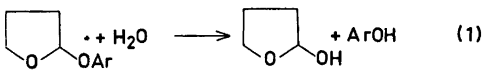
pH-Independent Hydrolysis of Some 2-Aryloxytetrahydrofurans

HARRI LÖNNBERG and VEIJO POHJOLA

Department of Chemistry and Biochemistry, University of Turku, SF-20500 Turku, Finland

It is well-known that acetals are generally stable under alkaline conditions.[1] However, several hemicyclic carbohydrate acetals, glycosides, are cleaved quite readily in aqueous base solutions.[2] Especially, aryl aldofuranosides exhibit a marked lability to alkali.[3] To further the understanding of the factors influencing the hydrolysis of these compounds the cleavage of the corresponding tetrahydrofuran derivatives in aqueous sodium hydroxide solutions (eqn. 1) has been studied in this work.



(1)

The kinetic data obtained with the 2-aryloxytetrahydrofurans studied are given in Table 1. The hydrolysis rate of each investigated compound is almost independent of the hydroxide ion concentration. The slight decrease in the first-order rate constants with the increasing base concentration is probably due to specific salt effects. Routes involving rate-limiting nucleophilic attack by hydroxide ion can thus be excluded as the major reaction pathways. In consistence with this conclusion, two kinetically indistinguishable mechanisms can be suggested for the hydrolysis of these compounds; a unimolecular decomposition of the substrate to a phenoxide ion and a cyclic oxo-carbenium ion (eqn. 2), or water, acts as a general acid donating a proton to the *exo* cyclic oxygen atom concerted with the covalent bond rupture (eqn. 3).

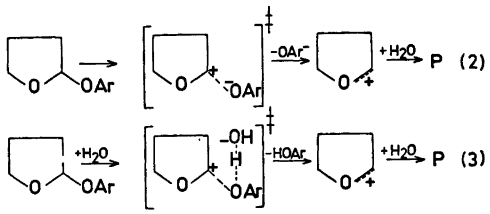


Table 1. First-order rate constants [$k(H_2O)$ and $k(D_2O)$] for the hydrolysis of 2-aryloxytetrahydrofurans in sodium hydroxide and sodium deuteroxide solutions of different concentrations. The ionic strength was adjusted to 0.1 mol dm^{-3} with sodium chloride. $T = 358.15$ K if not otherwise stated; number of runs 2 if not otherwise stated.

Substituent	$C(OH^-)$/mol dm^{-3}			$C(OD^-)$/mol dm^{-3}
	0.1	0.01	0.001	0.1
	$k(H_2O)/10^{-4}$ s^{-1}			$k(D_2O)/10^{-4}$ s^{-1}
None	0.454	0.569		0.345
3-OCH_3	1.054	1.230	1.418	
4-Cl	1.643 [a]	1.952 [a]	1.979 [a]	1.194
3-Cl	5.61 [a]	5.70 [a]	5.77 [a]	3.71
4-$COCH_3$	61.2 [a]	61.2 [a]	59.6 [a]	41.4
	21.9 [b]			
	8.64 [c]			
	2.96 [d]			

[a] Number of runs: 3. [b] $T = 348.15$ K. [c] $T = 338.15$ K. [d] $T = 328.15$ K.

Electron-withdrawing substituents in the aryloxy group greatly accelerate the hydrolysis of 2-aryloxytetrahydrofurans. A plot of the logarithms of the rate constants against the substituent constants σ^- gives a fairly good linear correlation line with a slope of 2.4 ± 0.2 (Fig. 1). If normal substituent constants, σ°, are used instead, a curvilinear Hammett plot is obtained, the point for 4-acetyl group falling far above the straight line the other substituents yield. The need for σ^- values to correlate the hydrolysis rates indicates that resonance inter-

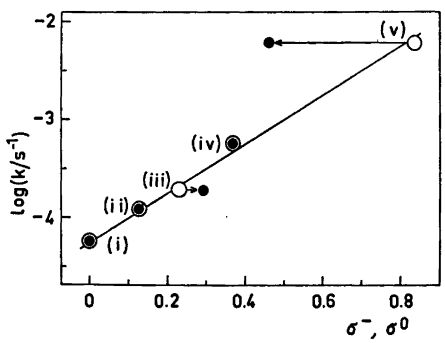


Fig. 1. Hydrolysis of 2-aryloxytetrahydrofurans in aqueous 0.01 mol dm^{-3} sodium hydroxide solution at 358.15 K. Logarithms of the first-order rate constants plotted against the substituent constants of the substituents in the aryl moiety. Open circles refer to σ^- and filled circles to σ° values. Notation: (i) phenoxy, (ii) 3-methoxyphenoxy, (iii) 4-chlorophenoxy, (iv) 3-chlorophenoxy, and (v) 4-acetylphenoxy derivative.

