Scientific Research

Hydroxyalkylation of Cyclic Imides with Oxiranes. Part II. The Mechanism of Reaction in Presence of Triethylamine

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ABSTRACT

The mechanism of reaction of cyclic monoimides with oxiranes was established based upon kinetic studies and product analysis. It has been established that the reaction proceeds through initial formation of an adduct of imide and triethylamine. The crucial bond in adduct has ionic character; in non-aqueous solvents it is present as ion pair, while in water the adduct dissociate and free ions are present. The adduct enables the proton transfer from imide to oxirane. The rate determining step is reaction of imide and this adduct. Different values of entropy of transition states obtained from thermodynamic calculations suggest slightly different structure of transition state of rate determining step.

Keywords: Imides; Oxiranes; Mechanism; Kinetics; Non-Kinetics Evidences

1. Introduction

The reaction of cyclic monoimides with oxiranes in presence of triethylamine (TEA) leads to N-(hydroxy-alkyl) imides of the general formula (I):
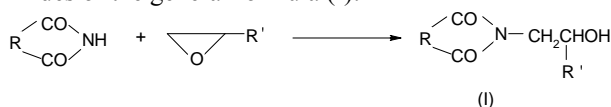
where R = (-CH$_2$-)$_2$, (-CH$_2$-)$_3$, -Ph

R' = -H, -CH$_3$

As it was presented in [1] the reaction follows the rate law (2):

$$V = k''_{1/2} c_K^{1/2} c_{AH}^{3/2} c_B^{1/2} \qquad (2)$$

where c_K, c_{AH}, and c_B mean the catalyst, imide groups, and oxirane concentrations, respectively.

The process can be considered to have the competitive and consecutive character consistent with reaction of N-(hydroxyalkyl)imides, which are the primary products, with oxirane. However the consecutive product is formed with low yield, *ca* 5 - 10 mol%. The rate law describing the reaction of N-(2-hydroxyalkyl)imides with oxiranes obeys another kinetics (first order related to oxirane concentration vs 1/2 for the first step), indicating that the reactions of oxiranes with N-(hydroxyalkyl)imides, which reveals the alcohol character, occur via different mechanism [2-6]. Based upon the rate constants the monoimides were ordered according to lowering reactivity as: PI ≥ SI > GI >HMSI. It has been also found that ethylene oxide (EO) was more reactive than propylene oxide (PO). The free energy of activation (ΔG$^{\neq}$) was also obtained for

those processes. The temperature dependence was linear which provided further evidence that the same mechanism operates for all studied systems.

Here we propose the mechanism of those reactions based on product analysis, intermediate identification and kinetic measurements.

2. Experimental

2.1. Substrates

The substrates were the same as in Part I.

2.2. Conductometric Measurements

The conductivity of imides, TEA, and their mixtures was studied in aqueous solutions at variable molar ratio in thermostated conductometric cells of 20 cm^3 capacity at 20°C (±0.1). The solutions were then diluted twice and conductivity was measured again. No PI solutions were measured due to its low solubility in water.

2.3. Cryoscopic Measurements

The cryoscpic measurements were done for 0.12-0.13-molal solutions of imide and TEA at 1:1 molar ratio (the total concentration of both was 0.25 mol/kg solvent in dioxane ($K_{cryos.}$ = 4.64). The method was standardized by determination of molar mass of imide and TEA. The presence of of imide-TEA adduct was deduced based on following approach. The total concentration of both reagents c_t was the sum of imide (c_{AH}) and catalyst (c_K) concentrations. The actual molal concentration of all com-

ponents (c_e) present in solution (imide, TEA, and adduct) were found from the measurements of decrease of the freezing point solution related to solvent from (3):

$$-\Delta T = K_k c_e \tag{3}$$

If the adduct is present in solution of mixture the $c_e < c_t$ is expected. If x is the concentration of adduct, the equilibrium:

