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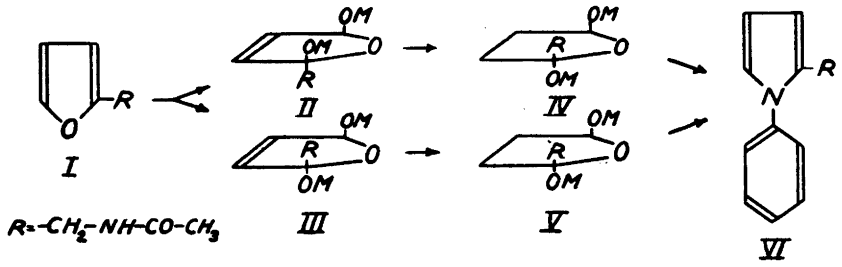
Preparation of *Cis* and *Trans* 2,5-Dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran, of *Cis* and *Trans* 2,5-Dimethoxy-2-(acetamidomethyl)-tetrahydrofuran and of 1-Phenyl-2-(acetamidomethyl)-pyrrole

NIELS CLAUSON-KAAS and ZDENĚK TYLE

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

A new electrolytic method for the methoxylation of furans has been described previously [1–4]. This has now been used to methoxylate 2-(acetamidomethyl)-furan (N-furfurylacetamide) (I) to the corresponding dimethoxydihydrofuran. The yield of distilled, analytically pure dimethoxy-2-(acetamidomethyl)-dihydrofuran was as high as 96 per cent. The product was partially crystalline and could be separated by crystallization from ether into about equal parts of a crystalline isomer (melting point 104°) and another isomer, which it was not possible to bring to crystallization. Both isomers were hydrogenated catalytically to the corresponding tetrahydrofurans. Crystalline dimethoxy-2-(acetamidomethyl)-dihydrofuran gave a crystalline dimethoxy-2-(acetamidomethyl)-tetrahydrofuran while the liquid isomer gave a liquid tetrahydrofuran.

When heated with aniline in acetic acid, both tetrahydrofurans gave a high yield of a compound with the formula $C_{11}H_{11}N_2(COCH_3)$. This compound, which could be distilled in vacuum and then crystallized from ether (melting point 88°), gave a positive Ehrlich reaction (for pyrroles with a free α-position), and must therefore be 1-phenyl-2-(acetamidomethyl)-pyrrole (VI). It follows that the tetrahydrofurans are *cis* and *trans* 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran (formulas IV and V) and that the dihydrofurans are *cis* and *trans* 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran (II and III). Compounds I—VI are all new.



The simple transformation of a 2,5-dimethoxytetrahydrofuran into a pyrrole probably proceeds through the corresponding 1,4-dicarbonyl compound, which then enters a Paal-Knorr pyrrole synthesis with the amine.

EXPERIMENTAL

Microanalyses by Kirsten Glens and Ernst Boss

2-(Acetamidomethyl)-furan (I). 75.0 g of acetic anhydride (technical product) in 75 ml of dry ether was added to a cooled (— 20°), stirred solution of 60.0 g of furfurylamine [5,6] in 100 ml of ether and the resulting amide isolated by distillation. Yield 82.0 g of 2-(acetamidomethyl)-furan = 95%; colourless liquid, b.p.$_9$ = 146—148°; n_D^{25} = 1.4998.

$C_5H_6ON(COCH_3)$ (139.2) Calc. C 60.4 H 6.5 N 10.1 $COCH_3$ 30.9
Found » 60.7 » 6.5 » 10.1 » 29.0

Cis *and* trans *2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran (II and III).* 5.00 g of ammonium bromide (0.051 mole) was dissolved in 260 ml of methanol (technical product) and 41.7 g of 2-(acetamidomethyl)-furan (0.30 mole) and the mixture electrolyzed with the set-up used previously for the electrolytic methoxylation of furan [1].

After electrolysis the liquid in the cell was colourless in the upper part of the cell and yellow near the bottom. The liquid was poured into a solution of sodium methoxide

Table 1.

