On the Rearrangement Mechanism of Cyclic *O,N*-Acetals derived from Acylquinones and Enamines

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A kinetic study of the acid-catalysed rearrangement of 4-acetyl-2,3-dihydro-3,3-dimethyl-5-hydroxy-2-(1-morpholino)- and 4-acetyl-2,3-dihydro-3,3-dimethyl-5-hydroxy-2-(1-piperidino)-benzo[*b*]furan (**1a** and **1b**, respectively) as a function of the hydrochloric acid concentration, the reaction medium, and the dialkylamino group of the substrate is reported. The substrate (**1a**) shows hydrolysis and rearrangement reactions in dioxane–water (5.3 mol dm^{-3} in water) mixture but (**1b**) does not exhibit hydrolysis reaction. Both substrates show a limiting [HCl] dependence in dioxane–water (5.3 mol dm^{-3} in water) mixture but in ethanol–water (5.3 mol dm^{-3} in water) (**1b**) shows a first order in [HCl] kinetic behaviour. In dioxane–ethanol (40% v/v ethanol) both substrates exhibit closely similar rate-constant values for the same HCl concentrations. The kinetic results are explained through a reaction scheme and discussed taking into account the basicity of the amino groups and the stabilisation of the ionic species involved in the probable rearrangement mechanism.

The acid-catalysed rearrangement of 4-acyl-2,3-dihydro-5-hydroxybenzo[*b*]furans containing a cyclic *O,N*-acetal group has been studied by us in connection with quinone synthesis,[1-3] and also in order to obtain information about the chemistry of the *O,N*-acetal group.[4] In a previous paper[4] on the kinetics of the acid-catalysed rearrangement of 4-acetyl-2,3-dihydro-3,3-dimethyl-5-hydroxy-2-(1-morpholino)benzo[*b*]furan (**1a**) leading to 5,8-dihydroxy-4,4-dimethyl-1(4*H*)-naphthone (**2**), we reported a set of reactions which described this process. The study of the reaction (**1a**)⟶(**2**) showed the existence of 2,3-dihydro-2,5-dihydroxy-3,3-dimethylbenzo[*b*]furan (**3**) as an intermediate, and the kinetic results were discussed assuming the existence of ethylketal and immonium ion intermediates. The kinetic data were evaluated on the basis of two first-order parallel reactions (**2**)⟵(**1a**)⟶(**3**), since the reaction (**3**)⟶(**2**) is very slow.

Following our studies on cyclic *O,N*-acetals derived from quinones and enamines, we found that, under the same conditions, the intermediate (**3**) is not detected in the acid-catalysed rearrangement of 4-acetyl-2,3-dihydro-3,3-dimethyl-2-(1-piperidino)-5-hydroxybenzo[*b*]furan (**1b**) leading to the naphthone (**2**). This result, which implies the absence of hydrolysis reactions and is obviously a simplification of the proposed model, led us to study the effect of the addition of water on the kinetics of the transformation (**1b**)⟶(**2**) in dioxane and ethanol solutions.

Taking into account the fact that the reaction is acid-catalysed, we also examined the effect of [HCl] on the kinetics of the reactions of (**1b**) in dioxane–ethanol, dioxane–water, and ethanol–water solutions, and on the kinetics of the reactions of (**1a**) in dioxane–ethanol and dioxane–water solutions.

Experimental

The u.v.-visible spectra of different kinetic samples were obtained in a Pye Unicam SP-1800 spectrophotometer, using 10 mm cuvettes. Elemental analysis of (**1b**) was carried out at the Instituto de Química General (CSIC), Madrid, Spain. The m.p.s were determined on a Kofler hot-stage microscope melting-point apparatus. I.r. (KBr) spectra were obtained on a Perkin-Elmer 567 spectrophotometer, and ^1H n.m.r. spectra were taken with a Varian XL-100 spectrometer.

Ethanol, dioxane, and hydrochloric acid were reagent grade; hydrochloric acid in ethanol was prepared by bubbling HCl through ethanol, and was standardised by titration with aqueous NaOH.

