HYDRATION OF 2,2-DICHLORO-1-ARYLETHANONES IN WATER AND TETRAHYDROFURAN–WATER MIXTURES.

RENATO WENDHAUSEN, JR, EDUARDO ZAMPIRÓN, JOSÉ F. VIANNA, CÉSAR ZUCCO, MARCOS CAROLI REZENDE* AND FARUK NOME.*

Departamento de Química, Universidade Federal de S. Catarina, Florianópolis, SC 88049, Brazil

The hydration of 2,2-dichloro-1-arylethanones was studied in water and tetrahydrofuran (THF)–water mixtures and the equilibrium constants in water were estimated for four ethanones. The process is subject to specific acid and to general base catalysis. The proton inventory technique was applied to the study of the reaction in L_2O and $THF-L_2O$ solutions (L = H or D). In pure water and water-rich mixtures, a very large number of protons participate in the open transition state, this number decreasing gradually with increasing water content in the mixture, until the minimum value of 2 is reached, corresponding to a cyclic, closed transition-state structure.

INTRODUCTION

Nucleophiles are known to add to the carbonyl group of aldehydes and ketones to form tetrahedral species. When the nucleophile is water, hydrates are obtained which are stable in solution and in many cases can be isolated.

Although equilibrium constants of hydration for various halogenoketones have been determined by several methods,[1] detailed mechanistic studies of the hydration of this class of compounds are scarce. Among *gem*-polyhalogenoketones, the hydration of trifluoroethanones has attracted the attention of different groups. Studies on the hydration of 2,2,2-trifluoro-1-arylethanones have been published[2-5] and the hydration of 1,1,1-trifluoroacetone has been compared with that of acetone.[6,7]

Studies on the hydration of chloroketones have been restricted to a few propanone derivatives, including 1-chloropropanone,[8] 1,1-dichloropropanone[9] and 1,3-dichloropropanone.[10-13] The mechanism of hydration of the last compound has been investigated in detail in a series of now classical papers by Bell and co-workers.[10-12] More recently, the influence of surfactants on the hydration of the same substrate has also been investigated.[14,15]
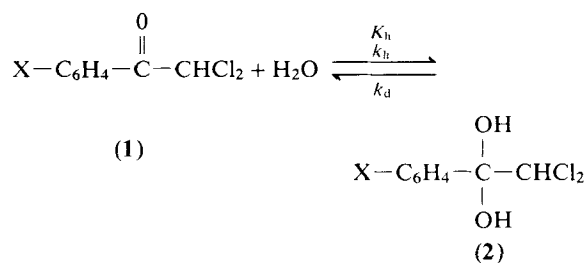
We have been concerned for some time with the chemistry of *gem*-polychloroarylethanones. The reaction of 2,2,2-trichloro-1-arylethanones with amines and alcohols has been studied in our laboratories from both the preparative and mechanistic points of view.[16,17] The

mechanism of the basic hydrolysis of these ethanones was also investigated.[18] In all cases tetrahedral intermediates were postulated, which are formed by an initial nucleophilic attack at the carbonyl group.

In continuation of our interest in this topic, we decided to examine the mechanism of hydration of this class of compounds, as this is a reversible process in neutral or acidic solutions, uncomplicated by further decomposition of the hydrate formed. This paper deals with the hydration of 2,2-dichloro-1-arylethanones (**1**) in water and tetrahydrofuran (THF)–water mixtures.

RESULTS AND DISCUSSION

The observed rate constants for the hydration of the dichloroethanones (**1**) in water to form the corresponding hydrates (**2**) at 25 °C are given in Table 1.

$$X-C_6H_4-\overset{\overset{\displaystyle O}{\|}}{C}-CHCl_2 + H_2O \underset{k_d}{\overset{K_h \atop k_h}{\rightleftharpoons}}$$

(**1**)

$$X-C_6H_4-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}-CHCl_2$$

(**2**)

X = H (a)
$p-CH_3$ (b)
$p-Br$ (c)
$m-NO_2$ (d)

---

* Authors for correspondence.

