

Note on the Preparation of Acetals of Alkoxysuccinaldehydes

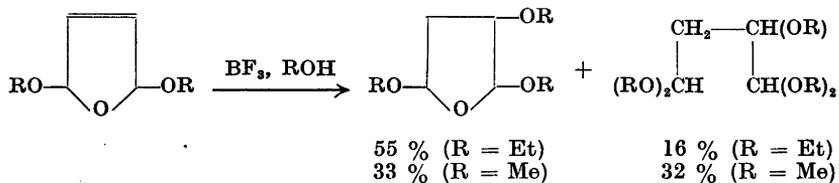
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Acetals of alkoxy succinaldehydes have been prepared by interaction of alcohols and 2,5-dialkoxy-2,5-dihydrofurans in the presence of catalytic amounts of boron fluoride etherate. The use of a new setup for laboratory fractional batch distillations is demonstrated.

Stoll, Lindenmann and Jucker¹ have prepared 2,3,5-trialkoxytetrahydrofurans by interaction of equimolar amounts of 2,5-dialkoxy-2,5-dihydrofurans and hydrogen bromide in alcoholic solution. These authors suggest that the reaction takes place through an intermediate 2,5-dialkoxy-3-bromo-tetrahydrofuran in which the bromine is replaced by a metathetic reaction with the solvent.

We have obtained trimethoxy- and triethoxytetrahydrofurans by interaction of the alcohol and the dihydrofuran in the presence of an acid catalyst, preferably boron fluoride etherate (*cf.*²). At the same time a certain amount of the tetraalkyl acetal of the alkoxy succinaldehyde is formed



The reaction mixtures were analyzed by fractional distillation and, as expected (*cf.*³), it was found that the trialkoxytetrahydrofurans consisted of mixtures of two or more stereoisomers. It was also found that the reaction mixture from 2,5-dimethoxy-2,5-dihydrofuran contained 9 % of malealdehyde tetramethyl acetal.

We believe that the experiments of Stoll, Lindenmann and Jucker¹ are also acid-catalyzed alcohol additions rather than two-step reactions proceeding through an intermediate bromo compound.

The results of the distillations are given in detail in order to demonstrate the use of a new setup for laboratory fractional batch distillations⁴.

Table 1. Distillation of 56.76 g of ethyl acetals under 14 mm; heat input 4.0 watt; take-off every 2.4 minutes; change of fraction every 1.0 hour; total yield of distillate 55.75 g (98.2 %).

Fraction (g)	B. p. °C	n_D^{25}	C %	H %	OC ₂ H ₅ %
1 (1.10)	< 89	1.4243			
2 (1.82)	89 — 100.1	1.4230			
3 (1.86)	100.1 — 100.4	1.4220	59.3	10.1	65.0
C ₄ H ₈ O(OC ₂ H ₅) ₂ (204.3) requires			58.8	9.9	66.2
4 (1.84)	100.4 — 100.6	1.4219			
5 (1.85)	100.6	1.4219			
6 (1.85)	100.6 — 100.7	1.4219			
7 (1.83)	100.7 — 100.8	1.4218			
8 (1.83)	100.8 — 100.9	1.4219			
9 (1.79)	100.9	1.4219	59.0	10.2	65.5
10 (1.79)	100.9	1.4219			
11 (1.85)	100.9 — 101.0	1.4219			
12 (1.79)	101.0	1.4220			
13 (1.82)	101.0 — 101.1	1.4220			
14 (1.76)	101.1 — 101.2	1.4220			
15 (1.79)	101.2 — 101.6	1.4222			
16 (1.83)	101.6 — 102.0	1.4227			
17 (1.75)	102.0 — 102.3	1.4229			
18 (1.81)	102.3 — 102.4	1.4231			
19 (1.79)	102.4 — 102.7	1.4231			
20 (1.82)	102.7 — 103.1	1.4231			
21 (1.85)	103.1 — 104.0	1.4231	59.4	10.1	65.0
22 (1.74)	104.0 — 120	1.4231			
23 (1.78)	120 — 135.0	1.4202			
24 (1.74)	135.0 — 136.0	1.4171			
25 (1.70)	136.0	1.4167	60.4	10.8	80.3
C ₄ H ₈ (OC ₂ H ₅) ₂ (278.4) requires			60.4	10.9	80.9
26 (1.73)	136.0	1.4166			
27 (1.69)	136.0 — 136.1	1.4165			
28 (1.72)	136.1	1.4164	60.7	10.9	80.3
29 (1.65)	136.1	1.4164			
30 (1.69)	136.1 — 136.2	1.4164			
31 (1.68)	136.2	1.4163	61.3	11.3	80.4
32 (1.21)	136.2 — 135.0	1.4167			