Materials.—4-Acetyl-2,3-dihydro-3,3-dimethyl-5-hydroxy-2-(1-morpholino)benzo[*b*]furan (**1a**) and 5,8-dihydroxy-4,4-dimethyl-1(4*H*)-naphthone (**2**) were obtained as previously reported.[4]

4-*Acetyl*-2,3-*dihydro*-3,3-*dimethyl*-5-*hydroxy*-2-(1-*piperidino*)*benzo*[b]*furan* (**1b**).—*N*-(2-Methylprop-1-enyl) piperidine (200 mg, 1.44 mmol)[5] in dry benzene (10 ml) was added dropwise at room temperature to a stirred solution of 2-acetyl-1,4-benzoquinone[6] (200 mg, 1.33 mmol) in the same solvent (40 ml). After 2 h, the reaction mixture was evaporated under reduced pressure and the oily residue was allowed to solidify in the presence of cyclohexane. The crude product was recrystallised from cyclohexane to yield (**1b**) (200 mg, 0.69 mmol, 52%), m.p. 162—164 °C (Found: C, 70.8; H, 7.85; N, 4.65. $C_{17}H_{23}NO_3$ requires C, 70.56; H, 8.01; N, 4.84%); $\nu_{max.}$(KBr) 3 340 (OH) and 1 655 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$; standard Me_4Si) 1.32 (3 H, s), 1.42 (3 H, s), 1.30—1.60 (6 H, m), 2.30—2.80 (4 H, m), 2.62 (3 H, s), 4.75 (1 H, s), 6.57 (1 H, d, *J ca.* 8 Hz), and 6.66 (1 H, d, *J ca.* 8 Hz); the signal corresponding to the hydroxylic proton was not observed but its presence was detected by D_2O addition.

Kinetic Measurements.—The kinetics were determined by measuring the absorbance increase at 420 nm in accordance with the general procedure previously described.[4] The reactions were studied at 80 ± 0.1 °C and in all cases excellent first-order plots were obtained using Guggenheim's method.[7] The absorption spectra of the reaction mixtures of (**1b**) at infinity corresponded to within 2% to the 'mock' infinity prepared by using (**2**). In the case of (**1a**) the spectra of the reaction mixtures corresponded only qualitatively with the 'mock' infinity but at very long times also corresponded to within 2%. In some runs the ionic strength was modified by KCl addition; no differences in the observed rate constants were detected.

Results and Discussion

The reaction of the *O,N*-acetal (**1a**) was studied in dioxane–water mixtures, and in the presence of different concentrations

Table 1. Rearrangement (k_R) and hydrolysis (k_H) rate constants for the reaction of (**1a**) in dioxane–water (5.3 mol dm^{-3} in water) at different concentrations of HCl

[HCl]/mol dm^{-3}	10^4k_R/s^{-1}	10^5k_H/s^{-1}
0.015	0.77	5.60
0.024	1.18	5.33
0.029	1.48	4.67
0.058	2.90	3.70
0.073	3.75	3.30
0.116	5.40	2.83
0.131	5.83	
0.145	6.33	

Table 2. Rearrangement rate constants for the reaction of (**1a,b**) in dioxane–ethanol (40% v/v ethanol) at different hydrogen chloride concentration

	10^4k_R/s^{-1}	
[HCl]/mol dm^{-3}	(**1a**)	(**1b**)
0.025	3.45	3.55
0.050	4.92	4.78
0.100	6.23	5.92
0.251	11.2	
0.502	18.0	18.6
0.753	26.8	26.8

Table 3. Empirical rate equations established for the reactions of (**1a,b**) in different solvents with different HCl concentrations