Table 1. Equilibrium and rate constants for the hydration of 2,2-dichloro-1-arylethanones (1) in water at 25 °C

Ketone	$10^2 k_{obs}$ (s^{-1})	$10^3 k_h$ (s^{-1})	$10^2 k_d$ (s^{-1})	K_h
1a	6·64	16·4	5·00	0·33
1b	6·74	9·8	5·76	0·17
1c	9·25	36·0	5·65	0·64
1d	29·34	24·10	5·24	4·60

The rate constants of hydration (k_h) and dehydration (k_d) may be obtained with the aid of the following equations:

$$k_{obs} = k_h + k_d \qquad (1)$$

$$K_h = k_h/k_d \qquad (2)$$

where K_h is the equilibrium constant between the hydrate (2) and the ketone (1).

Combination of equations (1) and (2) yields k_d and k_h as functions of k_{obs} and K_h;

$$k_d = k_{obs}/(K_h + 1) \qquad (3)$$

$$k_h = k_{obs}K_h/(K_h + 1) \qquad (4)$$

The K_h values may be calculated from the equation

$$K_h = (a_M^{ketone} - a_M^{equil.})/(a_M^{equil.} - a_M^{hydrate}) \qquad (5)$$

where the molar absorptivities a_M^{ketone}, $a_M^{hydrate}$ and $a_M^{equil.}$ refer to the ketone (1), the hydrate (2) and the equilibrium mixture, respectively.

Values for a_M^{ketone} could be obtained by extrapolation of the absorbance values of 1 in water to reaction time zero. Once the equilibrium had been attained, the absorbance reading at the same wavelength yielded the corresponding $a_M^{equil.}$. Unfortunately, the $a_M^{hydrate}$ values could not be determined with the same precision, because species 2 could not be isolated from the aqueous solution. This difficulty was overcome by taking the molar absorptivities of the corresponding 2,2,2-trichloro-1-arylethanols (3)[19] as good approximations of the molar absorptivities of the hydrates 2, following a procedure employed previously.[17] The values of $a_M^{hydrate}$ were then 400, 570, 350 and 4930 for the species 2a, 2b, 2c and 2d, respectively.

With these approximations, values of K_h, k_h and k_d were estimated for all substrates 1 in water. These values are also given in Table 1.

The equilibrium constant of hydration for 1a (0.33) is seen to be approximately ten times smaller than the corresponding value for the 2,2-dichloropropanone (2.9), determined by Bell and McDougall.[9] This decrease in the ease of hydration when a methyl is substituted by a phenyl group may be a result of both the increased steric protection of the carbonyl group in 1a and the decreased electrophilicity of this group when conjugated with an aromatic system. This second effect is particularly im-

portant, as shown by the comparison of the K_h values of hydration of 2,2-dichloropropanone (2.9) and of 2,2-dichloro-1-(3-nitrophenyl)ethanone (1d) (4.6). Conjugation with the more electron-withdrawing 3-nitrophenyl substituent increases the electrophilicity of the carbonyl group, thus rendering this dichloroarylethanone (1d) even more susceptible to hydration than the analogous 2,2-dichloropropanone.

The values of k_h, k_d and K_h allow the determination of the Hammett ρ values for the hydration and dehydration processes. The corresponding Hammett plots (not shown) yield ρ values of 1·59, −0·03 and 1·62 for the hydration and dehydration steps, and for the equilibrium constants, respectively. As expected, the forward hydration step is fairly dependent on the nature of the substituent, being facilitated by electron-withdrawing groups, whereas the reverse dehydration step is almost independent of the nature of the phenyl substituent. Our values are very close to those reported by McClelland and Coe[20] for the hydration of benzaldehydes. They obtained a ρ value of 1·7 for the hydration step and a ρ value near zero in the dehydration direction.

We next turned our attention to the investigation of acid or base catalysis in the hydration process. The influence of the pH of the medium on the observed rate constant of hydration of 1a was investigated in aqueous HCl solutions. The k_{obs} values obtained are given in Table 2. As can be seen, the hydration does not depend on the hydronium concentration in the pH range 7–1. In more acidic solutions, a linear dependence of the observed rate constant on the acid concentration was observed. This points to the existence of a spontaneous hydration constant $k_0 = 0·066\,s^{-1}$, and a specific acid-catalysed rate contant $k_H = 0·3961\,mol^{-1}\,s^{-1}$.

