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The Uncatalyzed Alcoholysis of Furyl-2-oxirane. A Mechanistic Study Based on Kinetic Data

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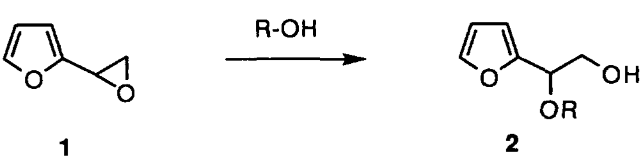
Abstract.- A kinetic study of the uncatalyzed methanolysis of furyl-2-oxirane has been achieved, giving information about the mechanism of a "pure" (uncatalyzed) ring opening of a heteroaromatic oxide. Solvent and salt effect are compatible with a solvent assisted process with a solvent-separated ion-pair intermediate.

The reaction of epoxides with alcohols constitutes a well known method for the preparation of diol monoethers.[1] In the case of aryl-substituted epoxides the reaction is always a catalytic process and catalysts like mineral acids,[2] Al_2O_3,[3] acidic resins,[4] Lewis acids,[5] metallic salts,[6] organometallic reagents,[7] quinones,[8] amine-borane complex,[9] and others[10] have been used. Mechanistic considerations for these catalytic processes have been also discussed.[11]

Furyl-2-oxirane **1**[12] constitutes an exception to the general behaviour of arylsubstituted epoxides and reacts smoothly with alcohols without any catalyst[13] (Scheme). This uncatalyzed reaction had only one precedent due to Kotsuki *et al.* who have performed the hydrolysis of aliphatic and aromatic epoxides without catalyst and under high pressure conditions (10 Kbar).[14] The uncatalyzed alcoholysis of furyl-2-oxirane at room pressure and temperature should be suitable in order to gain information about the general features of the "pure" ring opening of hetaryl oxides with alcohols. The study of the process on the basis of kinetic considerations[15] is the objective of the present report.



Scheme

Kinetic measurements of methanolysis reactions were performed in pseudofirst order conditions by measuring the concentration of 2 (R = CH_3) by G.L.C. and using naphthalene as an internal standard. The modification of the reaction rate with the solvent polarity measured by the increase of %H_2O in the mixtures

$MeOH-H_2O^{16}$ is quoted in the Table 1. The small increase of rate with the solvent polarity (increase of % H_2O in the mixture $MeOH-H_2O^{16}$) may be adscribed to a "S_N2 (intermediate)" mechanism[17] with a weak nucleophilic assistance and presence of ion pair intermediates. Nucleophilic assistance helps heterolysis of the C-X bond as in the S_N2 (one stage) mechanism. The nucleophilic assistance of the solvent may be supported on the basis of the following consideration: Grunwald and Winstein proposed a linear free energy relationship (Equation 1) for the variation of S_N1 solvolysis rate with the solvent,[18] where k is the solvolysis reaction rate constant in a solvent of ionizing power Y, and k_o is the specific solvolysis reaction rate constant at 25°C in the standard solvent (Y = 0 in 80% aqueous ethanol). The parameter m_{RX} depends upon the substrate and specific solvent interaction. A high value of m_{RX} means a more S_N1 character of the process (1.20 for the solvolysis of adamantyl bromide, for instance). In our case a value of m_{RX} = 0.45 was obtained (Figure 1). This value is close to that obtained for the solvolysis of 2-propylbromide (m_{RX} = 0.43) where the ionization is strongly assisted by the nucleophilic solvent.[19] Notewhorthy no trace of diol **2** (R = H), arising from competitive reaction of **1** with water was isolated. This compound was isolated by reaction of **1** with a saturated solution of NaCl in THF-H_2O.

$$\log (k/k_o) = m_{RX} \cdot Y \qquad \text{[Equation 1]}$$

Table 1. *Rate constants for the methanolysis of 1 in water-methanol mixtures[a]*

Run	% H_2O(V/V)	$k_1.10^6(sc^{-1})$
1	0.0	2.1±0.3
2	9.09	4.3±0.1
3	16.7	5.9±0.3
4	28.6	16.6±0.6
5	33.3	19.0±0.6

a) At 272.0±0.5°K

The presence of ion pairs has been demonstrated by measuring the rate constants in the presence of KI. The results are collected in Table 2. From the inspection of the data and from the plotting of ($6+\log k_1$) vs [KI] (Figure 2), a sharp increase of the rate at concentration of KI about 0.45M was deduced. This phenomenon is typical of the intermediacy of a solvent-separated ion pair and indicates the operation of a salt effect.[20] In this case the external anion traps the ion pair, reducing the return to the starting material and increasing the overall reaction rate.

Table 2. *Rate constants for the methanolysis of 1 in the presence of KI[a]*

Run	[KI](M)	$k_1.10^6(sc^{-1})$
1	0.0	4.3±0.1
2	0.09	27.4±0.5
3	0.18	31.3±0.9
4	0.36	36.6±0.6
5	0.45	134.0±2.0
6	0.55	56.3±0.7
7	0.64	35.2±0.7
8	0.73	19.4±0.6

a) All measurements were performed in a mixture water-methanol with 9.09% water(V/V), at 272.0±0.5°K.

In summary, kinetic data for the uncatalyzed methanolysis of furyl-2-oxirane in solvolytic conditions indicates that the reaction occurs by a solvent-assisted S_N process through a solvent-separated ion pair intermediate.