Solvent mixture	Substrate	Equation
Dioxane–water	(**1b**)	$k_R^{-1} = C_1[HCl]^{-1} + C_2$
(5.3 mol dm^{-3} in water)	(**1a**)	$k_R^{-1} = C_3[HCl]^{-1} + C_4$
		$(k_H - C_5)^{-1} = C_6[HCl] + C_7$
Ethanol–water (5.3 mol dm^{-3} in water)	(**1b**)	$k_R = C_8[HCl]$
Dioxane–ethanol (40% v/v ethanol)	(**1a**) and (**1b**)	$k_R = C_9[HCl] + C_{10}$

of hydrochloric acid as catalyst. Analysis of the reaction mixtures showed that the concentration ratio of (**2**) to the stable intermediate (**3**), measured before the substrate (**1a**) was consumed {not at very long reaction times because the reaction (**3**)$\rightarrow$(**2**) is dependent on the catalyst concentration and thus the higher this is, the lower the [(**3**)]:[(**2**)] ratio}. This is inconsistent with the existence of a common intermediate for both reactions (hydrolysis and rearrangement) unless the latter reaction is acid catalysed. Naphthone formation *via* an immonium intermediate, as has been suggested,[4] requires an aldol condensation of the acetyl group with the immonium function; such a process should be acid catalysed, but the nucleophilic attack of water upon the immonium intermediate, leading to (**3**), does not require an acid catalyst.

The reaction of the *O,N*-acetal (**1b**) was studied in ethanol–water and dioxane–water mixtures, and in the presence of hydrochloric acid as catalyst. Analysis of the reaction mixtures showed only the presence of (**1b**) and (**2**); no intermediates were detected. This behaviour, different from that shown by (**1a**), was confirmed by visible spectrophotometry since (*a*) a stable isosbestic point was observed and (*b*) all the equilibrium spectra were identical under different conditions. It was also kinetically different since only a single kinetic equation was observed for the change (**1b**)$\rightarrow$(**2**).

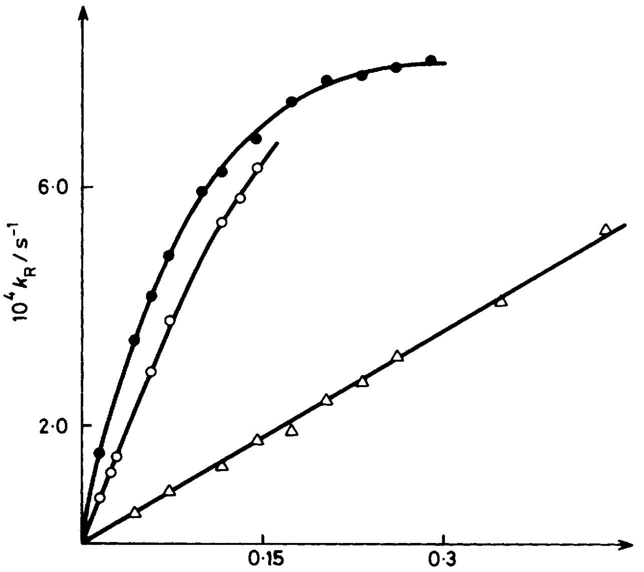


Figure 1. Variation of k_R with HCl concentration. (○) for (**1a**) in dioxane–water (5.3 mol dm^{-3} in water) solution; (●) for (**1b**) in dioxane–water (5.3 mol dm^{-3} in water) solution; (△) for (**1b**) in ethanol–water (5.3 mol dm^{-3} in water) solution

Assuming that the set of reactions proposed for the rearrangement of (**1a**)[4] is valid for that of (**1b**), the above results show that the hemiacetal formation paths are not significant and only the rearrangement paths are important. The Scheme shows the probable pathway for the rearrangement reactions of (**1a,b**). Although in the previous paper[4] the hydrolysis product (**3**) was isolated as a cyclic compound, when the acidity of the reaction medium is taken into account it seems possible that this product takes one of the equilibrium forms shown as (**4**) in the Scheme. Thus it is possible that an acetalic intermediate, if indeed there is one, could take any of the equilibrium forms (**8**) shown in the Scheme. The rate constants k_2, k_4, and k_6 are those of water attack upon (**5a,b**), (**6a,b**), and (**8**), respectively, and k_5 and k_7 are those of ethanol attack upon (**6a,b**) and (**5a,b**), respectively, all in the solvolytic pathway.

Since the furan oxygen in (**1a,b**) is less basic than the amino groups (morpholino and piperidino)[8] and considering the hydrochloric acid concentrations used throughout the study, it is probable that both substrates are protonated at the nitrogen atom and $K_1[HCl] \gg K_2[HCl]$.