Isotopic effects on the acid-catalysed hydration of 2,2-dichloro-1-(4-bromophenylethanone) (1c) and 2,2-dichloro-1-(3-nitrophenyl)ethanone (1d) were studied in LCl–L2O solutions (L = H or D), in the acid concentration range 0·2–1·0 M. The k_H/k_D ratios for substrates 1c and 1d were 1·96 and 2·24, respectively. These small values are in agreement with the existence of specific acid catalysis in the process, indicating that

Table 2. Observed rate constants for the hydration of 2,2-dichloro-1-phenylethanone (1a) in aqueous HCl solutions at 25 °C

[HCl] (M)	$10^2 k_{obs}$ (s^{-1})	[HCl] (M)	$10^2 k_{obs}$ (s^{-1})
a	6·6	0·2	9·7
b	6·5	0·4	20·6
0·001	6·6	0·6	24·1
0·01	6·7	0·8	34·6
0·1	6·8	1·0	42·6

[a] pH 7·0, phosphate buffer.
[b] pH 5·0, phthalate buffer.

protonation of the carbonyl oxygen occurs before the attack by a water molecule.

The specific base catalysis was not studied because at basic pH 2,2-dichloro-1-arylethanones decompose to mandelic acid derivatives.[21]

The existence of general acid or base catalysis in the pH range 1–7 was next checked using the equation

$$(k_{obs} - k_0)/[HB]_T = k_{HB}(1 - f) + f k_B \qquad (6)$$

where k_{HB} and k_B are the catalytic rate constants for the general acid and base [HB] and [B], respectively, $[HB]_T$ is the total concentration of the acid–conjugate base pair, $[HB]_T = [HB] + [B]$, and f is the fraction of conjugate base at a given pH. A plot of $(k_{obs} - k_0)/[HB]_T$ vs f allows the determination of k_{HB} and k_B for a given general acid or base catalyst as the intercepts on the ordinate at $f = 0$ and 1, respectively. This procedure yielded negligible k_{HB} values for all acids utilized in this range, an indication that the process exhibits almost no acid catalysis. On the other hand, general base catalysis was observed in the hydration of 1a in the pH range 1–7. The k_B values obtained for seven bases are given in Table 3. A Brønsted plot of these data yielded a β value of 0.47, which is again very close to the β value of $0 \cdot 4$ reported for the hydration of benzaldehydes.[20]

In order to gain more insight into the structure of the transition state for the hydration of the 2,2-dichloro-1-arylethanones (1), we applied the proton inventory technique to the study of the process in water and in THF–water mixtures.

As discussed above, the rate constants for the hydration (k_h) and dehydration (k_d) steps, and the equilibrium constants K_h, derived from the k_{obs} values with aid of equations (3), (4) and (5), are only approximate, since they rely on $a_M^{hydrate}$ values which cannot be measured directly.

Although this approximation might seem at first sight to invalidate all subsequent data treatment, it was found that the exact determination of these constants in all solvent mixtures was not essential for the rigorous application of the proton inventory technique.

In fact, the position of maximum absorbance, λ_{max}, in H_2O–D_2O mixtures for the ketones under study was found to be constant, within $0 \cdot 1$ nm, over the whole composition range. As shown by Bell and Critchlow,[12] this observation implies that the molar absorptivities of the ketone and of the hydrate are not affected by the atom fraction of deuterium in the solvent mixture. Further, when the absorbances of the equilibrium mixture in all solvent mixtures listed in Tables 4 and 5 were measured, we found that, within a precision of $0 \cdot 002$ absorbance unit, for a final reading of about $0 \cdot 700$, no change was observed on changing the atom fraction of deuterium from 0 to 1. Accordingly, since the absorptivities in equation (5) do not depend on the atom fraction of deuterium for all H_2O–D_2O and H_2O–D_2O–THF mixtures, it follows that the value of K_h, whatever it may be, is constant over the whole H_2O–D_2O composition range. We may then simply

Table 4. Observed rate constants for the hydration of 2,2-dichloro-1-arylethanones (1) in H_2O–D_2O mixtures at 25 °C

	$10^2 k_n^{obs}$ (s^{-1})			
n	**1a**	**1b**	**1c**	**1d**
0	6·65	6·74	9·21	29·4
0·1	5·75	5·88	7·94	26·6
0·2	5·30	5·23	7·49	24·1
0·3	4·93	4·66	7·20	21·9
0·4	4·22	4·10	6·12	20·2
0·5	3·84	3·83	5·78	17·3
0·6	3·42	3·17	5·14	16·2
0·7	2·99	2·81	4·80	13·8
0·8	2·80	2·56	4·56	12·5
0·9	2·51	2·21	4·20	11·2
1·0	2·38	1·74	3·97	10·6

