*Acta Chemica Scandinavica, 1998: 52: 964 965*
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ACTA
CHEMICA SCANDINAVICA
*ISSN 0904-213X*

*Short Communication*

# Cationic Protection Against Decomposition in Acidic Media: On the Acid-Stability of an Aminoalkyl-Substituted Furan

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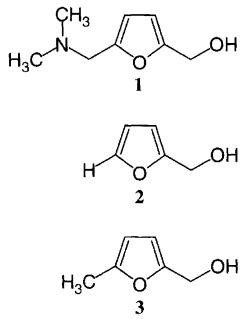
Aasen, A. J., Storesund, H. J., Klaveness, J. and Skramstad, J., 1998. Cationic Protection Against Decomposition in Acidic Media: On the Acid-Stability of an Aminoalkyl-Substituted Furan. – Acta Chem. Scand. 52: 964–965. © Acta Chemica Scandinavica 1998.

Furan derivatives are normally very reactive towards electrophilic reagents provided there are no electron-withdrawing groups in the ring. Thus, many furans react violently with decomposition with strong acids (e.g., conc. sulfuric acid) and also with Lewis acids such as aluminium chloride.[1–6] Certain furans with alkyl groups, e.g., 2,5-di-*tert*-butylfuran, have, however, been reported to yield stable (>10 days) furanonium ions in strongly acidic media.[7,8]

Although apparently obvious,[9] the literature seems to be devoid of studies on intrinsic cationic protection against decomposition of furans in acidic media. A comparative study on the stabilities of the three furan derivatives 5-(dimethylaminomethyl)furfuryl alcohol (**1**), furfuryl alcohol (**2**) and 5-methylfurfuryl alcohol (**3**) in acidic solutions constitutes the subject of the present paper.




*Scheme 1.*

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## Results and discussion

$D_2O$ solutions containing both 5-(dimethylaminomethyl)furfuryl alcohol (**1**) and furfuryl alcohol (**2**) were acidified with conc. hydrochloric acid to pH ca. 0 and their stabilities monitored by nuclear magnetic resonance spectroscopy ($^1$H NMR). The integrals of the signals of the dimethylamino group of **1** and the C(5)H of **2** were measured relative to the integral of dimethyl sulfoxide (DMSO), which was added as an internal standard that was seemingly stable under the prevailing conditions.[10] The presence of both furans in the same NMR tube ought to ensure identical environments for the two compounds.

Preliminary experiments employing both $^1$H and $^{13}$C NMR revealed only minor decomposition of the amino alcohol **1**. Furfuryl alcohol (**2**), however, rapidly polymerized to dark, insoluble, resinous products which did not affect the analyses of the remaining signals in the spectrum. Consequently, reliable integrals of the signals of **1** and **2** were acquired[11] permitting the calculation of the rate of disappearance of **2** at pH 0 in water at 20 °C to be $6.5 \times 10^{-3}$ min$^{-1}$, i.e. the reaction follows first-order kinetics.

The relative stabilities of furfuryl alcohol (**2**) and 5-methylfurfuryl alcohol (**3**) in $D_2O$ containing catalytic amounts of HCl were studied in comparable NMR experiments. The observed faster decomposition of 5-methylfurfuryl alcohol (**3**) compared with furfuryl alcohol (**2**) indicates that the methyl group of **3** probably rendered no, or little, steric protection against different kinds of nucleophilic attack (e.g., polymerization). The relative instability of **3** may indicate that the inductive effect by the methyl group facilitates protonation, which is followed by rapid reaction with nucleophiles.

These results demonstrate that 5-(dimethylaminomethyl)furfuryl alcohol (**1**) resists destruction in strongly acidic solutions. The lack of decomposition is attributed to the fact that the dimethylamino group of (**1**) is present predominantly as the corresponding dimethylammonium ion **4**. The unusual stability might be rationalized by (i) electrostatic rejection of 'approaching' hydroxonium ions by the positively charged dimethylammonium group in **4** and (ii) weak inductive effects exerted by the dimethylammonium group possibly rendering the furan ring less susceptible to electrophilic attack (electron-withdrawal; cf. Fig. 1). Furthermore, the protecting potential of the dimethylammonium group is supported by the fact that 5-methylfurfuryl alcohol (**3**) and 2,5-dialkylsubstituted furans, e.g., 2,5-dimethylfuran, rapidly decompose[6,12] in acid media (exceptions: *vide supra*).

