Table IX. Calculation of the Differential Change in Internal Enthalpy, $\delta_o\Delta H_i$, Relative to 2-Pyridone as a Reference Catalyst[a]

Catalyst	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\delta_o\Delta H^{\ddagger}$	$\delta_o\Delta S^{\ddagger}$	$\delta_o\Delta H_e$	$\delta_o\Delta H_i$	K_2, M^{-1}[b]
Picric acid	12.7	−28.4	−0.5	−5.7	−1.6	1.1	1.8
2-Aminopyridine	13.2	−24.6	0	−1.9	−0.5	0.5	2.2
Pyrazole	13.2	−30.2	0	−7.5	−2.1	2.1	7.5
2-Pyridone (ref)	13.2	−22.7	0	0	0	0.0	41
Benzoic acid	13.2	−21.4	0	1.3	0.4	−0.4	82
Trichloroacetic acid	(14.1)	(−15.4)	(0.9)	(7.3)	(2.0)	(−1.1)	
Benzenephosphinic acid	14.9	−8.8	1.7	13.9	3.9	−2.2	(560)[c]
Diphenyl phosphate	14.1	−10.8	0.9	11.9	3.3	−2.4	(1050)[c]

[a] Enthalpies in kcal/mol and entropies in gibbs/mol at a standard state of 1 mol/l. at 25° and 1 atm. [b] At 25°. [c] These values are probably too large.

Experimental rate constants for the mutarotation of tetramethylglucose in five different solvent systems are summarized in Table IV. Based on this table, we conclude the following: (a) Diphenyl phosphate, benzene-phosphinic acid, benzenephosphonic acid, and toluene-sulfonic acid monohydrate possess comparable catalytic activities in the solvent systems examined; all probably act in a similar fashion. (b) All of the tetraalkyl-ammonium salts act as general base catalysts in acetonitrile (the bisulfate ion, with a $pK_{acetonitrile}$ of 25.9, is known to be a strong base;[23] the dihydrogen phosphate and dihydrogen arsenate ions should be even stronger bases[24]). (c) It is not possible to make a distinction between the various types of catalytic mechanisms on the basis of changes in catalytic activity as a function of solvent. (d) The more polar the solvent, or the better it is at hydrogen bonding with the catalyst, the lower the rate constant. We hoped that the tautomeric catalysts would all behave in a similar fashion as a function of solvent. Their common behavior could then be distinguished from that of general acid or general base catalysis. Unfortunately, we were not able to make a distinction between the various types of catalytic mechanisms. At best, therefore, the data in Table IV supplement the rate constant and activation parameter determinations in benzene and also provide information of possible synthetic utility.

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(24) M. K. Chantooni, Jr., private communication.

Acid-Catalyzed and Base-Catalyzed Hydration of β-Oxy-α,β-unsaturated Ketones[1,2]

L. R. Fedor,* N. C. De, and S. K. Gurwara

Contribution from the Department of Medicinal Chemistry, School of Pharmacy, State University of New York at Buffalo, Buffalo, New York 14214. Received July 25, 1972

Abstract: Hydrations of 20 β-oxy-α,β-unsaturated ketones to β-keto aldehydes or β-diketones in acidic solution are catalyzed only by hydronium ions; general acid catalysis is not observed. This result coupled with that of insensitivity of rates of hydration to structural changes in the ketones is offered in support of a mechanism involving equilibrium protonation of the carbonyl oxygen atom followed by rate-determining addition of water to the β carbon of the cation; decomposition of the hemiacetal or β elimination of the oxy group gives products. Hydrations of 4-(para-substituted phenoxy)-3-buten-2-ones to phenols and 3-ketobutanal in alkaline solution are postulated to occur *via* rate-determining Michael addition of hydroxide ion to the β-carbon atom followed by ketonization of the enolate anion concerted with elimination of para-substituted phenoxides.

Earlier work of Noyce, *et al.*, on the acid-catalyzed hydration of α,β-unsaturated carbonyl compounds, summarized in a paper on the hydration of phenylbenzoylacetylenes,[3] established that unsaturated acids undergo hydration *via* rate-determining protonation of the olefin bond, as occurs for para-substituted styrenes,[4] while unsaturated ketones undergo hydration *via* rate-determining ketonization of the enediol formed by addition of water to the β-carbon atom of the carbonyl-protonated substrate or *via* rate-determining protonation of the olefin bond when β-carbonium ion stabilization is sufficiently great.[5] Previously, 4-methoxy-3-buten-2-one, formally a vinyl ether for which the A-SE2 mechanism is established,[6] and an

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(5) D. S. Noyce and W. L. Reed, *ibid.*, 80, 5539 (1958).
(6) A. J. Kresge, H. L. Chen, Y. Chiang, E. Murrill, M. A. Payne, and D. S. Sagatys, *ibid.*, 93, 413 (1971), and references therein.

unsaturated ketone, was found to undergo specific acid-catalyzed hydration to give 3-ketobutanal.[7] The kinetics results were interpreted using a modified Noyce ketonization mechanism whereby rapid protonation of the carbonyl group was followed by rate determining Michael addition of water to the β-carbon atom of the cation, although the less likely olefin protonation mechanism was not ruled out. The present study reports kinetics results of the hydration of substituted β-oxy-α,β-unsaturated ketones of diverse structure (eq 1, Table I), which are capable of undergoing hydration via diverse mechanisms.