Table 5. Observed rate constants for the hydration of 2,2-trichloro-1-(3-nitrophenyl)ethanone in THF–L_2O with different deuterium molar fractions n

	$10^3 k_n^{obs}$ (s^{-1})		
n	$L_2O = 10$ M	$L_2O = 20$ M	$L_2O = 30$ M
0	2·36	5·77	12·4
0·1	2·16	5·21	11·3
0·2	1·97	4·72	10·0
0·3	1·80	4·28	9·2
0·4	1·60	3·97	8·1
0·5	1·40	3·70	7·6
0·6	1·23	3·28	6·7
0·7	1·08	3·02	5·9
0·8	0·95	2·78	5·3
0·9	0·78	2·52	4·9
1·0	0·67	2·30	4·5

Table 3. Catalytic rate constants, k_B, for the base-catalysed hydration of 2,2-dichloro-1-phenylethanone (1a) in water in the pH range 1–7

Base	pK_b	k_B (l mol^{-1} s^{-1})
$Cl_2CHCO_2^-$	12·52	0·014
$NCCHCO_2^-$	11·55	0·028
$ClCH_2CO_2^-$	11·15	0·057
HCO_2^-	10·25	0·155
$CH_3CO_2^-$	9·24	0·285
HCO_3^-	7·63	3·090
HPO_4^{2-}	6·79	5·880

write the equality $K_n = K_0$, where the subscripts n and 0 refer to the equilibrium constant in H_2O–D_2O mixtures, with atom fractions of deuterium equal to n and 0 respectively.

The proton inventory technique is based on the analysis of the variations of rate/equilibrium constants in H_2O–D_2O mixtures, as the atom fraction of deuterium n is varied.[22] Relationships (7) and (8), known as the Gross–Butler equations, show the dependence of the equilibrium K_n and rate constants k_n in H_2O–D_2O mixtures on the value of n:

$$K_n = K_0 \left[\prod_i^\nu (1 - n + n\phi_i^P) \Big/ \prod_j^\nu (1 - n + n\phi_j^R) \right] \quad (7)$$

$$k_n = k_0 \left[\prod_i^\nu (1 - n + n\phi_i^T) \Big/ \prod_j^\nu (1 - n + n\phi_j^R) \right] \quad (8)$$

where $\phi_{i(j)}$ is the fractionation factor for every proton which exchanges with the solvent during the process under study and the superscripts R, P, and T refer to reagents, products and transition state, respectively.

For the hydration of ketones (1), the denominator of equation (7) equals unity because our reagent does not have any hydrogen atoms which exchange with the solvent during the hydration process. Since $K_n = K_0$, the numerator of equation (7) must also be unity, a conclusion which implies that the fractionation factor for the hydroxyl protons on the product hydrate is unity. This value is in complete agreement with tabulated values for fractionation factors of $C-O-L$ groups.[22]

We may now simplify equation (8), in our particular case, to equations (9) and (10), which apply to the hydration and dehydration rate constants, k_n^h and k_n^d, respectively:

$$k_n^h = k_0^h \prod_i^\nu (1 - n + n\phi_i^T) \quad (9)$$

$$k_n^d = k_0^d \prod_i^\nu (1 - n + n\phi_i^T) \quad (10)$$

Since the transition state for both processes, according to the principle of microscopic reversibility, is the same, we may combine the two equations to obtain

$$k_n^h + k_n^d = (k_0^h + k_0^d) \prod_i^\nu (1 - n + n\phi_i^T) \quad (11)$$

which may be written as equation (12), the observed rate constant k_n^{obs} being equal to $k_n^h + k_n^d$:

$$k_n^{obs} = k_0^{obs} \prod_i^\nu (1 - n + n\phi_i^T) \quad (12)$$

It is now clear that we do not need to determine k_h and k_d values in various H_2O–D_2O mixtures in order to obtain direct information regarding the number of protons involved in the transition state. It suffices to analyse the variation of k_n^{obs} in such mixtures with the molar fraction of deuterium oxide, n.

Values of these observed rate constants as n is varied

in H_2O–D_2O mixtures are given for substrates 1a–1d in Table 4. Table 5 lists the observed rate constants for the hydration of 2,2-trichloro-1-(3-nitrophenyl)ethanone in aqueous THF mixtures with variable L_2O molar concentrations.