EXPERIMENTAL

Microanalyses in part by K. Glens

Addition of ethanol to diethoxydihydrofuran. Diethoxydihydrofuran⁵ (150.0 g), ethanol (anhydrous, 560 ml) and boron fluoride etherate (15.0 ml) were mixed and heated under reflux (90 min). A solution of sodium ethoxide [from sodium (7.5 g) and ethanol (60 ml)] was added and the mixture heated further under reflux (30 min). This was done in order to destroy traces of compounds with a free aldehyde group. After cooling, the borofluoride was removed by filtration and washed with ether. The ethanol and the ether were distilled in a vacuum from a water-bath (70°). The excess of sodium ethoxide was removed by centrifugation and washed twice with ether. The reaction product combined with the ethereal washings was then distilled. The yield was 167.0 g of a colorless liquid, b.p.₁₇ 101–135°. The product slowly forms peroxides on standing.

The product was fractionally distilled in a previously described setup including a 12 cm column⁴. The result of the distillation is shown in Table 1.

The yield of triethoxytetrahydrofuran (fractions 3–22) was 36.24 g (55 %) and of ethoxysuccinaldehyde tetraethyl acetal (fractions 24–32) 14.81 g (16 %). The yield of the mixture of acetals is 52.83 g (fractions 3–32) (74 %).

It is apparent from Table 1 that the triethoxytetrahydrofuran consists of a mixture of two or more stereoisomers. Stoll, Lindenmann and Jucker¹ report b.p.₁₅ 91–98° for their triethoxytetrahydrofuran.

Addition of methanol to dimethoxydihydrofuran. A mixture of acetals of methoxysuccinaldehyde was prepared from dimethoxydihydrofuran⁶ (100.0 g), methanol (dried with magnesium, 400 ml) and boron fluoride etherate (10.0 ml) as described above. The yield was 121.0 g of a colorless liquid, b.p.₁₅ 75–102°. The product was distilled through a 25 cm column⁴ (Table 2). During the distillation a low boiling product (0.58 g in all, n_D^{25} 1.3531), probably consisting mainly of methanol, accumulated in the cooling trap. In order to reduce this splitting off of methanol, the product rate was increased towards the end of the distillation.

In the article describing the setup for fractional distillation⁴ it was claimed that when a pure compound is distilled at constant boil-up rate and a fixed setting of the timer, the product rate remains constant within 3 %. In the above distillations this is only true for the distillation shown in Table 1, but not for the distillation shown in Table 2. We believe that the reason for this is the very slight decomposition which takes place during the latter distillation. The formation of gas causes small variations of the pressure in the still-pot and the column, whereby the boil-up rate and thereby the product rate is changed. In our experience, a slight decomposition is actually indicated more clearly by variations of the product rate, rather than by variations of the boiling point or the purity of the product (*e. g.* as measured by the refractive index).

The yield of trimethoxytetrahydrofuran (fractions 2–12) was 40.79 g (33 %), of malealdehyde tetramethyl acetal (fractions 15–18) 12.28 g (9 %) and of methoxysuccinaldehyde tetramethyl acetal (fractions 20–32) 50.46 g (32 %). The yield of the mixture of acetals (fractions 2–32) is 113.76 g (81 %).

