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KINETICS OF DEUTERIUM EXCHANGE OF FURAN AND METHYLFURANS IN DIMETHYLSULFOXIDE

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Rates of exchange between deuterium in 2D-, 3D-, 2D-3CH_3-, and 2D-5CH_3-furan and a solution of potassium tert-butoxide in dimethylsulfoxide are measured. Protophilic deuterium exchange at position 2 in the furan molecule is 600 times faster than that at position 3, while a methyl group at position 3 or 5 retards it 10-fold. Catalytic activities of potassium and lithium butoxides are compared.

The existing information in the literature regarding the reactivities of furan and its homologs in protophilic hydrogen replacement derives from synthetic work on metallation [1–4]. With alkali metal organometallic compounds, the hydrogen at position 2 in furan and at position 5 in sylvan is replaced by metal. Under certain conditions low yields of 2, 5-dimetallated derivatives of furan are obtained [2, 4]. Judging by the yields of organolithium compounds obtained by the action of phenyllithium on furan and sylvan, introduction of the Me group weakens the acidity of the ring [2]. According to [1], furan itself occupies an intermediate place, in respect of acidity, between phenylacetylene (pK = 22) and triphenylmethane (pK = 28.5). The pK values in parentheses are obtained from [5]. Simultaneous metallation shows [6] that thiophene is much more acid than furan, since a mixture of 1 mole of each, when treated with 1 mole butyllithium, leads to 96.3% metallation of the thiophene, and only 3.7% metallation of the furan.

Table 1

Deuterium Exchange Average Velocity Constants, using 0.4 Molar tert-BuOK at 25°

Compound	k, sec^{-1}	Compound	k, sec^{-1}
2D-furan *	$2.1 \cdot 10^{-7}$	3D-furan**	$1.2 \cdot 10^{-5}$
2D-furan	$5.5 \cdot 10^{-4}$	5CH_3-2D-furan	$5.8 \cdot 10^{-5}$
3D-furan	$9.8 \cdot 10^{-7}$	3CH_3-2D-furan	$5.8 \cdot 10^{-5}$

* Catalyst, tert-BuOLi (0.4 molar).

** At 50°.

Hitherto there has been inadequate investigation of the reactivities of furan compounds. The great advantages of the hydrogen isotope exchange technique [7] raised the question of applying it to investigate furan and its derivatives. A solution of potassium or lithium tert-butoxide in dimethylsulfoxide (DMSO) [8] proved to be a suitable medium for this. Such research is all the more interesting as it offers the possibility of directly determining the reactivities of furan and thiophene for protophilic hydrogen replacement, since thiophene and its derivatives undergo deuterium exchange in that medium. For example, it has previously been pointed out [8], in agreement with conclusions reached in [6], that α deuterium atoms in furan exchange 500 times slower than those in thiophene.

The present authors have embarked on a systematic investigation of the kinetics of isotopic exchange in furan compounds, and the first results are given in this paper.

To compare hydrogen mobility in CH bonds differing markedly in reactivity, exchange rates between 2D-furan and potassium and lithium tert-butoxides in 0.4 molar solution were measured. The velocity constants set out above (Table 1) show that there is a 2000-fold difference in catalytic activity between the two butoxides, and this is due to the O–K link being more polar than the O–Li one [9], and the difference being preserved in DMSO solution, despite the great capacity of this solvent for solvating alkali metal cations, and its high dielectric constant of 48.9 at 20°. The specific conductivity of a 0.4 molar solution of the tert-BuOK in DMSO is greater, by a factor of 10, than that of a like solution of tert-BuOLi (preliminary figures of 6×10^{-4} and 5×10^{-5} ohm^{-1} were obtained at 20°). A marked dependence of catalytic activity of tert-butoxides on the alkali metal is also observed with other reactions in the same solvent [10, 11].

The 3D-furan exchange rate is low at 25°, even with tert-BuOK as catalyst, so that the value at 50° was also found.

Table 2

Kinetics of Exchange of Deuterium with an 0.4 Molar tert-BuOK Solution at 25°

τ	C_v	k, sec^{-1}
	2D- furan (C_w^0 = 2.97 aт. % D)	
331 hr	2.27; 2.27*	$2.3 \cdot 10^{-7}$; $2.3 \cdot 10^{-7}$
432 hr	2.20; 2.20*	$1.9 \cdot 10^{-7}$; $1.9 \cdot 10^{-7}$
20 min.	1.63; 1.67	$5.0 \cdot 10^{-4}$; $4.8 \cdot 10^{-4}$
25 "	1.23	$5.9 \cdot 10^{-4}$;
27 "	1.18	$5.7 \cdot 10^{-4}$
41 "	0.67	$6.0 \cdot 10^{-4}$
	3D-furan (C_w^0 = 3.68 aт. % D)	
168 hr	2.05; 2.02	$9.7 \cdot 10^{-7}$; $9.9 \cdot 10^{-7}$
20 "	1.41; 1.41**	$1.3 \cdot 10^{-5}$; $1.3 \cdot 10^{-5}$
48 "	0.58**	$1.1 \cdot 10^{-5}$
67.5 hr	0.35**	$0.9 \cdot 10^{-5}$
	$5CH_3$-2D- furan (C_w^0 = 2.09 aт. % D)	
120 min.	1.36; 1.33	$5.9 \cdot 10^{-5}$; $6.3 \cdot 10^{-5}$
180 "	1.14; 1.14	$5.6 \cdot 10^{-5}$; $5.6 \cdot 10^{-5}$
180 "	1.16; 1.13	5.5; 5.7
	$3CH_3$-2D- furan (C_w^0 = 2.06 aт. % D)	
100 min.	1.43	$6.1 \cdot 10^{-5}$
150 "	1.23; 1.19	$5.7 \cdot 10^{-5}$; $6.1 \cdot 10^{-5}$
154 "	1.17	$6.1 \cdot 10^{-5}$
200 "	1.05; 1.06	$5.6 \cdot 10^{-5}$; $5.5 \cdot 10^{-5}$