In Figure 1 the data in Table 4 for substrate 1a are plotted and compared with theoretical curves for the Gross–Butler equation (12), calculated for various values of n. It is readily seen that our data fit best a theoretical curve which predicts a very large ('infinite') number of protons participating in the transition state of hydration. If all the protons contribute to a small and approximately equal extent to the overall isotopic effect, equation (12) may be written in the form[22]

$$\ln k_n^{obs} = \ln k_0^{obs} - n[m(1 - \phi^T)] \quad (13)$$

Accordingly, $\ln k_n^{obs}$ is expected to show a linear dependence on the molar fraction n, as the number of protons, m, involved is very large. Linearity tests for the data in Table 4, according to equation (13), yielded in all cases straight lines with correlation coefficients greater than 0.99.

Different results were obtained when the data in Table 5 were treated according to equation (12). As seen in Figure 2, the degrees of curvature obtained when k_n^{obs} values are plotted against n are different in the three aqueous THF solutions. Indeed, the data for solutions with 10, 20 and 30 M L_2O concentrations are consistent with 2, 8 and an infinite number of protons, respectively, participating in the transition state of the hydration reaction. A linearity test is provided by equation (14) for the case of two protons being involved in the transition state.[22]

$$(k_n^{obs}/k_0^{obs})^{1/2} = 1 + (\phi^T - 1)n \quad (14)$$

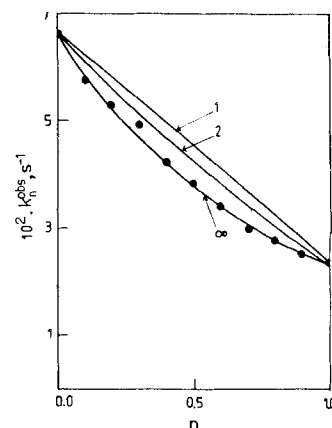Figure 1. Hydration of 2,2-dichloro-1-phenylethanone (1a) in H_2O–D_2O mixtures. Variation of the observed rate constant with the deuterium molar fraction, n. Theoretical curves drawn according to equation (12) for one, two and an infinite number of protons (ν) involved in the transition state
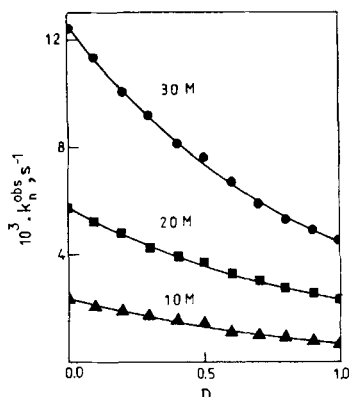
Figure 2. Hydration of 2,2-dichloro-1-(3-nitrophenyl)ethanone (**1d**) in THF–L_2O mixtures. Variations of the observed rate constants with the deuterium molar fraction, n, for $L_2O = 10$, 20 and 30 M. Theoretical Gross–Butler curves correspond to (▲) two, (■) eight and (●) an infinite number of protons (ν) intervening in the transition state

Figure 3 Plot of log k_{obs} vs log[H_2O] for the hydration of (●) 2,2-dichloro-1-(3-nitrophenyl)ethanone (**1d**) and (■) 2,2-dichloro-1-(4-bromophenyl)ethanone (**1c**) in H_2O–THF mixtures

Here again a straight line is obtained when $(k_n^{obs}/k_0^{obs})^{1/2}$ is plotted against n (figure not shown). The data for the 30 M aqueous solution were tested according to equation (13) and the straight line obtained, with a correlation coefficient greater than 0·99, confirmed the assignment of an infinite number of protons in this case.

The analysis of the data in THF–water solutions clearly indicates that the number of protons participating in the transition state for the hydration reaction of compounds **1** depends on the composition of the solvent.

We might then expect the same conclusion from the determination of the order of reaction in water as the solvent composition is changed. Unfortunately, in our case, this method is not as rigorous and reliable as the proton inventory technique, because the individual rate constants k_h and k_d cannot be determined precisely for each solvent mixture. Nevertheless, the plot shown in Figure 3, of log k_{obs} vs log [H_2O] in THF–water mixtures, shows a strong curvature, a result which points in the same direction as the proton inventory experiments.