The malealdehyde tetramethyl acetal (previously found⁷ b.p.₇₆₀ 198–199°, n_D^{25} 1.4282) was identified by transformation into malealdehyde bis-phenylhydrazone as described previously⁸. The yield was 74 mg (72 %), m. p. 170–171° (Kofler stage, corr.). The hydrazone was further characterized by the infrared absorption spectrum (in potassium bromide), which was identical with that of an authentic specimen prepared from dimethoxydihydrofuran. (Found: C 72.3; H 6.2; N 21.5. Calc. for C₁₆H₁₆N₄ (264.3): C 72.7; H 6.1; N 21.2).

It is apparent from Table 2 that the trimethoxytetrahydrofuran is a mixture of two or more stereoisomers. Stoll, Lindenmann and Jucker¹ report b.p.₁₅ 78–82° for their product. Kebrle and Karrer⁸ report b.p.₁₅ 85–86° and n_D^{20} 1.4300 for a product prepared by methylation of a 2,5-dimethoxy-3-hydroxytetrahydrofuran.

Table 2. Distillation of 119.6 g of methyl acetals under 25 mm; heat input 3.6 watt; take-off every 6.9 minutes; change of fraction every 8 hours. After about half of fraction 26 was collected and until the end of the distillation the take-off valve was opened every 1.7 minutes and the fractions changed every 4 hours. The total yield of distillate, including the product in the cooling trap, was 116.9 g (97.7 %).

Fraction (g)	B.p. °C	n_D^{25}	C %	H %	OCH ₃ %
1 (2.52)	65.5— 81.3	1.4296			49.0
2 (3.87)	81.3— 88.3	1.4233			54.7
3 (3.74)	88.3— 88.5	1.4228	52.0	8.9	55.8
C ₂ H ₅ O(OCH ₃) ₂ (162.2) requires			51.8	8.7	57.4
4 (3.65)	88.5— 88.6	1.4223			55.3
5 (3.72)	88.6	1.4225			56.3
6 (3.67)	88.6— 88.9	1.4222			57.7
7 (3.65)	88.9— 89.0	1.4226	51.7	9.0	56.4
8 (3.57)	89.0— 89.2	1.4226			56.7
9 (4.03)	89.2— 90.1	1.4230			56.4
10 (3.73)	90.1— 92.3	1.4241			55.9
11 (3.68)	92.3— 93.5	1.4260	51.3	8.8	56.4
12 (3.48)	93.5— 95.2	1.4264			57.0
13 (3.41)	95.2— 101.3	1.4252			59.5
14 (3.18)	101.3— 103.2	1.4233			65.3
15 (3.10)	103.2— 104.3	1.4242			67.0
16 (3.05)	104.3— 104.8	1.4252			68.5
17 (3.04)	104.8— 105.1	1.4259	54.5	9.2	69.0
C ₂ H ₄ (OCH ₃) ₄ (176.2) requires			54.5	9.2	70.4
18 (3.09)	105.1— 111.5	1.4261			69.0
19 (3.64)	111.5— 119.1	1.4191			71.5
20 (3.48)	119.1— 119.2	1.4169	52.1	10.1	73.0
C ₄ H ₉ (OCH ₃) ₅ (208.3) requires			51.9	9.7	74.5
21 (2.94)	119.2	1.4169			
22 (3.01)	119.2	1.4168			
23 (3.10)	119.2	1.4168	52.4	9.9	74.5
24 (2.95)	119.2	1.4167			
25 (3.07)	119.2	1.4167			
26 (4.39)	119.2	1.4167			
27 (5.47)	119.2	1.4166	52.4	9.8	74.0
28 (5.51)	119.2	1.4167			
29 (5.84)	119.2	1.4166			
30 (5.92)	119.2	1.4168			
31 (3.90)	119.2	1.4167	51.8	9.7	73.2
32 (0.88)	119.2	1.4176			72.8

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