actions between the *exo* cyclic oxygen atom and the substituted benzene nucleus are altered on going from reactant molecule to activated complex. Of the substituents employed, the 4-acetyl group is the only one that exerts a $-R$ effect, or in other words, tends to withdraw electrons by resonance. Because the rate-enhancing effect of this substituent is far greater than predicted by its σ° value, it seems probable that the decomposition of 2-aryloxytetrahydrofurans occurs with formation of an electron-rich center in direct conjugation with the benzene ring. This is what would happen, if mechanism (2) is followed. As the phenoxy group begins to depart a partial negative charge will develop on the *exo* cyclic oxygen atom. Resonance acceptors, such as the 4-acetyl group, will therefore induce a greater through conjugation in the activated complex than in the reactant molecule. In contrast, no marked change in resonance interactions would take place if the *exo* cyclic oxygen atom were protonated by water concerted with the covalent bond fission, and the rate constants would be expected to correlate with σ° rather than with σ^- values. This is the case, for example, in the general acid-catalyzed hydrolysis of 2-(4-substituted phenoxy)tetrahydropyrans.[4]

The activation entropy of -21 ± 3 J K^{-1} mol^{-1} obtained at 298.15 K for the hydrolysis of 2-(4-acetylphenoxy)tetrahydrofuran is also consistent with route (2). According to this mechanism a separation of charges takes place on going from reactant molecule to transition state. Since the developing charges would be solvated, a slightly negative $\Delta S^{\neq}$ value seems reasonable. Participation of water as a proton donating agent would be expected to give rise to a more negative entropy of activation.

One may also consider the possibility that 2-(4-acetylphenoxy)tetrahydrofuran, which exhibits an exceptionally high reactivity, undergoes a spontaneous decomposition, whereas the other investigated substrates, having poorer leaving groups, react by mechanism (3). The values obtained for the kinetic solvent deuterium isotope effect, however, argue against this suggestion. All reactions studied exhibit a ratio $k(D_2O)/k(H_2O)$ of the magnitude 0.7, the differences between separate values being less than experimental errors. Similar values have been reported for uncatalyzed hydrolyses of other acetals.[5] Furthermore, the high positive value of 2.4 for the Hammett ϱ^--parameter conflicts with the proton-transfer catalysis by water. Polar substituents in the leaving group exert opposing effects on the basicity of the *exo* cyclic oxygen atom and on the ease of the carbon-oxygen bond rupture. If water would donate a proton to the *exo* cyclic oxygen atom concerted with the covalent bond cleavage these two influences would, at least partially, cancel each other, and a smaller reaction constant, ϱ^-, would be expected. On this basis it seems probable that the hydrolysis of all the compounds studied occurs with a spontaneous formation of a cyclic oxo-carbenium ion.

Experimental. The 2-aryloxytetrahydrofurans were synthesized by the procedure of Woods and Kramer.[6] The products were purified by repeated distillations under reduced pressure. 3-Chloro-, 4-chloro-, and 4-acetylphenoxy derivatives were further crystallized from dry methanol. The following compounds were prepared:

2-Phenoxytetrahydrofuran, b.p. 346 – 348 K at 0.2 kPa;
2-(3-Methoxyphenoxy)tetrahydrofuran, b.p. 373 – 375 K at 0.2 kPa;
2-(4-Chlorophenoxy)tetrahydrofuran, m.p. 300 – 301 K;
2-(3-Chlorophenoxy)tetrahydrofuran, m.p. 308 – 309 K;
2-(4-Acetylphenoxy)tetrahydrofuran, m.p. 335 – 337 K.

Aqueous sodium hydroxide solutions were prepared from standard Titrisol solutions (E. Merck) by diluting with distilled water. Sodium deuteroxide solutions were prepared from metallic sodium and deuterium oxide under toluene.

Hydrolyses were followed spectrophotometrically at the absorption maxima of the liberated phenoxide ions. The measurements were performed on a Unicam SP 800 spectrophotometer equipped with a scale expansion accessory. The temperature of the cell housing block was adjusted with water circulation from a Lauda thermostat and controlled by a thermoelement. The initial substrate concentration was in the $10^{-4} - 10^{-5}$ mol dm^{-3} range. The first-order rate constants were calculated by the method of Guggenheim.

Acknowledgements. The financial aid from the Finnish Academy, Division of Sciences, is gratefully acknowledged.

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Received June 10, 1976.