$$\underset{(c_{oAH}-x)}{AH} + \underset{(c_{oK}-x)}{K} = \underset{x}{A^-, HK^+} \tag{4}$$
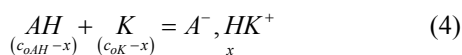
takes place and hence the association constant K_a can be obtained from (5):
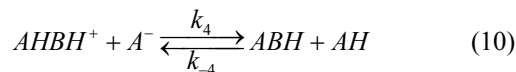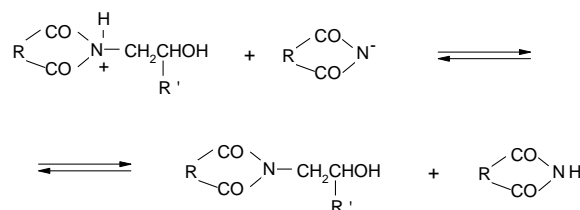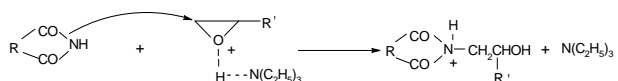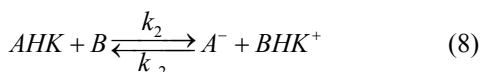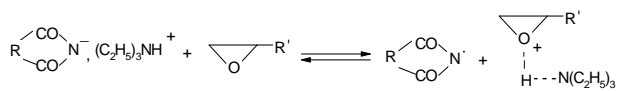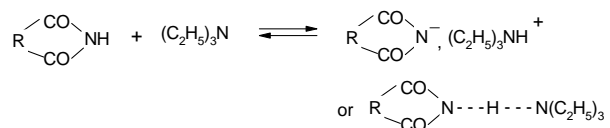
$$K_a = \frac{x}{(c_{0AH} - x)(c_{0K} - x)} \tag{5}$$

where the association degree β is defined as the ratio of adduct concentration (x) to component concentration (c_o) which is present in lower concentration:

$$\beta = (x/c_o)100\% \tag{6}$$

3. Results and Discussion

3.1. Mechanism of Reaction

The mechanism of the reaction of imides with oxiranes can be deduced based on experimental kinetic law Equation (2). It was assumed that adducts (ion pairs or hydrogen bonded complexes of imides (AH) and catalyst (K) take part in elementary reactions. The crucial adduct is formed between imide group and nitrogen of TEA. The products are formed upon reaction of imide with adduct of triethylammonium cation and oxirane molecule (AHK) according to the scheme (the acronyms under the reaction were introduced to be later used in kinetic equation):

$$AH + K \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AHK \tag{7}$$

$$AHK + B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} A^- + BHK^+ \tag{8}$$

$$AH + BHK^+ \xrightarrow{k_3} AHBH^+ + K \tag{9}$$

$$AHBH^+ + A^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} ABH + AH \tag{10}$$

Thus the elementary steps are:

1) Formation of AHK adduct from imide and TEA (7), which plays the role of proton transfer agent from imide to oxirane;

2) Reaction of adduct with oxirane with formation of new adduct BHK^+;

3) Reaction of BHK$^+$ with next molecule of imide resulting in formation of the alcohol protonated on imide group and recovery of catalyst (9);

4) Neutralization of imide anion by proton transfer from protonated alcohol to imide anion (10).

3.2. Kinetic Evidences for Proposed Mechanism

If one assume that:

1) The equilibrium between adduct (AHK) and TEA is reached very fast

2) The protonation constant of oxirane (K_2) is low and equilibrium (8) establishes slower that that in reaction (7)

3) The rate determining step is reaction of AH with adduct BHK^+ the rate of oxirane consumption equals the rate of disappearance of BHK^+ adduct, *i.e.*:

$$V_{gen} = -\frac{dc_B}{dt} = -\frac{dc_{BHK^+}}{dt} = k_3 c_{AH} c_{BHK^+} \tag{11}$$

