SYNTHESIS OF DIALKYLAMINOMETHYLFURFURALS

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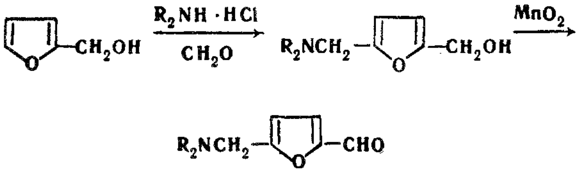
N, N-Dialkylaminomethylfurfuryl alcohols are synthesized by reacting furfuryl alcohol with dialkylamines in ethanol in the presence of paraformaldehyde. The N, N-dialkylaminomethylfurfurals are obtained by oxidizing the appropriate amino alcohols with active MnO_2.

It is known that treatment of amino alcohols with active manganese dioxide readily converts them to the carbonyl compounds [1]. It was of interest to investigate the possibility of synthesizing aminomethylfurfurals by oxidizing the appropriate furfuryl alcohols. Furan aminoaldehydes are interesting bifunctional compounds whose derivatives may possess biological activity, but hitherto they have been practically unknown. The literature describes [2] the synthesis of an extremely unstable material which the authors considered to be N,N-diethylaminomethylfurfural from chloromethylfurfural and diethylamine. They did not succeed in isolating the aminoaldehyde pure, and the paper gives only the analysis of the picrate. The present paper gives a method of synthesizing dialkylaminomethylfurfurals, comprising aminomethylating furfural alcohol with salts of secondary amines in the presence of synthesizing dialkylaminomethylfurfurals, comprising aminomethylating furfuryl alcohol with salts of secondary amines in the presence of paraform, and oxidation of the resultant amino alcohols to aldehydes with active manganese dioxide [3]. Not only furfuryl alcohol but also secondary alcohols can undergo the Mannich reaction, as was shown for furylmethylcarbinol.



All the aminomethylfurfurals were stable, slightly colored liquids which kept well in the cold, and which were rather soluble in water. Their structures were confirmed by IR spectra, which showed an intense band in the 1672–1686 cm^{-1} region, characteristic of the carbonyl group of furfurals. Further the melting point of the picrate of diethylaminomethylfurfural was the same as that given in the literature [2]. Aminomethylfurfurals react with great difficulty with 2,4-dinitrophenylhydrazine, but readily give hydrazones with the hydrazide of isonicotinic acid. These derivatives have considerable tuberculostatic action.

EXPERIMENTAL

5-(N, N-Dialkylaminomethyl)furfuryl alcohols. A mixture of equimolecular amounts of freshly distilled furfuryl alcohol, piperidine hydrochloride, and a 1.5 fold excess paraform was refluxed in ethanol for 2 hr, a further 1 mole paraform added, and refluxing continued for 12 hr more. The solvent was vacuum-distilled off, the residue made strongly alkaline, and extracted with ether. The solution was dried over $MgSO_4$, the solvent distilled off, and the residue vacuum-distilled. Yield of 5-(piperidinomethyl)furfuryl alcohol (I) 62.4%, bp 145° (2 mm), n_D^{20} 1.5199. Found: C 67.60, H 8.84, N 7.17%. Calculated for $C_{11}H_{17}NO_2$: C 67.66, H 8.78, N 7.17%.

The other amino alcohols were prepared similarly. 5-(N, N-Dimethylaminomethyl)furfuryl alcohol, yield 53.0%, bp 128°–133° (15 mm), n_D^{20} 1.4900. Found: C 62.00, H 8.56, N 8.84%. Calculated for $C_8H_{13}NO_2$: C 61.91, H 8.44, N 9.03%. The literature gives [2] 125°–135° (15 mm), n_D^{20} 1.4900. 5-(N, N-dimethylaminomethyl)furfuryl alcohol, yield 54.8%, bp 142°–146° (15 mm), n_D^{20} 1.4766. Found: C 65.32, H 9.23, N 7.83%. Calculated for $C_{10}H_{17}NO_2$: C 65.54, H 9.35, N 7.64%. Similarly 1-[5'-(N, N-dimethylaminomethyl) furyl-2']ethanol-2 was prepared from furylmethylcarbinol, yield 75.1%, 116°–117° (6 mm), n_D^{20} 1.4869. Found: C 63.95, H 8.87%. Calculated for $C_9H_{15}NO_2$: C 63.88, H 8.93%. The iodomethylate had mp 200°–201° (absolute ether).

5-(N, N-Dialkylaminomethyl)furfurals. 1 mole carbinol I was refluxed in dry benzene with four times the necessary amount of MnO_2, in a vessel fitted with a Dean and Stark moisture apparatus, the end of the reaction being judged by cessation of water formation. The precipitate was filtered off, the benzene vacuum-distilled off, and the oxidation product vacuum-distilled. Yield of 5-(piperidinomethyl)furfural (II) 88.4%, bp 126°-127° (1 mm), n_D^{20} 1.5379. Found: C 68.45, H 8.06, N 7.26%. Calculated for $C_{11}H_{15}NO_2$: C 68.37, H 7.82, N 7.25%.

The other aminofurfurals were prepared similarly. 5-(N, N-dimethylaminomethyl)furfural (III), yield 83.6%, purified through its bisulfite compound, bp 78° (2 mm), n_D^{20} 1.5211. Found: C 62.42, H 7.25, N 9.34%. Calculated for $C_8H_{11}NO_2$: C 62.73, H 7.24, N 9.14%.

5-(N, N-diethylaminomethyl)furfural (IV), yield 73.5%, After purifying through the bisulfite derivative it had 82° (1 mm), n_D^{20} 1.5086. Found: C 65.88, H 8.36, N 7.68%. Calculated for $C_{10}H_{15}NO_2$: C 66.27, H 8.34, N 7.73%. The picrate was obtained by heating the aldehyde with ethanolic picric acid, mp 99°–100° (ex ethanol). Found: N 13.45%. Calculated for $C_{10}H_{15}NO_2 \cdot C_6H_3N_3O_7$: N 13.65%. The literature [2] gives mp 101°–102°.

The N-isonicotinylhydrazones of the aminofurfurals were prepared by refluxing together for 4 hr in ethanol solution equimolecular proportions of the aldehyde and isonicotinic hydrazide.

III hydrazone, mp 122°–123° (ex EtOH). Found: C 61.43, H 5.94%. Calculated for $C_{14}H_{16}N_4O_2$: C 61.75, H 5.92%.

II hydrazone, mp 165.5°–166.5°. Found: C 65.47, H 6.53, N 17.94%. Calculated for $C_{17}H_{20}N_4O_2$: C 65.37, H 6.45, N 17.94%.

IV hydrazone, mp 127°–128°. Found: C 64.16, H 6.79, N 18.69%. Calculated for $C_{16}H_{20}N_4O_2$: C 63.98, H 6.71, N 18.65%.

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