The variation of the transition state structure for the hydration of **1** with the solvent composition may be interpreted as reflecting changes in the structure of the solvent mixture. While the activity of water remains approximately constant for THF solutions with 10, 20 and 30 M water,[23,24] the excess thermodynamic properties of the system change dramatically in the same range.[25,26] A plot of the excess enthalpy of the system vs the molar fraction of water in the mixture exhibits an S-shaped curve with a negative minimum value at a molar fraction of water of 0·8 and a maximum at a molar fraction of 0·1.[25,26] Between these two points the
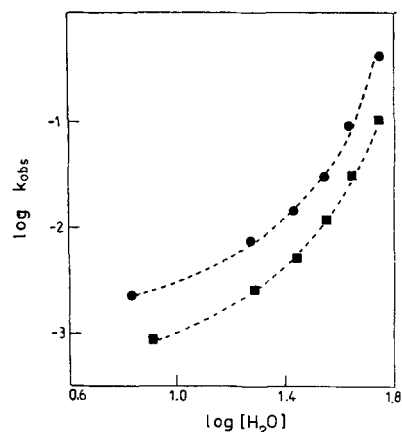
excess enthalpy increases almost linearly with the increase in the molar fraction of THF in the mixture. This linear increase has been explained by Glew and co-workers in terms of the gradual replacement of H_2O–H_2O by H_2O–THF hydrogen bonds,[26] an explanation that has been supported by NMR experiments.[26-28]

Glew and co-workers' rationalization, applied to the same range of water concentration in which we carried out our experiments, is entirely consistent with our findings. In pure water, or in water-rich solvent mixtures, water-to-water hydrogen bonds predominate and a very large number of protons participate in the transition state of hydration, represented by the open structure I. As this homogeneous, infinite structure is disrupted by the addition of the organic co-solvent, the number of protons participating in the transition state gradually decreases, until it reaches the minimum value of 2, which corresponds to the cyclic structure II.
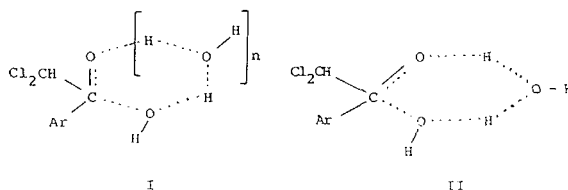
Hence our results show that hydration reactions in mixed solvents have a variable transition-state structure, in which the number of intervening protons is a function of the structure of the solvent system.

This statement probably applies to other *gem*-polyhalogenoketones, such as 2,2,2-trichloro-1-arylethanones, the hydration of which is currently being investigated.

EXPERIMENTAL

Melting points were obtained with a Koffler hot-stage apparatus and were not corrected. Chromatographic analyses were carried out with a CG-370 instrument.

The following compounds were prepared by methods described previously: 2,2-dichloro-1-phenylethanone (**1a**), b.p. 134–136 °C (10 mmHg), lit.[29] b.p. 138–140 °C (13 mmHg); 2,2-dichloro-1-(4-methyl-phenyl)ethanone (**1b**), m.p. 54–55 °C, lit.[30] m.p. 54.5–55.3 °C; 2,2-dichloro-1-(4-bromophenyl)ethanone (**1c**), m.p. 61–62 °C, lit.[30] m.p. 61·6–62 °C; 2,2-dichloro-1-(3-nitrophenyl)ethanone (**1d**), m.p. 56–57 °C lit[31] m.p. 57–58 °C.

Aqueous solutions were prepared from deionized, doubly distilled water. Deuterium oxide with a minimum isotopic purity of 99·96 atom-% of deuterium was purchased from Aldrich. The concentration of HCl and DCl solutions were determined by titration. Molar fractions of deuterium were determined by neutron activation analysis.

The observed reaction rates were determined spectroscopically with a Shimadzu UV-210A spectrophotometer equipped with thermostated ($\pm 0 \cdot 1$ °C) water-jacketed cell compartments. In a typical run, 15 μl of a 10^{-2} M stock solution of the substrate in dry THF were added to 3 ml of water or the aqueous solvent mixture in the cell, and the absorbance (A) decay was recorded simultaneously at 254, 264, 267 and 247 nm for **1a**, **1b**, **1c** and **1d**, respectively. The linear plots ($r > 0 \cdot 99$) of $\ln(A_t - A_\infty)$ vs time yielded pseudo-first-order rate constants with errors smaller than 3%.