The concentration of c_{BHK} can be found from stationary state condition [7]:

$$\frac{dc_{BHK}}{dt} = k_2 c_{AHK} c_B - k_{-2} c_{A^-} c_{BHK^+} - k_3 c_{AH} c_{BHK^+} = 0 \tag{12}$$

Because

$$c_{A^-} = c_{BKH^+} \tag{13}$$

then:

$$\frac{dc_{BHK}}{dt} = k_2 c_{AHK} c_B - k_{-2} c_{BHK^+}^2 - k_3 c_{AH} c_{BHK^+} = 0 \tag{14}$$

After rearrangement the Equation (14) is:

$$k_{-2} c_{BHK^+}^2 + k_3 c_{AH} c_{BHK^+} - k_2 c_{AHK} c_B = 0 \tag{15}$$

The solution for c_{BHK} gives:

$$c_{BHK^+} = \frac{-k_3 c_{AH} + \sqrt{k_3^2 c_{AH}^2 + 4k_{-2}k_2 c_{AHK} c_B}}{2k_{-2}} \tag{16}$$

Taking into account the Assumption 3 the relationship:

$$k_3 c_{AH} \lll 4k_{-2} k_2 c_B c_{AHK}$$

is obvious, which furthermore allows to simplify Equation (16) to:

$$c_{BHK} = \frac{\sqrt{4k_{-2} k_2 c_{AHK} c_B}}{2k_{-2}} = \sqrt{K_2 c_{AHK} c_B} \qquad (17)$$

Putting (17) into (11) the rate of reaction becomes:

$$V_{gen} = k_3 \sqrt{K_2} c_{AH} c_{AHK}^{1/2} c_B^{1/2} \qquad (18)$$

As before, the concentration of adduct AHK can be obtained from stationary state condition:

$$\frac{dc_{AHK}}{dt} = k_1 c_K c_{AH} - k_{-1} c_{AHK} - k_2 c_{AHK} c_B + k_{-2} c_{BHK^+}^2 = 0 \quad (19)$$

Introducing Equation (17) for c_{BHK^+} the relationship:

$$k_1 c_K c_{AH} - k_{-1} c_{AHK} - k_2 c_{AHK} c_B + k_{-2} K_2 c_{AHK} c_B = 0 \quad (20)$$

is obtained, from which:

$$c_{AHK} = \frac{k_1 c_K c_{AH}}{k_{-1}} \qquad (21)$$

or:

$$c_{AHK} = K_1 c_K c_{AH} \qquad (22)$$

Thus:

$$V_{gen.} = k_3 \sqrt{K_1 K_2} c_K^{1/2} c_{AH}^{3/2} c_B^{1/2} \qquad (23)$$

when

$$c_{AH} \gg c_B \qquad (24)$$

the latter equation can be simplified into:

$$V_{gen.} = k_3'' c_K^{1/2} c_B^{1/2} \qquad (25)$$

where:

$$k_3' = k_3 \sqrt{K_1 K_2} c_{AH}^{3/2} \qquad (26)$$

The obtained kinetic equation is in agreement with the experimental one, which suggests that proposed mechanism operates in the studied systems.

At this step the small differences of reactivity of PI and SI (cf. Part I) with oxiranes can be explained on the basis of proposed mechanism. Higher reactivity of PI is electronic in origin; phtalimide anion is mesomerically stabilized, thus the lifetime of AHK is larger in case of phtalimide, which enables the reactions (8) and (9).