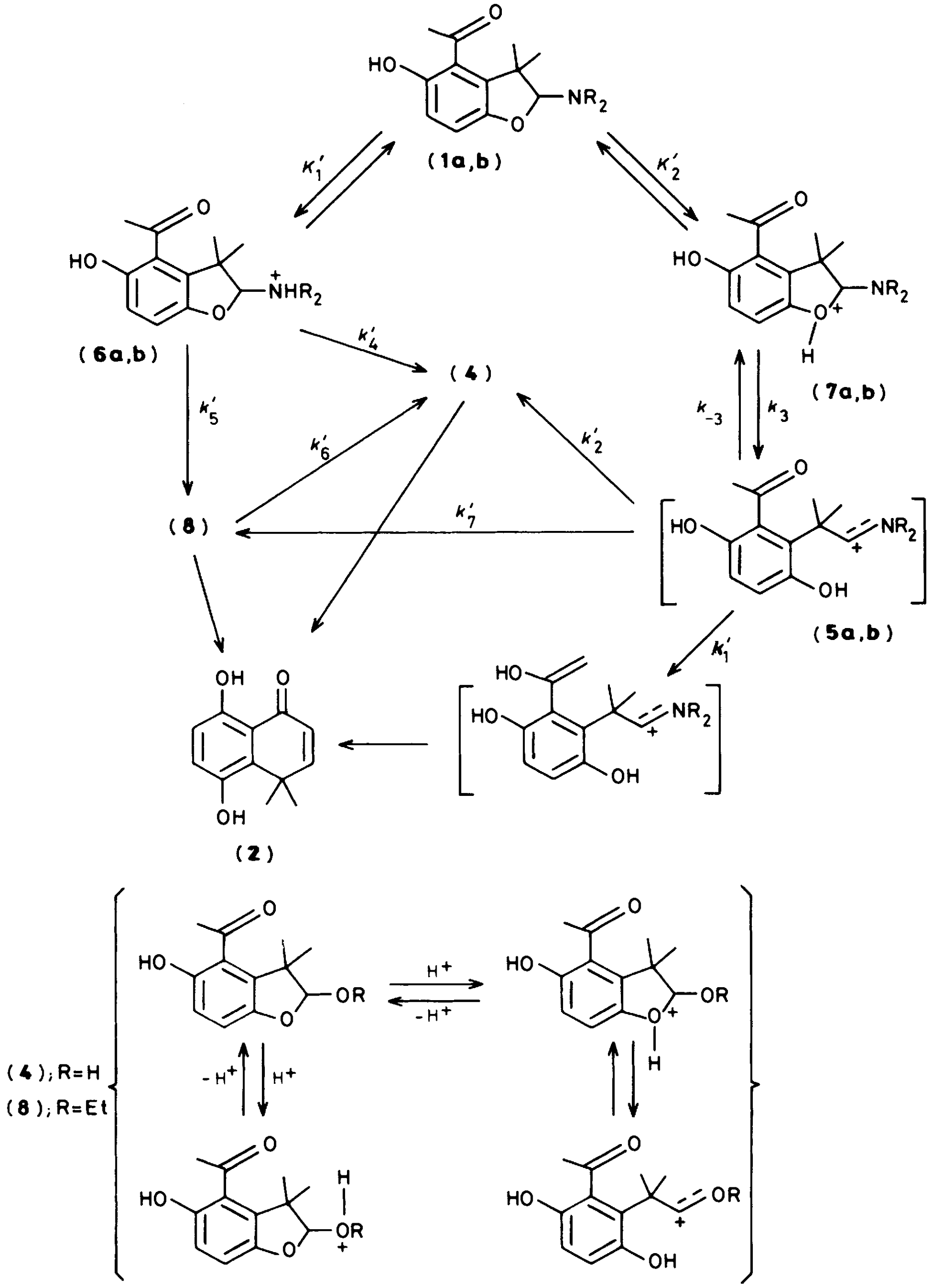
In order to verify the possible intervention of chloride ions as a competitive nucleophile in solvolytic reactions, some experiments were carried out in the presence of potassium chloride; however, no difference in the kinetic behaviour was observed.