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*Catalyst tert-Bu Li (0.4 molar).

**At 50°.

For furan, deuterium at position 2 is exchanged 600 times faster than that at position 3. Thus the conclusion reached in papers on metallation of furan, that α-CH is much more highly acidic than β-CH, and that it is characteristic of the α hydrogen atom of furan that its substitution is independent of whether the reagent is protophilic or electrophilic (cf. [12]), is confirmed.

When the electron-donating methyl group is introduced into the furan ring, its protophilic substitution is retarded, just as obtains with the benzene ring (see [7], p. 350). It is noteworthy that the deuterium exchange reaction is identically retarded (ten-fold) for exchange of a deuterium atom adjacent to a Me group in $3CH_3$-2D-furan, or separated from one, by an oxygen atom, as in $5CH_3$-2D-furan.

Identical chemical shifts for corresponding hydrogen atoms are found in the NMR spectra [13] of the methyl furan isomers; hence they have similar electron densities.

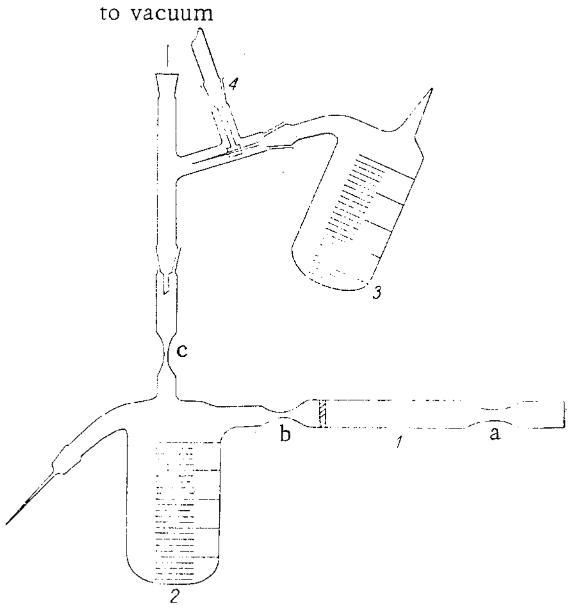
It is assumed [14] that in the furan ring the electronic inductive effect of a substituent is transmitted from one α position to another primarily through the hetero atom, as well as through space. This may be the reason for the identical mobilities of the deuterium atoms in $3CH_3$-2D-furan and $5CH_3$-2D-furan.

Experimental

Furan (I), sylvan (II), and 3-methylfuran (III) were dried over $CaCl_2$, and twice distilled over Na, the boiling points being respectively 31.4°, 63°, and 62°, and n_D^{20} 1.4216, 1.4300 and 1.4318. Gas liquid chromatography (GLC) showed that only II contained a small amount of impurity. These compounds were used for the syntheses and for diluting the deuterium preparations. In deuterium exchange experiments where the ratio of the number of moles of II to number of moles of catalyst was varied 2.5-fold, the rate constant was unaltered.

I was used for preparing [15] 2-chloromercurifuran, which was converted to 2D-furan [16]. 3D-furan was prepared by the method of [17]. II was used to synthesize [18] 2-chloromercuri-5-methylfuran, converted by a stoichiometric quantity of DCl in D_2O, to 2D-5CH_3-furan (60% yield). 2D-3CH_3-furan was prepared similarly. The purities of the preparations were checked by GLC.

The catalyst was prepared, as described in [20], by dissolving the alkali metal, with applications of heat, in pure tert-BuOH. Then the alcohol was distilled off, and the butoxide thrice sublimed at 10^{-3} mm Hg.



Apparatus for determining the solution of catalyst in DMSO.

The present experimental method differed from that previously [21] described in the method of preparing the solution of catalyst in DMSO. The butoxide was introduced, in an argon atmosphere, into the side arm 1 of flask 2, a No. 1 glass filter being interposed between the two, after which there was sealing off at the constriction a. Pure DMSO was vacuum-distilled over CaH_2 into flask 3, which was then sealed off. Then the butoxide was vacuum-distilled into flask 2, and the side tube sealed off at constriction b. Tap 4 was turned, the DMSO run into flask 2, which was then sealed off at constriction c. The concentration of catalyst in solution was determined by titrating samples withdrawn.

Table 2 summarizes the experimental results. There C_W and C_W^0 are the deuterium concentrations (atoms, %) in the water obtained by burning the compound before the experiment, and at time τ. During the experiments the compounds were unchanged.

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