Different values of entropy of transition states obtained from thermodynamic calculations (cf part I, **Table 7**) suggest slightly different structure of transition state of rate determining step. The value of −150 J/mol s can be attributed to transition State (II) which results straightforward from reaction (9), while the values < −200 J/mol

s suggest the cyclic transition State (III) exists, in which imide anion participates: participates:


(II)

(III)
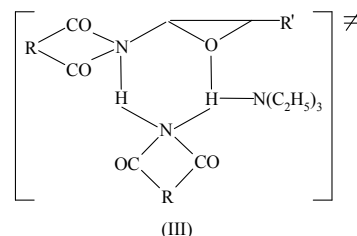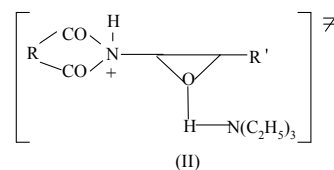
It has been observed, that the studied reaction are the fastest in DMF in comparison to other solvents (DMSO or dioxane; see Part I., **Table 8**). Presumably the reason is an involvement of solvent molecule in hydrogen cation transfer from imide to oxirane, *i.e.* the same as the catalytic role of TEA in reactions (7) and (8).

3.3. Non-Kinetics Evidences

The crucial points in proposed mechanism are the formation of 1:1 imide-TEA adduct and fast equilibria. Conductivity of aqueous solution of TEA is related to the equilibrium according the to scheme of reaction:

$$(C_2H_5)_3 N + H_2O \rightleftharpoons (C_2H_5)_3 NH^+ + OH^- \qquad (27)$$
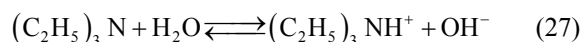
Introducing the imide or HMSI to the solution of TEA results in considerable increase of conductivity (**Table 1**), which is not additive, *i.e.* it is higher than the sum of conductivities of single components. This suggests that reaction (28) occurs:

(28)
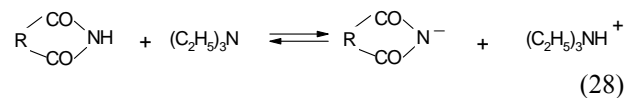
The measurements performed with variable composition indicated that in imide—TEA mixtures the maximum conductivity is reached immediately at equimolar solution of imide and TEA for the SI-TEA system (**Figure 1**). This was expected result for the stoichiometry of adduct.

Yet another kind of association takes place in non-aqueous solvents. Cryoscopic measurements revealed that all mixtures of imides with TEA follow the non-equality $c_e < c_t$, thus in these conditions the single species (ionic pair or hydrogen bonded adduct) is formed at the 5.2 - 7.7 mol% level in equimolar solutions (**Table 2**). The association is the highest at the PI-TEA system due to mesomeric stabilization of phtalimide anion. This causes shifting of the equilibrium (7) to the right. It should also be noted that association occurs also in the system

Table 1. Changes of conductivity of aqueous solutions of imides, TEA, and equimolar mixtures imide—TEA.

Concentration [mol/dm^3]	Equivalent conductivity [S cm^2] of									
	SI	GI	HMSI	TEA	adduct SI -TEA		adduct GI-TEA		adduct HMSI-TEA	
					additive	experim.	additive	experim.	additive	experim.
0.500	0.018	0.023	-	5.944	5.962	22.729	5.967	22.079	-	-
0.250	0.030	0.026	0.041	6.458	6.488	28.558	6.484	28.038	6.499	16.242
0.125	0.014	0.034	0.053	9.841	9.855	31.117	9.875	31.117	9.394	18.725
$6.25 \cdot 10^{-2}$	0.073	0.042	0.063	13.427	13.500	36.234	13.469	34.154	13.490	20.643
$3.13 \cdot 10^{-2}$	0.083	0.062	0.073	17.430	17.513	37.107	17.492	37.107	17.503	21.826
$1.56 \cdot 10^{-2}$	0.104	0.104	0.133	22.318	22.422	40.934	22.422	39.686	22.451	23.683