Tables 1 and 2 and Figures 1 and 2 summarise the experimental results of this work, where k_R and k_H are the rearrangement and hydrolysis rate constants, respectively. In Table 1 the values of k_H when [HCl] > 0.116 mol dm^{-3} are not included because at this concentration the hydrolysis reaction is less than 5% and k_H determination is not accurate.

The empirical equations obtained in this study are summarised in Table 3.

(1) *Effect of* HCl *Concentration on the Rearrangement Reaction of* (**1b**) *in Dioxane–Water* (5.3 *mol dm*$^{-3}$ *in Water*).—As was mentioned above, this reaction gives no hydrolysis product and the Scheme can be simplified to equation (1).

$$(\mathbf{6b}) \underset{}{\overset{K_1[HCl]}{\leftrightharpoons}} (\mathbf{1b}) \overset{K_2[HCl]}{\rightleftharpoons} (\mathbf{7b}) \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} (\mathbf{5b}) \xrightarrow{k_1[HCl]} (\mathbf{2}) \quad (1)$$



NR_2. **a** = Morpholino
b = Piperidino
$K_1' = K_1[H^+]$
$K_2' = K_2[H^+]$
$k_1' = k_1[H^+]$

$k_2' = k_2[H_2O]$
$k_4' = k_4[H_2O]$
$k_5' = k_5[EtOH]$
$k_6' = k_6[H_2O]$
$k_7' = k_7[EtOH]$

Scheme.

Equation (2) can be derived from equation (1), assuming a steady-state condition for (**5b**) and that $K_1[HCl] \gg (1 + K_2[HCl])$ (see above).

$$k_R = k_1k_3K_2[HCl]K_1^{-1}(k_{-3} + k_1[HCl])^{-1} \quad (2)$$

This limiting [HCl] dependence is in accord with the results shown in Figure 1. This equation is also in accord with the empirical equation (Table 3) if it is written as equation (3).

$$k_R^{-1} = K_1k_{-3}(k_1k_3K_2)^{-1}[HCl]^{-1} + K_1(k_3K_2)^{-1} \quad (3)$$

The values of the combined rate constants are summarised in Table 4. From the empirical equation the maximum k_R value is

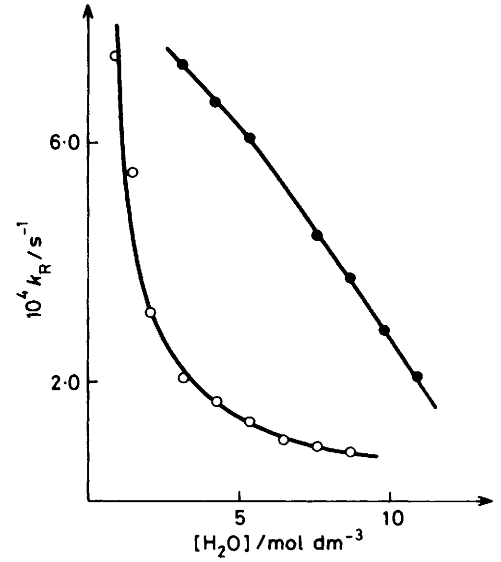


Figure 2. Variation of k_R in the reaction of (**1b**) with water concentration. (○) In ethanol–water; (●) in dioxane–water

The hydrolysis rate constant k_H derived from equation (4) is given by equation (7), which suggests a decrease in k_H with [HCl] increase, which is in accord with the experimental results (Table 1), and a lack of dependence on [HCl] at very low concentrations (not observed).

$$k_H = k_2k_3K_2[H_2O]K_1^{-1}(k_{-3} + k_1[HCl] + k_2[H_2O])^{-1} + k_4[H_2O] \quad (7)$$

Equation (7) is also in accord with the empirical equation (Table 3) if it is written as equation (8).

$$(k_H - k_4[H_2O])^{-1} = K_1(k_{-3} + k_2[H_2O])(k_2k_3K_2[H_2O])^{-1} + K_1k_1(k_2k_3K_2[H_2O])^{-1}[HCl] \quad (8)$$

The linearity of experimental results plotted as equation (8) with a non-zero $k_4[H_2O]$ value ($k_4[H_2O] = 1.75 \times 10^{-5}$ obtained by iterative fitting) confirms the existence of a hydrolysis reaction from (**6a**) resulting from the nucleophilic attack of a water molecule without ring opening.

