetal<sup>9</sup> (0.080 mole), 270 ml of methanol and 5.0 g of ammonium bromide were electrolyzed and the reaction mixture worked up in the usual way *cf.* 3.

Hours	Current (ampere)	Potential across the cell during electrolysis (volt)	Temperature in the cell °C	Ampere hours (per cent of theoretical amount)
0.5	1.9	3.4	- 18	1.0 (20 %)
1.5	1.8	3.5	- 17	2.8 (65 %)
2.5	1.4	3.8	- 19	4.4 (102 %)

Fraction (g)	B. p. 0.1	$n_D^{25}$	OCH <sub>3</sub> Calc. 50.4 %
1 (1.1)	62-64°	1.4449	46.6
2 (14.7)	64-65.5°	1.4440	49.6
3 (0.7)	66-67°	1.4446	49.2

All fractions were colourless. Yield (fraction 2) 14.7 g of dimethoxy-isopropyl-dihydro-furaldehyde dimethyl acetal = 75 %; current efficiency 73 %.

$C_8H_{10}O(OCH_3)_4$  (246.3) Calc. C 58.5 H 9.0  
Found » 58.7 » 9.2

*Dimethoxy-4-isopropyl-tetrahydro-2-furaldehyde dimethyl acetal.* 4.06 g of dimethoxy-isopropyl-dihydro-furaldehyde dimethyl acetal and 20 ml of anhydrous methanol were shaken with 0.6 g of Raney nickel under 105-120 atmospheres of hydrogen at 120-130° for 21 hours. The reaction product was isolated as usual. Yield 2.31 g of dimethoxy-4-isopropyl-tetrahydro-2-furaldehyde dimethyl acetal = 56 %; colourless liquid, b. p. 0.1 = 58-60°;  $n_D^{25} = 1.4349$ .

$C_8H_{12}O(OCH_3)_4$  (248.3) Calc. C 58.0 H 9.7 OCH<sub>3</sub> 50.0  
Found » 58.2 » 10.0 » 48.5

*Methyl 2,5-dimethoxy-4-isopropyl-2,5-dihydro-2-furoate (V).* 12.6 g of methyl 4-isopropyl-2-furoate<sup>9</sup> (0.075 mole), 280 ml of methanol and 1.87 g of concentrated sulfuric acid were electrolyzed and the reaction mixture worked up in the usual way<sup>Cf. 3</sup> (see p. 577).

Yield 10.5 g of methyl dimethoxy-isopropyl-dihydrofuroate = 61 %; current efficiency 47 %; colourless liquid, b. p. 0.1 = 69-71°;  $n_D^{25} = 1.4520$ .

$C_8H_9O_2(OCH_3)_3$  (230.3) Calc. C 57.4 H 7.9 OCH<sub>3</sub> 40.4  
Found » 57.9 » 7.9 » 39.5

*Methyl 2,5-dimethoxy-tetrahydro-2-furoate (VI).* 4.20 g of methyl dimethoxy-isopropyl-dihydrofuroate and 20 ml of anhydrous methanol were shaken with 0.7 g of Raney nickel under 100-120 atmospheres of hydrogen at 120-125° for 20 hours. Yield 3.05 g

Hours	Current (ampere)	Potential across the cell during electrolysis (volt)	Temperature in the cell °C	Ampere hours (per cent of theoretical amount)
0.7	1.0	4.0	- 19	0.8 (20 %)
1.5	0.9	4.0	- 19	1.6 (40 %)
2.9	0.8	4.1	- 19	2.8 (70 %)
6.2	0.7	4.2	- 20	5.2 (129 %)

of methyl dimethoxy-isopropyl-tetrahydrofuroate = 72 %; colourless liquid, b. p. 0.1 = 68–70°;  $n_D^{25} = 1.4401$ .

$C_8H_{11}O_2(OCH_3)_3$  (232.3) Calc. C 56.9 H 8.7  $OCH_3$  40.1  
Found » 57.1 » 8.9 » 39.1

232 mg of methyl dimethoxy-isopropyl-tetrahydrofuroate in 4 ml of anhydrous methanol was added to a solution of 500 mg of dinitrophenylhydrazine in 7 ml of methanol and 1 ml of concentrated sulfuric acid. After 1.5 hours a few mg of a red precipitate was removed by filtration. The next day a yellow precipitate was filtered off, washed 5 times with methanol and dried. Yield 360 mg of bis-dinitrophenylhydrazone = 66 %. Crystallization from acetone-petroleum ether gave 270 mg; m. p. 178–181°. Recrystallization gave 205 mg; m. p. 179–181°.

$C_{20}H_{19}O_9N_8(OCH_3)$  (546.5) Calc. C 46.2 H 4.1 N 20.5  $OCH_3$  5.7  
Found » 46.5 » 4.5 » 20.2 » 6.0

#### SUMMARY

Some  $\beta$ -substituted furans have been methoxylated by electrolysis to the corresponding 2,5-dimethoxy-2,5-dihydrofurans.

#### REFERENCES

1. Clauson-Kaas, N. (to Kemisk Værk Køge A/S). Belg. patent 500356 (1951).
2. Clauson-Kaas, N., Limborg, F., and Glens, K. *Acta Chem. Scand.* **6** (1952) 531.
3. Clauson-Kaas, N., Limborg, F., and Dietrich, P. *Acta Chem. Scand.* **6** (1952) 545.
4. Clauson-Kaas, N. *Acta Chem. Scand.* **6** (1952) 556.
5. Meinel, K. *Ann.* **516** (1935) 231.
6. Clauson-Kaas, N., and Fakstorp, J. *Acta Chem. Scand.* **1** (1947) 415.
7. Clauson-Kaas, N., and Limborg, F. *Acta Chem. Scand.* **6** (1952) 551.
8. Jones, D. G., and Imperial Chemical Industries Ltd. Brit. patent 595041; *C. A.* **42** (1948) 2992.
9. Elming, N. *Acta Chem. Scand.* **6** (1952) 602.

Received January 29, 1952.