

Nuclear Oxidation of Silvan and Furfuryl Alcohol

Preparation of 3-Methylpyridazine and 3-Hydroxymethylpyridazine

NIELS CLAUSON-KAAS and FRANZ LIMBORG

Universitetets Kemiske Laboratorium, København, Denmark

The nuclear oxidation of furfural has recently been investigated with special regard to the structure of addition products formed by the oxidation¹. In this communication the oxidation of silvan and furfuryl alcohol is discussed and the preparation of stable addition compounds of these furans described.

By acid hydrolysis the addition products yield yellow unsaturated 1,4-dicarbonyl compounds which proves the former to be derivatives of 2,5-dihydrofuran.

In analogy with the synthesis of pyridazines introduced by Paal and Schultze² 3-methylpyridazine and 3-hydroxymethylpyridazine, respectively, are formed by the addition of hydrazine to the dicarbonyl compounds.

SILVAN

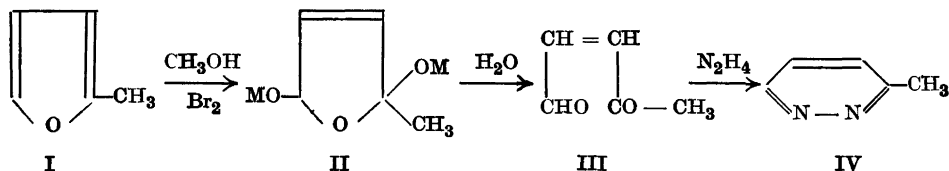
The formation of an addition compound by oxidation of silvan (I) has so far not been reported. Meinel³ mentions, that silvan is not methoxylated in the usual manner with bromophthalimide in methanol but yields a product which contains a considerable amount of bromine. However, we have prepared, a dimethoxydihydrosilvan in a 65 per cent yield by methoxylation with bromine in methanol. The acetal is a colourless liquid with properties similar to the corresponding dihydrofuran derivative described earlier⁴. The analysis, a methoxy and a molecular weight determination demonstrate that two methoxy groups have been added to silvan.

By acid hydrolysis and distillation of the reaction product a yellow liquid is collected boiling at 55—75°/10 mm. No doubt it consists mainly of β -acetylacrolein (III) but did not give the correct analytical values. The best determination was obtained of a fraction boiling at 68°/10 mm. which contained

59.9 % carbon and 6.58 % hydrogen (calc. for $C_5H_6O_3$: 61.2 % and 6.14 %). It is an established fact that carbonyl compounds of this type may retain water or alcohol firmly. We therefore believe that our product also contains a small amount of water or methanol which is sufficient to account for the diverging analysis.

The β -acetylacrolein was not subjugated to a closer study but it may be said, that this ketoaldehyde is more stable than malealdehyde (Wohl and Mylo⁵).

When dimethoxydihydrosilvan is hydrolyzed and hydrazine added to the reaction mixture, 3-methylpyridazine (IV) is formed in analogy with the synthesis of pyridazines introduced by Paal and Schulze². The base was obtained in a 56 per cent yield. It has previously been prepared by Poppenberg⁶ and his description of the properties of this compound is in perfect agreement with our observations. The synthesis of 3-methylpyridazine proves that the dihydrosilvan is 2,5-dimethoxy-2,5-dihydrosilvan (II).



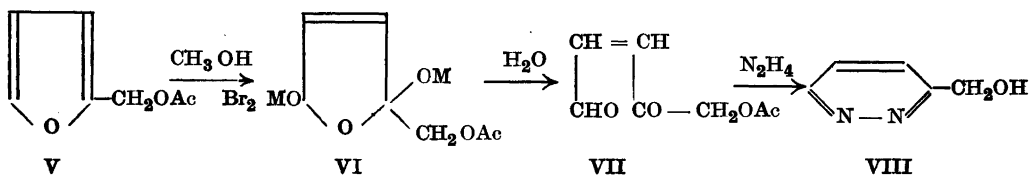
FURFURYL ALCOHOL

Meinel³ has prepared a dimethoxydihydrofurfuryl alcohol by the action of methanolic bromine on furfuryl alcohol. He believed this addition product to be 4,5-dimethoxy-4,5-dihydrofurfuryl alcohol but it has recently been suggested that Meinel's compound is the corresponding 2,5-derivative⁴.

We have methoxylated furfuryl acetate (V) and obtained a dimethoxydihydrofurfuryl acetate (yield 66 %). It is a viscous colourless oil boiling at about $112^\circ/9$ mm. The analysis, a methoxy, an acetoxy and a molecular weight determination demonstrate the addition of two methoxy groups to furfuryl acetate.