Hours	Current (ampere)	Potential across the cell during electrolysis (volt)	Temperature in the cell °C	Ampere hours (per cent of theoretical amount)
0.5	3.3	4.5	— 11	1.7 (11 %)
2.2	3.0	4.8	— 13	7.3 (45 %)
5.3	2.3	5.1	— 12	16.3 (101 %)
6.0	2.0	5.2	— 12	17.7 (110 %)

(1.20 g of sodium (0.052 mole) in 20 ml of methanol) and the methanol and the ammonia evaporated in vacuum. The residue was distilled further in vacuum without filtering off the precipitate of sodium bromide. Yield 57.8 g of 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran = 96 %; colourless, partially crystalline product, $b.p._{0.6} = 119-134°$.

$C_5H_6ON(COCH_3)(OCH_3)_2$ (201.2) Calc. C 53.7 H 7.5 N 7.0 $COCH_3$ 21.4 OCH_3 30.9
Found » 53.6 » 7.8 » 6.5 » 21.1 » 30.5

Crystallization from 100 ml of ether gave 23.8 g of white crystals, m.p. 99—101° (Hershberg apparatus, corr.). Recrystallization gave a product melting at 104—105° (another crystallization did not change the m.p.).

Found C 53.8 H 7.8 N 6.7 $COCH_3$ 21.2 OCH_3 31.0

The mother liquid from the crystals was distilled in vacuum. Yield 31.6 g of a colourless, very viscous liquid, $b.p._{0.1} = 119-124°$ (no fore-run and no residue).

Found C 54.0 H 7.7 N 7.2 $COCH_3$ 21.1 OCH_3 30.1

Cis *and* trans *2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran (IV and V).* 20.0 g of crystalline 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran and 80 ml of methanol were shaken with 5 g of Raney nickel under 100 atmospheres of hydrogen for 4 hours at room temperature. Yield 19.6 g of crystalline 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran = 97 %; colourless product, $b.p._{0.1} = 117-124°$; m.p. 53—54°. M.p. after crystallization from ether 58—60° (further crystallization did not change the m.p.).

$C_5H_8ON(COCH_3)(OCH_3)_2$ (203.2) Calc. C 53.2 H 8.4 N 6.9 $COCH_3$ 21.2 OCH_3 30.5
Found. » 53.0 » 8.6 » 6.8 » 20.9 » 30.9

20.0 g of liquid, 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran gave in the same way 19.4 g of liquid 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran = 96 %; colourless, very viscous oil, $b.p._{0.1} = 111-117°$.

Found C 53.0 H 8.4 N 6.9 $COCH_3$ 21.4 OCH_3 30.2

1-Phenyl-2-(acetamidomethyl)-pyrrole (VI). 2.03 g of crystalline 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran (0.01 mole), 0.93 g of aniline (0.01 mole) and 3.0 ml of glacial acetic acid were refluxed for 30 minutes and the resulting clear, reddish-brown solution distilled. Yield 1.88 g of 1-phenyl-2-(acetamidomethyl)-pyrrole = 88 %; colourless product, $b.p._{0.4} = 166-171°$; m.p. 85—89°; Ehrlich reaction for pyrroles with a free α-position positive.

$C_{11}H_{11}N_2(COCH_3)$ (214.3) Calc. C 72.9 H 6.6 N 13.1 $COCH_3$ 20.1
Found » 72.4 » 6.7 » 13.3 » 19.8

Crystallization from ether gave 1.50 g; m.p. 88—91° (further crystallizations did not change the m.p.).

Found C 72.6 H 6.7 N 13.3 $COCH_3$ 19.1

2.03 g of liquid 2,5-dimethoxy-2-(acetamidomethyl)-tetrahydrofuran gave in the same way 2.08 g of 1-phenyl-2-(acetamidomethyl)-pyrrole = 97 %; $b.p._{0.1} = 159-166°$; m.p. 84—88°; Ehrlich reaction positive. Crystallization from ether gave 1.40 g; m.p. and mixed m.p. with the above sample 88—90°.

Found C 73.0 H 6.5 N 13.2 $COCH_3$ 19.1

SUMMARY

2-(Acetamidomethyl)-furan (I) has been methoxylated by electrolysis to a mixture of *cis* and *trans* 2,5-dimethoxy-2-(acetamidomethyl)-2,5-dihydrofuran (II and III). Catalytic hydrogenation of the dihydrofurans gave the

corresponding *cis* and *trans* tetrahydrofurans IV and V. Both tetrahydrofurans gave 1-phenyl-2-(acetamidomethyl)-pyrrole with aniline in acetic acid. All the above compounds are new.

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