The reversibility of all reactions was established by chromatographic analysis of the products. After the equilibrium between the ketone and its hydrate had been attained, the samples were injected into the gas chromatograph. In every case only one peak was detected, corresponding to the original 2,2-dichloro-1-arylethanone (**1**).

REFERENCES

1. R. P. Bell, in *Advances in Physical Organic Chemistry*, edited by V. Gold, Vol. 4, pp. 1–29. Academic Press, London (1966).
2. R. Stewart and R. Van der Linden, *Can. J. Chem.* **38**, 399 (1960).
3. R. Stewart and J. D. Van Dyke, *Can. J. Chem.* **48**, 3961 (1970).
4. R. S. McDonald, C. K. Teo and R. Stewart, *J. Chem. Soc., Perkin Trans. 2* 297 (1983).
5. C. D. Ritchie, *J. Am. Chem. Soc.* **106**, 7187 (1984)
6. M. P. Jansen and T. T. Tidwell, *J. Fluorine Chem.* **20**, 791 (1982).
7. H. J. Buschmann, H. H. Fueldner and W. Knoche, *Ber. Bunsenges. Phys. Chem.* **84**, 41 (1980).
8. U. Haldna, H. Kuura and L. Erreline, *Reakts. Sposobon. Org. Soedin. Tartu* **4**, 678 (1967); *Chem. Abstr.* **69**, 100218v (1968).
9. R. P. Bell and A. O. McDougall, *Trans. Faraday Soc.* **56**, 1281 (1960)
10. R. P. Bell and M. P. Jansen, *Proc. R. Soc. London, Ser. A* **261**, 38 (1961).
11. R. P. Bell, J. P. Millington and J. M. Pink, *Proc. R. Soc. London, Ser. A* **303**, 1 (1968).
12. R. P. Bell and J. E. Critchlow, *Proc. R. Soc. London, Ser. A* **325**, 35 (1971).
13. E. H. Cordes and M. Childers, *J. Org. Chem.* **29**, 968 (1964).
14. O. A. El-Seoud, M. J. da Silva, L. P. Barbur and A. Martins, *J. Chem. Soc., Perkin Trans. 2* 331 (1978).
15. O. A. El-Seoud and M. J. da Silva, *J. Chem. Soc., Perkin Trans.* 127 (1980).
16. R. A. Rebelo, M. C. Rezende, F. Nome and C. Zucco, *Synth. Commun.* **17**, 1741 (1987).
17. M. Uieara, C. Zucco, D. Zanette, M. C. Rezende and F. Nome, *J. Chem. Soc., Perkin Trans. 2* 175 (1987).
18. C. Zucco, C. F. Lima, M. C. Rezende, J. F. Vianna and F. Nome, *J. Org. Chem.* **52**, 5356 (1987).
19. H. S. Lins, F. Nome, I. de Souza and M. C. Rezende, *J. Chem. Soc., Perkin Trans. 2* 1521 (1984).
20. R. A. McClelland and M. Coe, *J. Am. Chem. Soc.* **105**, 2718 (1983).
21. E. B. Ayres and C. R. Hauser, *J. Am. Chem. Soc.* **65**, 1095 (1943).
22. K. B. J. Showen, in *Transition States of Biochemical Processes*, edited by R. D. Gandour and R. L. Showen, p. 225. Plenum Press, New York (1978).
23. K. L. Pinder, *J. Chem. Eng. Data* **18**, 275 (1973).
24. C. Treiner, J. Bocquet and M. Chemla, *J. Phys. Chim.* 72 (1973).
25. J. Matous, J. P. Novak, J. Sobr and J. Pick, *Collect Czech. Chem. Commun.* **37**, 2653 (1972).
26. D. N. Glew and H. Watts, *Can. J. Chem.* **51**, 1933, (1973)
27. D. N. Glew, H. D. Mak and N. S. Rath. *J. Chem. Soc.* 264 (1968).
28. D. N. Glew, H. D. Mak and N. S. Rath. *Can. J. Chem.* **45**, 3059 (1967).
29. *Beilsteins Handbuch der Organischen Chemie*, Vol. 7, p. 220. (1925).
30. R. N. McDonald and R. C. Cousins, *J. Org. Chem.* **45**, 2976 (1980).
31. *Beilsteins Handbuch der Organischen Chemie*, Vol. 7, Part II, p. 224. (1948).