Table 2. Analysis of imide—TEA adduct in dioxane by cryoscopic method.
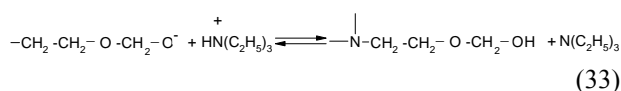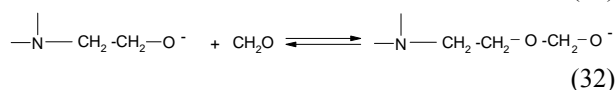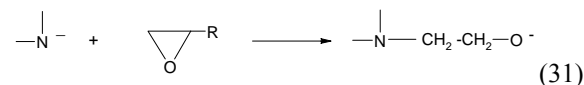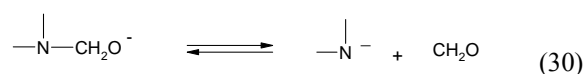
Imide	Molal concentration [mol/kg]		Sum of molal concentrations [mol/kg]		Equilibrium constant	Association degree β [%]
	Imide	TEA	Calculated from weight	Determined cryoscopically		
SI	0.1309	0.1238	0.2547	0.2462	0.60	6.8
PI	0.1286	0.1253	0.2539	0.2441	0.72	7.8
GI	0.1427	0.1457	0.2884	0.2797	0.49	6.1
HESI	0.1180	0.1181	0.2361	0.2300	0.48	5.2
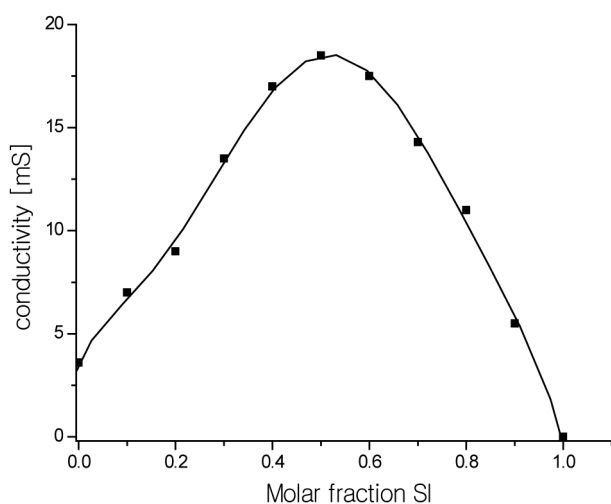
Figure 1. Changes of conductivity of solutions for the SI—TEA system of variable composition.

HESI-TEA. This suggests that proton donor to oxirane can be not only the imide but also its product of reaction, the alcohol, while the TEA catalyst mediates the transfer of proton from imide or alcohol to oxirane.

It has been noted that upon addition of oxirane to HMSI partial release of formaldehyde from N-hydroxy-methyl group occurred accompanied by its migration to the end of hydroxyalkyl chain. Based upon cryoscopic data and previous studies it was possible to determine the mechanism of this rearrangement. Previously we have focused on kinetic models for initial steps of oxirane re-actions with N-(hydroxymethyl) derivatives of some aza-cyclic compounds (barbituric, isocyanuric, and uric acids) leading to the formation of polyetherols [8-11]. The per-centage of N-hydroxymethyl and groups in HMSI and O-hydroxymethyl groups in the product of its reaction with oxirane was determined as weakly bound formalde-hyde. According to the data the HMSI contained 1 mole of formaldehyde per mole of HMSI (%CH$_2$O$_{calc}$ = 23.3, %CH$_2$O$_{found}$ = 23.2). It was also found that upon ad- di-tion of 1 mole of EO to HMSI *ca* 0.3 mole of unstable bonded formaldehyde as O-(hydroxymethyl) groups re-mains, but after addition of 2 moles EO practically whole formaldehyde is blocked by oxirane. These results sug-gest, that either O-(hydroxymethyl) groups are formed as the result of partial dissociation of formaldehyde from N-(hydroxymethyl) groups of HMSI and then added to N-(hydroxyalkyl) group ac- cording to the scheme:

$$\overset{|}{-N}—CH_2OH \; + \; N(C_2H_5)_3 \; \rightleftharpoons \; \overset{|}{-N}—CH_2O^- \; + \; \overset{+}{HN(C_2H_5)_3}$$