The lumped rate constants derived from the comparison of equations (6) and (8) with the empirical results (Table 3) are summarised in Table 4.

Table 4. Combined rate constants

Solvent	Substrate	From gradient	From intercept	Plot of equation
Dioxane–water	(**1b**)	$K_1k_{-3}(k_1k_3K_2)^{-1} = 84.7$	$k_3K_2K_1^{-1} = 1.1 \times 10^{-3}$	3
	(**1a**)	$K_1(k_{-3} + k_2[H_2O])(k_1k_3K_2)^{-1} = 192.8$	$k_3K_2K_1^{-1} = 5.2 \times 10^{-3}$	6
		$K_1k_1(k_2k_3K_2[H_2O])^{-1} = 6.39 \times 10^5$	$K_1(k_{-3} + k_2[H_2O])(k_2k_3K_2[H_2O])^{-1} = 1.44 \times 10^4$	8[a]
Ethanol–water	(**1b**)	$K_2k_1k_3(K_1k_{-3})^{-1} = 1.2 \times 10^{-3}$		9
Ethanol–dioxane	(**1a,b**)	$K_2k_1k_3K_1^{-1}(k_{-3} + k_7[EtOH])^{-1} = 3.14 \times 10^{-3}$	$k_5[EtOH] + \frac{k_7[EtOH]k_3K_2}{(k_{-3} + k_7[EtOH])K_1} = 2.97 \times 10^{-4}$	14

[a] For $k_4[H_2O] = 1.75 \times 10^{-5}$ obtained by iterative fitting.

$K_2k_3K_1^{-1} = 1.1 \times 10^{-3}$, not very different from the tendency of k_R in Figure 1 (*ca.* 8.4×10^{-4}).

(2) *Effect of* HCl *Concentration on the Rearrangement and Hydrolysis Reactions of* (**1a**) *in Dioxane–Water* (5.3 *mol dm*$^{-3}$ *in Water*).—Assuming this reaction to be the parallel reactions (**2**)⟵(**1**)⟶(**4**), since reaction (**4**)⟶(**2**) is negligible,[4] equation (4) represents the model of the reactions derived from the Scheme.

$$\begin{tikzcd}
(\mathbf{6a}) \arrow[r, shift left, leftarrow, "K_1[HCl]"] \arrow[r, shift right] \arrow[dr, "k_4[H_2O]"'] & (\mathbf{1a}) \arrow[r, shift left, "K_2{[HCl]}"] \arrow[r, shift right, leftarrow] & (\mathbf{7a}) \arrow[r, shift left, "k_3"] \arrow[r, shift right, leftarrow, "k_{-3}"'] \arrow[dl, "k_2[H_2O]"] & (\mathbf{5a}) \arrow[d, "k_1[HCl]"] \\
 & (\mathbf{4}) & & (\mathbf{2})
\end{tikzcd} \quad (4)$$

Assuming a steady-state condition for (**5a**) and $K_1[HCl] \gg (1 + K_2[HCl])$ (see above), equation (5) can be derived for the rearrangement rate constant. This equation shows a limiting dependence on [HCl] in accord with the experimental results (Figure 1), and if written as equation (6) it takes the same form as the empirical equation (Table 3).

$$k_R = k_1k_3K_2[HCl]K_1^{-1}(k_{-3} + k_1[HCl] + k_2[H_2O])^{-1} \quad (5)$$

$$k_R^{-1} = K_1(k_{-3} + k_2[H_2O])(k_1k_3K_2)^{-1}[HCl]^{-1} + K_1(k_3K_2)^{-1} \quad (6)$$

(3) *Effect of* HCl *Concentration on the Rearrangement of* (**1b**) *in Ethanol–Water* (5.3 *mol dm*$^{-3}$ *in Water*).—Taking into account the absence of a hydrolysis reaction (see above), and although the ethanolysis reactions cannot be disregarded *a priori*, the experimental results (Figure 1) suggest that equations (1) and (2) with $k_{-3} \gg k_1[HCl]$ over the whole range of [HCl] values used are valid in this reaction medium; this leads to equation (9).

$$k_R = K_2k_1k_3(K_1k_{-3})^{-1}[HCl] \quad (9)$$

The ethanolysis reaction of (**6b**) requires an intercept different from zero in the empirical equation. The lack of intercept permits us to disregard this reaction pathway.