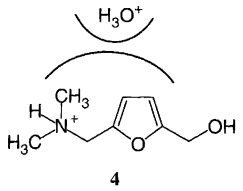


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*Fig. 1.* Dimethylammonium ion (**4**) of the amino alcohol **1**. Electrostatic repulsion of hydroxonium ions.

## Experimental

*General.* $^1$H NMR and $^{13}$C NMR spectra were recorded on a Varian XL-200 instrument at 200 MHz and 50 MHz, respectively, using deuterium oxide ($D_2O$) as the solvent and dimethyl sulfoxide (DMSO) as an internal reference ($^1$H, 2.5 ppm; $^{13}$C, 39.5 ppm). All experiments on stability were performed at ambient temperature. pH measurements were made by use of Merck Universalindikator pH 0–14 (pH paper).

*Stabilities of 5-(dimethylaminomethyl)furfuryl alcohol* (**1**) *and furfuryl alcohol* (**2**). *Preliminary experiments.* Initial experiments disclosed that the stabilities of 5-(dimethylaminomethyl)furfuryl alcohol (**1**) and furfuryl alcohol (**2**) in acidic (pH ca. 0) aqueous solutions at room temperature were readily monitored by comparing appropriate integrals of $^1$H or $^{13}$C NMR signals with the $^1$H and $^{13}$C signals of dimethyl sulfoxide (DMSO; internal reference). The $^1$H NMR signals of the C(5)H multiplet of furfuryl alcohol (**2**) at 7.30 ppm, the dimethylamino singlet of the amino alcohol **1** at 2.65 ppm, and the dimethyl singlet of DMSO at 2.50 ppm were well separated from other signals in the spectra and adequate for integration. The ratios of the integrals of the $^1$H NMR signals of the amino alcohol (**1**) and DMSO at 2.65 ppm and 2.5 ppm, respectively, and the $^{13}$C NMR signals of (**1**) and DMSO at 42.5 ppm and 39.5 ppm, respectively, did not change appreciably over a period of 24 h. All the $^1$H and the $^{13}$C NMR signals of furfuryl alcohol (**2**) vanished within a short time. The decomposition products of furfuryl alcohol (**2**) appeared to be practically insoluble in $D_2O$ (tarry material deposited), and thus did not seem to interfere with the remaining signals.

*Kinetic measurements.* 5-(Dimethylaminomethyl)furfuryl alcohol [(**1**), ca. 0.42 mmol, base] and furfuryl alcohol [(**2**), ca. 0.86 mmol; 150 µl from a mixture of **1** and **2** in the ratio 49.4:100] were dissolved in $D_2O$ (1 ml). HCl (ca. 1.6 mmol; 100 µl from a stock solution comprising 42 ml conc. HCl and 30 ml water] was added to the $D_2O$ solution and the mixture transferred to an NMR tube, pH ca. 0. $^1$H NMR spectra were recorded at suitable intervals and the intensities of the appropriate signals (*vide supra*) measured by integration.

*Stabilities of 5-methylfurfuryl alcohol* (**3**) *and furfuryl alcohol* (**2**) $^{13}$C NMR spectra (50 MHz) of a solution of 5-methylfurfuryl alcohol [(**3**), 32 mg; 0.29 mmol],[13] furfuryl alcohol [(**2**), 29 mg; 0.30 mmol] and DMSO (26 mg, 0.33 mmol) in $D_2O$ (1.0 ml) were recorded prior to, and after the addition of catalytic amounts of HCl: 0.05 µl (0.0042 mmol) and 0.1 µl (0.0083 mmol) after '0' and 6 h, respectively, of a stock solution prepared by diluting 1 ml conc. HCl to 150 ml with $H_2O$.

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10. The ratio between the integrals of the dimethyl group of the amino alcohol **1** and the dimethyl group of DMSO did not change during the experiments. Furthermore, the signal-to-noise ratio did not seem to deteriorate.
11. All the $^1$H NMR signals (and the $^{13}$C NMR signals recorded in the preliminary experiments) of furfuryl alcohol **2** seemed to vanish simultaneously, implying that acid-catalyzed deuteriation was negligible.
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13. 5-Methylfurfuryl alcohol (**3**) was prepared from 5-methylfurfural by $NaBH_4$ reduction in $H_2O$–$CH_3OH$. Micovic, V. M., Mamuzic, R. I., Jeremic, D. and Mihailovic, M. Lj. *Tetrahedron 20* (1964) 2279 prepared **3** by $LiAlH_4$ reduction.

Received November 3, 1997.