(29)

$$\overset{|}{-N}—CH_2O^- \; \rightleftharpoons \; \overset{|}{-N}^- \; + \; CH_2O$$

(30)

$$\overset{|}{-N}^- \; + \; \underset{O}{\triangle}^R \; \rightarrow \; \overset{|}{-N}—CH_2\text{-}CH_2\text{-}O^-$$

(31)

$$\overset{|}{-N}—CH_2\text{-}CH_2—O^- \; + \; CH_2O \; \rightleftharpoons \; \overset{|}{-N}—CH_2\text{-}CH_2—O\text{-}CH_2O^-$$

(32)

$$-CH_2\text{-}CH_2—O\text{-}CH_2\text{-}O^- \; + \; \overset{+}{HN(C_2H_5)_3} \; \rightleftharpoons \; \overset{|}{-N}\text{-}CH_2\text{-}CH_2—O\text{-}CH_2—OH \; + N(C_2H_5)_3$$

(33)

or first the oxirane is attached to N-(hydroxymethyl) group with formation of (IV), from which the formal-dehyde is released and rearranged into the end of chain

according to the scheme:

(34)

(35)
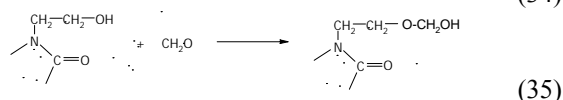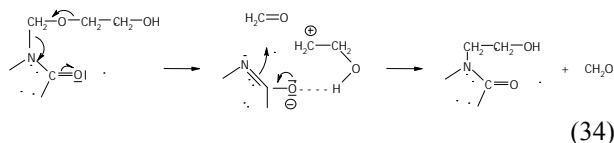
Cryoscopic determination of molar mass of HMSI in dioxane and DMSO indicated, that in both solvents the molar mass of HMSI was equal to calculated one (128.9 and 128.5 g/mol, respectively; calc. 129.1). This suggests that no dissociation of formaldehyde from N-(hydroxymethyl) groups occurs and the formaldehyde rearrangement takes place after blocking with oxirane (reaction 34). This corroborate well with our previous studies on the reaction of hydroxymethylated derivatives of uric acid with oxiranes [11]. The system HMSI-TEA was also studied by cryoscopic method (**Table 2**). As in other cases the relation $c_e < c_t$, was kept valid, what confirms that dissociation of formaldehyde from alcoholate did not occur upon TEA.