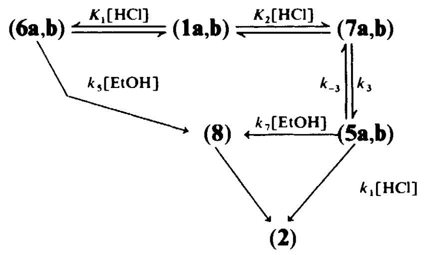
Also, the ethanolysis of (**5b**) can be ruled out, because this would require another term in equation (9) which would imply a decrease in k_R with [HCl] increase [equation (10)]. This equation was obtained assuming no ethanolic reaction of (**6b**), no hydrolysis reactions, steady-state approximation for (**5b**), and $K_1[HCl] \gg (1 + K_2[HCl])$. If $(k_{-3} + k_7[EtOH]) \gg k_1[HCl]$, equation (11) is obtained, showing a constant term which is not present in the empirical equation (Table 3).

$$k_R = k_1k_3[HCl](k_{-3} + k_7[EtOH] + k_1[HCl])^{-1} + k_3k_7K_2[EtOH]K_1^{-1}(k_{-3} + k_7[EtOH] + k_1[HCl])^{-1} \quad (10)$$

$$k_R = k_1k_3[HCl](k_{-3} + k_7[EtOH])^{-1} + k_3k_7K_2[EtOH]K_1^{-1}(k_{-3} + k_7[EtOH])^{-1} \quad (11)$$

This result permits us to disregard the contribution of the ethanolysis reaction for (**1b**) in the ethanol–water mixtures studied.

(4) *Effect of* HCl *Concentration on the* (**1a,b**) *Rearrangement Reaction in Dioxane–Ethanol* (40% *v*/*v Ethanol*).—It can be observed that both substrates exhibit closely similar values of k_R for the same HCl concentrations (Table 2), showing the lack of influence of the amine group in (**1a,b**). Taking into account the absence of hydrolysis products, equation (12) summarises the path involved in this reaction.



(12)

Assuming a steady-state condition for (**5a,b**), that the reaction (**8**)⟶(**2**) is very fast [(**8**) has not been observed], and that $K_1[\mathrm{HCl}] \gg (1 + K_2[\mathrm{HCl}])$, equation (13) can be obtained.

$$k_R = k_5[\mathrm{EtOH}] + k_1k_3K_2[\mathrm{HCl}]K_1^{-1}(k_{-3} + k_7[\mathrm{EtOH}] + k_1[\mathrm{HCl}])^{-1} + k_7k_3K_2[\mathrm{EtOH}]K_1^{-1}(k_{-3} + k_7[\mathrm{EtOH}] + k_1[\mathrm{HCl}])^{-1} \quad (13)$$

If, over the range of hydrochloric acid concentration used in this study, $(k_{-3} + k_7[\mathrm{EtOH}]) \gg k_1[\mathrm{HCl}]$, equation (14) can be obtained; this is in accord with the empirical equation (Table 3). The lumped rate constants are given in Table 4.

$$k_R = k_5[\mathrm{EtOH}] + k_3k_7K_2[\mathrm{EtOH}]K_1^{-1}(k_{-3} + k_7[\mathrm{EtOH}])^{-1} + k_1k_3K_2[\mathrm{HCl}]K_1^{-1}(k_{-3} + k_7[\mathrm{EtOH}])^{-1} \quad (14)$$

The intercept in the empirical equation confirms the ethanolysis reaction in this solvent although this result is not sufficient to decide if the solvolysis is for (**5a,b**) or (**6a,b**) or both, because their kinetic behaviour is indistinguishable.