When the addition product is boiled with diluted sulfuric acid the characteristic greenish-yellow colour of unsaturated 1,4-dicarbonyl compounds appears. By addition of semicarbazide to the hydrolysate a white semicarbazone, which exhibits the analytical values of a monosemicarbazone of 5-acetoxypentene-(2)-one-(4)-al-(1) (VII), is precipitated in a 22 per cent yield.

Addition of hydrazine to the hydrolysate yields 3-hydroxymethylpyridazine (VIII) (yield 49 %). This condensation as well as the above evidence proves that the structure VI must be ascribed to the addition compound.



3-Hydroxypyridazine has not previously been prepared. It is a colourless crystalline solid melting at 66°. It is only slightly soluble in benzene and ether but very soluble in alcohol and water. The structure was established by the analytical evidence, a molecular weight determination, and by the preparation and analysis of a crystalline *p*-nitrobenzoate.

Hydroxymethylpyridazine reduces Tollen's reagent immediately at room temperature. Methylpyridazine also reduces the reagent, but not quite so rapidly.

We are well aware of the fact, that our structure determinations do not exclude the possibility that the dimethoxydihydrofurans — in spite of their narrow boiling-range during distillation — are mixtures of isomers consisting mainly of the 2,5-derivatives. But as long as this has not been demonstrated, the addition products must be regarded as pure 2,5-dihydrofurans.

EXPERIMENTAL

2,5-Dimethoxy-2,5-dihydrofuran

Preparation. 9.0 ml of silvan (0.1 mole) were methoxylated exactly as described earlier for the preparation of the corresponding furan derivative ⁴. B. p. 46°/8 mm. Towards the end of the distillation the temperature was allowed to rise to 56°. Colourless liquid, yield 9.3 g = 65 %. The acetal may be distilled under atmospheric pressure without destruction; b. p. 152°. The freezing point depression of a benzene solution was measured.

C ₇ H ₁₂ O ₃	Calc. C 58.30	H 8.40	CH ₃ O 43.1	Mol. wt. 144.2
	Found » 58.06	» 8.81	» 41.3	» » 141

Hydrolysis; isolation of β-acetylacrolein. 7.2 g of dimethoxy dihydrofuran (0.05 moles) were boiled for 5 minutes with 5 ml of centinormal sulfuric acid. 5 ml of a saturated solution of calcium chloride was added and the mixture extracted with 100 ml of ether. The ethereal solution was dried with 15 g of calcium chloride for 30 minutes and the ether

removed on the steam bath through a Vigreux column. The residue was distilled in vacuum and a yellow liquid boiling from 55° to 75° under 10 mm was collected; yield 3.5 g. The theoretical amount calculated as β -acetylacrolein is 4.9 g. The fraction boiling at 68° was analyzed.

$C_5H_6O_2$ (98.1)	Calc. C 61.22	H 6.14
	Found » 59.91	» 6.58

Hydrolysis; preparation of 3-methylpyridazine. 7.2 g of dimethoxydihydrosilvan (0.05 moles) were boiled for one minute with 40 ml of decinormal sulfuric acid. After rapid cooling with ice water and addition of 2.50 ml of hydrazine hydrate (0.05 moles) the solution was refluxed for 30 minutes. 5 g of finely powdered potassium chromate and 30 g of potassium carbonate were added, the mixture shaken at room temperature for two hours and extracted three times with in all 200 ml of ether. The ethereal layer was dried with 50 g of potassium carbonate and the ether removed on the steam bath through a Vigreux column. The residue was distilled in vacuum. The methylpyridazine boiled sharply at 85°/9 mm. There was no forerun but a small amount of a higher boiling residue. Towards the end of the distillation the temperature was allowed to rise to 95°.

Colourless liquid; yield 2.6 g = 55 %.

$C_5H_6N_2$ (94.1)	Calc. C 63.81	H 6.44	N 29.77
	Found » 62.87	» 6.41	» 30.35

When boiled in the atmosphere 3-methylpyridazine rapidly turned brown. B. p. 207—211°/766 mm (Poppenberg⁶) 206°/760 mm).

2, 5 - Dimethoxy - 2, 5 - dihydrofurfuryl acetate

46.5 g of furfuryl acetate (0.33 moles) and 60 g of potassium acetate (0.6 moles) were dissolved in 400 ml of methanol. A solution of 15.0 ml of bromine (0.30 moles) in 300 ml of methanol was added at —7° during 50 minutes, and the addition product isolated in the usual manner⁴. B. p. 112—138°/20 mm.; yield 40 g = 66 %. There was a forerun of furfuryl acetate (5—6 g) and 7 g of a higher boiling residue (b. p. 140—165°/20 mm). The main fraction was a colourless liquid, which boiled sharply at 131°/20 mm by redistillation. The freezing point depression of a benzene solution was measured.