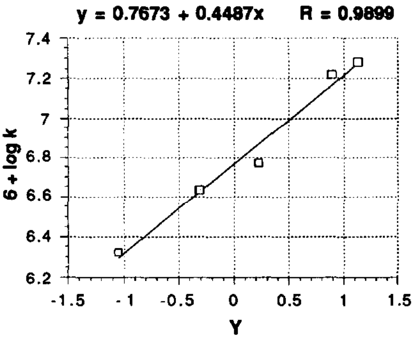


Figure 1

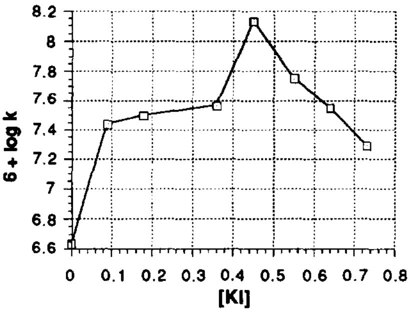


Figure 2

EXPERIMENTAL

Furyl-2-oxirane **1** and 2-(2-furyl)-2-methoxyethanol **2** (R = Me) were prepared by previously described procedures,[13] and distilled prior to use. Methanol was purified after distillation according to conventional procedures.[21] Naphthalene (internal standard for kinetic measurements) was recrystallized from ethanol. Kinetic measurements were performed by G.L.C. in a Perkin-Elmer Sigma 300 apparatus connected to a Perkin-Elmer Sigma 10 integrator, using a OV-101 column (methylsilicone, 25m).

General kinetic procedure.-The pseudo first order constant for the solvolysis of furyl-2-oxirane ($k_1\psi$) is $k_1\psi t = \ln \{[FO]_o/([FO]-[FA])\}$ (eq. 2) were $[FO]_o$ is the initial concentration of **1** and [FA] is the concentration of **2** at time t. At constant volume, eq. 2 can also be written as $k_1\psi t = \ln \{[nFO]_o/([nFO]-[nFA])\}$ (eq. 3).

The experimental procedure was as follows: 4 mmol of **1** were dissolved in MeOH (10 ml) at 272.0 ± 0.5 °K. At known reaction times, portions were removed and inmediately diluted in a solution of 20 mg of naphthalene (internal standard) in 2.5 mL of acetone. The mixture was injected in the G.L.C. apparatus, and the values of S_p (area corresponding to naphtalene) and S_{FA} (area corresponding to **2**) were obtained.

In order to obtain n_{FA} we used a calibration curve obtained from known amounts of **2** (m_{FAi}) and naphtalene (m_{pi}). From the equation $S_{FA}/S_p = x(m_{FAi}/m_{pi}) + y$ (eq. 3) and plotting S_{FA}/S_p *vs* m_{FAi}/m_{pi}, we obtain x and y. Thus, knowing S_{FA}, S_p, x, y, and m_{pi}, it is possible to obtain m_{FAi}—the amount of **2** contained in the portion of volume V_i obtained from the reaction medium. The value of m_{FA} at any time can be obtained from the equation $m_{FA} = m_{FAi}(V_t/V_i)$, V_t being the total volume of the reaction medium.

Kinetic measurements. ***The calibration curve.***-Solutions of **2** (R = CH_3) and naphthalene in acetone were prepared varying the ratio m_{FA}/m_{FP} from 0.05 to 1.30 (weight error ±0.1 mg). Aliquots of the solution were injected in the G.L.C. apparatus giving the values of S_{FA} and S_{FP}. Plotting S_{FA}/S_{FP} vs m_{FA}/m_{FP}, gave the following straight line: $S_{FA}/S_{FP} = 4.52\ 10^{-1}(m_{FA}/m_{FP}) - 3.10\ 10^{-3}$ (r = 0.9999)

Kinetics of the methanolysis of 1 in mixtures H_2O-MeOH. ***General Procedure.***- 440.0 mg (4 mMoles) of **1** was dissolved in methanol (10 mL) at 272°K. ***G.L.C. parameters.*** Injector temperature: 205°C. Oven temperature: 120°C. Detector temperature: 220°C. Retention time of 2 (R = CH_3): 3.1 min. Retention time of naphtalene: 6.3 min. The results are collected in Table 3.

Table 3. *Kinetics of methanolysis of 1 in water-methanol mixtures.*

Run	H_2O (mL; %)	n[a]	Equation	R
1	0	9	y = 0.0130 + 0.000124x	0.9843
2	1; 9.09	9	y = 0.0340 + 0.000260x	0.9941
3	2; 16.7	10	y = 0.1396 + 0.000350x	0.9776
4	4; 28.6	10	y = 0.0650 + 0.000996x	0.9899
5	5; 33.3	7	y = 0.1838 + 0.000114x	0.9892

a) Number of experimental points.

Kinetics of the methanolysis of 1 in the presence of KI. ***General Procedure.***- To a solution of **1** (440.0 mg, 4mMoles) in methanol (10 ml) at 272°K, a solution of KI in H_2O (1 ml) was added.The results are collected in Table 4.

Table 4. *Kinetics of the methanolysis of 1 in the presence of KI.*

Run	KI (mMoles)	[KI]	n[a]	Equation	R
1	0	0	9	y = 0.0340 + 0.000260x	0.9941
2	1	0.091	11	y = 0.0187 + 0.001642x	0.9963
3	2	0.182	11	y = 0.0161 + 0.001880x	0.9943
4	4	0.364	12	y = 0.0375 + 0.002157x	0.9957
5	5	0.454	9	y = 0.0403 + 0.008037x	0.9970
6	6	0.546	10	y = 0.0469 + 0.003378x	0.9987
7	7	0.636	9	y = 0.0226 + 0.002129x	0.9967
8	8	0.728	7	y = 0.02961 + 0.001162x	0.9924

a) Number of experimental points.

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