(5) *Solvent Effects on the Rearrangement Reaction of* (**1b**).—Taking into account the absence of hydrolysis and ethanolysis reactions in the rearrangement of (**1b**) (see above), the influence of the polarity of the solvent on the kinetics of the reaction (**1b**)⟶(**2**) was studied in dioxane and ethanol solutions as a function of water added to both solvents.

The scheme of reactions involved is shown in equation (1), and the rearrangement rate constant of equation (2) can be derived from this.

It is interesting to note that in equation (2) no dependence on water concentration is involved, but that the k_R values (Figure 2) in both media decrease when $[\mathrm{H_2O}]$ increases (polarity increases), and in both solvents with the same water concentration the k_R value is greater in dioxane than in ethanol. This behaviour probably can be by the greater stabilisation by solvation of the ionic species (**5b**) and (**7b**) than the transition states involved in the ring opening and in acid-catalysed enol formation from the acetyl group steps.

In spite of the errors involved in the determination of the lumped constants summarised in Table 4, it is interesting to note that the limiting value for the rearrangement rate constant ($k_3K_2K_1^{-1}$) in dioxane–water is higher for (**1b**) (Table 4). On this we must point out that the ring opening of (**7b**) should be favoured over that of (**7a**) since the more basic piperidino group[8] can more easily delocalise the positive charge, leading to a greater k_3 value for (**1b**). However, for the same reason a greater K_1 value for (**1b**) could be expected and although the electron-donating effect of the amine group leads also to a greater value of K_2 for (**1b**), the K_2/K_1 value will be more favoured for (**1a**) than for (**1b**). As a consequence the nature of the amine affects in both ways the upper limit of k_R, being greater for the morpholine derivative (**1a**).

In the same way, the $k_1(k_{-3})^{-1}$ value for (**1b**) is about eleven-times greater than $k_1(k_{-3} + k_2[\mathrm{H_2O}])^{-1}$ for (**1a**) in dioxane–water (Table 4). Taking into account that k_1 is the rate constant for the formation of the enol derivative from the acetyl group in (**5a,b**), it can be expected that the k_1 value for both substrates is not very different. The k_{-3} value must be different in both substrates because it depends on the ability of (**5a,b**) to form (**7a,b**) and this ability can be determined by the greater stability of (**5b**) relative to (**5a**), due to the greater basicity of the piperidino group. Therefore, k_{-3} is smaller for (**1b**). If one also considers that (**1b**) shows no hydrolysis reaction, there is a double reason for the experimental differences found.

In the rearrangement in dioxane–ethanol mixtures it is remarkable that the behaviour of both substrates is so similar in reactions involving solvolysis and rearrangement *via* immonium cation intermediates in spite of the different basicities of the amine moieties (piperidino and morpholino).[8] Regarding the ethanolysis reaction (k_5 path), it is noteworthy that the nucleophilic attack is at the carbon adjacent to the protonated amine nitrogen atom, and since both amine groups are very good leaving groups, the ethanol attack should be the rate-determining step in this reaction. In ethanolysis *via* the immonium cation (k_7 path) (**5b**), the attack of ethanol is at a more electrophilic carbon because of the greater basicity of piperidine than morpholine but also because the leaving group ability is worse in the piperidine adduct. In the rearrangement *via* the immonium cation (**5a,b**), however, k_1 would probably not be affected by the nature of the amine group because k_1 corresponds to the enolisation in the acetyl group; but the basicity of the piperidino group leads to increased values for k_3 and K_1 and K_2 relative to the morpholino group; this effect must be compensated so that both substrates show the same behaviour.

It is also interesting to note that the term $k_1k_3K_2(K_1k_{-3})^{-1}$ for (**1b**) is about ten times greater in dioxane–water than in ethanol–water mixtures (Table 4). Probably, owing to the greater stabilisation by solvation of H^+ (as was mentioned above in relation to the reaction media effect), the value for k_1 in ethanol–water media could be smaller.

In conclusion, according to the results obtained in this study of the dependence of the rearrangement reaction on catalyst concentration, solvent polarity, and the nature of the substrate dialkylamino group, the most probable rearrangement mechanism of (**1a,b**) and related *O,N*-acetals is the reaction scheme shown. Some paths, however, are more important than others depending on the solvent and for each case a simplified model is proposed.

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