$C_9H_{14}O_5$	Calc. C 53.46	H 6.99	CH ₃ COO 29.2	CH ₃ O 30.7	Mol. wt. 202.2
	Found » 53.21	» 7.12	» 28.2	» 29.7	» » 198

Hydrolysis; isolation of a monosemicarbazone of 5-acetoxypenten-(2)-one-(4)-al-(1). 220 mg of dimethoxydihydrofurfuryl acetate were boiled with 3 ml of centinormal sulfuric acid for 30 seconds. The solution, which had a faint greenish-yellow colour, was cooled and added to 0.30 g of semicarbazide hydrochloride and 0.35 g of potassium acetate. The mixture was heated slightly for a moment and then cooled rapidly. The semicarbazone, which precipitated immediately, was filtered off, washed thoroughly with water and dried over phosphorous pentoxide in vacuum over night. Yield 52 mg = 22 %. The crude product was recrystallized from 6 ml of alcohol. Yield 41 mg = 18 %. Colourless crystals, m. p. 160—165° (Kofler stage).

$C_8H_{11}O_4N_3$ (213.2)	Calc. C 45.07	H 5.21	N 19.72
	Found » 45.14	» 5.34	» 19.56

Hydrolysis; preparation of 3-hydroxymethylpyridazine. 10.1 g of dimethoxydihydrofurfuryl acetate (0.05 moles) were boiled for one minute with 40 ml of decinormal sulfuric acid. The solution was cooled rapidly, 5.00 ml of hydrazine hydrate (0.10 moles) were added and the mixture boiled for 20 minutes. After saturating with potassium carbonate (40 g) the hydroxymethylpyridazine was extracted with 600 cc. of ether, containing 7 % of methanol, the ethereal layer dried with potassium carbonate (20 + 50 g) and the ether removed on the steam bath. The residue was distilled under 1 mm. There was a colourless forerun (0.7 g) boiling at 110—120°, which crystallized readily (m. p. 40° (tube)). This substance was not further investigated. It was extremely hygroscopic.

The main fraction (b. p. 150°) consisted of the pure hydroxymethylpyridazine, which solidified to almost colourless crystals, m. p. 60°; yield 2.7 g = 49 %. M. p. after crystallisation from ether-petrolether 66° (tube, corr.). The freezing point depression of an aqueous solution was measured.

$C_5H_9ON_2$	Calc. C 54.51	H 5.50	N 25.43	Mol. wt. 110.1
	Found » 54.99	» 5.88	» 25.24	» » 105

If the synthesis was carried out with less than twice the theoretical amount of hydrazine hydrate, the reaction mixture turned dark, and the yield of hydroxymethylpyridazine was decreased considerably.

110 mg of 3-hydroxymethylpyridazine were dissolved in 0.3 ml of pyridine. 180 mg of p-nitrobenzoyl chloride were added and the mixture heated for one minute. 2 ml of water were added, the benzoate filteres off, washed thoroughly with acid sodium carbonate and water and dried over night in vacuum over phosphorous pentoxide. Yield 142 mg = 55 %. The crude product crystallized from acetone-ligroin or from methanol. M. p. 106° (tube, corr.).

$C_{12}H_9O_4N_3$ (259.2)	Calc. C 55.59	H 3.51	N 16.21 %
	Found » 55.58	» 3.63	» 16.58 »

During the investigation we have received financial aid from *Det teknisk-videnskabelige Forskningsraad* (N. Clauson-Kaas) and from *Kemisk Værk Køge A/S*, Copenhagen (F. Limborg).

We are grateful to the Director of the Chemical Laboratory of the University of Copenhagen, Prof. Dr. A. Langseth, for his kind interest in our work.

REFERENCES

1. Clauson-Kaas, N., and Fakstorp, J. *Acta Chem. Scand.* **1** (1947) 415.
2. Paal, C., and Schulze, H. *Ber.* **33** (1900) 3795.
3. Meinel, K. *Ann.* **516** (1935) 231.
4. Clauson-Kaas, N. *Kgl. Danske Vidensk. Selsk. Math.-Fys. Medd.* **22** (1947) 6.
5. Wohl, A., and Mylo, B. *Ber.* **45** (1912) 1746.
6. Poppenberg, O. *Ber.* **34** (1901) 3257.

Received July 10, 1947.