It is not possible to define the character of the bond in adduct on the basis of cryoscopic measurements. Therefore the IR and ^{1}H-NMR spectra were recorded. The IR spectrum of SI shows the valence band of NH at about 3200 cm^{-1} (**Figure 2(b)**). When 3-fold excess of TEA was added, the band disappeared (**Figure 2(d)**) accom-panied by appearance of weak band from ammonium cation $(C_2H_5)_3NH^+$ in the region 2300 - 2500 cm^{-1}. Undo-ubtedely, the proton transfer to TEA from imide took place. This band was more pronounced in the mixture of HESI and TEA (**Figures 2(c)** and (**e**)). The spectral features were: the disappearance of hydroxyl valence band at 3500 cm^{-1}, and simultaneous appearance of absorption at 2400 cm^{-1}. Thus, the product of reaction can also be the proton donor, which agrees well with cryoscopic data.
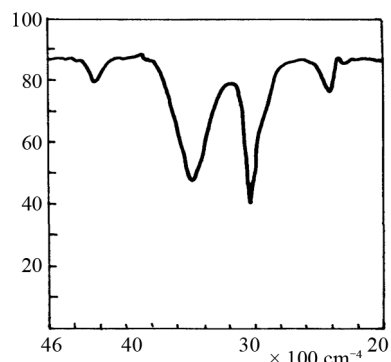
IR spectra rather preclude the formation of hydrogen bonded adduct; in such a case the broadening of the N-H
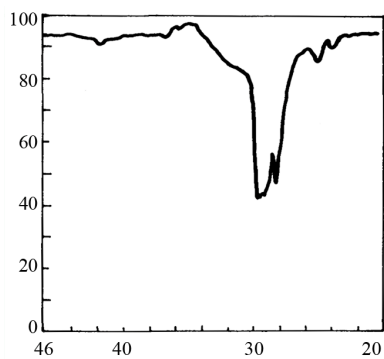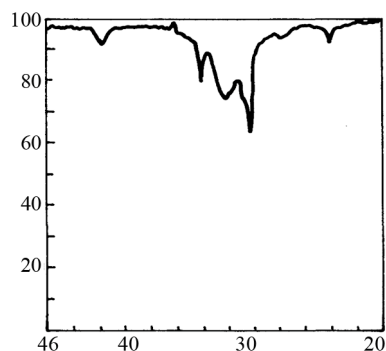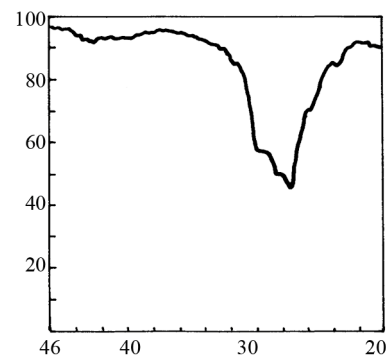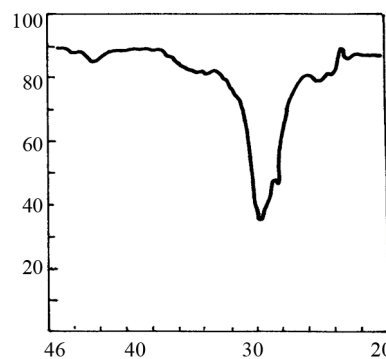

(b)

(c)

(d)

(e)

Figure 2. The relevant region of IR spectrum of TEA (a), SI (b), HESI (c), and mixtures of TEA with SI (d) and HESI (e).

(a)

band should be observed, while only the disappearance was the case. ^{1}H NMR spectra provide further evidences on the presence of ion pair. Addition of TEA to imide solution in DMSO-d_6 resulted in disappearance of imide group proton resonance >NH and simultaneous grow of resonance from $(C_2H_5)_3NH^+$ cation shifted upfield. The resonances are separated by 4.2 ppm in SI/SI-TEA system and by 6.1 ppm PI/PI-TEA. This spectroscopic picture also indicates the formation of ion pair instead of hydrogen bonding. Individual chemical shifts for the system SI/SI-TEA and PI/PI -TEA are as below:

SI (2.8, 4H, CH_2; 11.4, 1H, NH); SI/TEA (1.05, 9H, CH_3; 2.55, 6H, CH_2 from TEA, 2.8, 4H, CH_2 from SI; 7.2, 1H, NH^+).

PI (7.8, 4H, Ph; 11.6, 1H, NH); /PI-TEA (1.05, 9H, CH_3; 2.55, 6H, CH_2 from TEA, 7.8, 4H, Ph; 5.5, 1H, NH^+).

4. Summary and Conclusions

1) Based upon experimental kinetic the mechanism of the reaction of cyclic imides and oxiranes was proposed and verified by instrumental and analytical methods.

2) The initial step of reaction is the formation of 1:1 imide: TEA adduct, which intermediates the proton transfer from imide to oxirane. The adducts could not be isolated, although their presence in solutions was demonstrated experimentally.

3) The crucial bond in adduct has ionic character; in non-aqueous solvents it is present as ion pair, while in water the adduct dissociate and free ions are present.

4) The suggested mechanisms can be applied in expalantion of first stages of obtaining of polyetherols in reaction of oxiranes with cyclic imides containing a couple of imide groups such as isocyanuric acid, parabanic acid and barbituric acid etc.

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