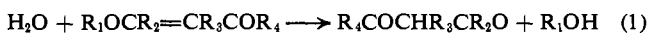$$H_2O + R_1OCR_2{=}CR_3COR_4 \longrightarrow R_4COCHR_3CR_2O + R_1OH \quad (1)$$

Table I. β-Oxy-α,β-unsaturated Ketones with General Structure $R_1OCR_2{=}CR_3COR_4$

Compd	R_1	R_2	R_3	R_4
1	C_6H_5	H	H	CH_3
2	$p\text{-}CH_3C_6H_4$	H	H	CH_3
3	$p\text{-}(CH_3)_3CC_6H_4$	H	H	CH_3
4	$p\text{-}CH_3OC_6H_4$	H	H	CH_3
5	$p\text{-}ClC_6H_4$	H	H	CH_3
6	$p\text{-}CNC_6H_4$	H	H	CH_3
7	$p\text{-}NO_2C_6H_4$	H	H	CH_3
9	CH_3	H	H	C_6H_5
10	CH_3	H	H	$4'\text{-}CH_3C_6H_4$
11	CH_3	H	H	$4'\text{-}ClC_6H_4$
12	CH_3	H	H	$4'\text{-}CH_3OC_6H_4$
14	CH_3	H	H	$4'\text{-}(CH_3)_2NC_6H_4$
16	CH_3	H	H	$p\text{-}NO_2C_6H_4$
17	CH_3CO	H	H	CH_3
18	$(CH_3)_3CCO$	H	H	CH_3
20	CH_3CO	H	H	$4'\text{-}CH_3OC_6H_4$
21	CH_3	H	CH_3	CH_3
22	CH_3	H	H	$C(CH_3)_3$
23	CH_3	H	H	$HC(CH_3)_2$
24	CH_3	CH_3	H	CH_3

Experimental Section[8]

Reagents and Compounds. Certified ACS grade inorganic salts were purchased from Fisher Scientific Co. 3-Butyn-2-one was purchased from Farchan Research Laboratories. Phenols were purchased from Aldrich Chemical Co., Inc. Triethylamine, N-ethylmorpholine, and tetramethylammonium chloride were supplied by Eastman Organic Chemials. Sodium lauryl sulfate was supplied by Ruger Chemicals. Deuterium chloride and deuterium oxide were purchased from Diaprep Inc. All the solvents were Fisher supplied and were dried and distilled before use. Analytical data for new compounds are provided in Table II. Spectral data were in agreement with structural assignments. The 4-(para-substituted phenoxy)-3-buten-2-ones (1-8) were synthesized using a modification of a published procedure.[9] Para-substituted phenols (100 mmol) were added to a 20% molar excess of 3-butyn-2-one in tetrahydrofuran in the presence of 0.2-0.4 ml of triethylamine. The progress of the reactions, carried out at 60-70° for 16-36 hr, was monitored using nmr spectroscopy. Mixtures of cis and trans isomers were detected during the courses of the reactions; $J = 6$ Hz and 12 Hz, respectively, for vinyl protons. Prolonged heating during the reactions converted cis isomers to trans isomers. 4-(p-Nitrophenoxy)-3-buten-2-one-d_5 was similarly synthesized from nitrophenol-d_1 and 3-butyn-2-one-d_1 (from 3-butyn-2-one equilibrated in D_2O) in refluxing (3 hr) tetrahydrofuran-D_2O (1:1) in the presence of 0.5 ml of N-ethylmorpholine. For 1-7, α-vinyl H had δ 5.75-6.1; β-vinyl H had δ 7.6-7.75 (CDCl$_3$, TMS). 3-Methoxy-

4'-substituted-acrylophenones (9-12, 14, and 16) were synthesized by literature procedures[10,11] as were p-N,N-dimethylaminobenzoylacetaldehyde and p-nitrobenzoylacetaldehyde (mp 104-106°, lit.[12] 98-99).[12] 3-Methoxyacrylophenone had bp 112-115° (2 mm), lit.[10] 112° (1.8 mm). For 9-12, 14, and 16, α-vinyl H had δ 6.28-6.4; β-vinyl H had δ 7.75-7.9 (CDCl$_3$, TMS). Sodium formylacetone and sodium formyl-p-methoxyacetophenone were prepared by the method of Mariella.[13] 4-Acetoxy- and 4-pivaloyloxy-3-buten-2-one (17 and 18) were synthesized from equimolar quantities of sodium formylacetone, acyl chloride, and pyridine in benzene (12 hr, 25°). 3-Acetoxy-4'-methoxyacrylophenone was similarly synthesized. 3-Hydroxy-4'-methoxyacrylophenone was prepared by acidification with aqueous acetic acid of the sodium salt. 2,2-Dimethyl-5-methoxy-4-penten-3-one (22), bp 63° (2.5 mm), lit.[14] 61° (3 mm), and 2-methyl-5-methoxy-4-penten-3-one (23), bp 70-72° (10 mm), lit.[14] 61-62° (3.5 mm), were synthesized by the method of Royals.[14] 2-Methyl-3-ketobutyraldehyde, mp 68-71°, lit.[15] 73°, prepared by the method of Diels,[15] was heated at reflux with K_2CO_3 and dimethyl sulfate in acetone to give 3-methyl-4-methoxy-3-buten-2-one (21). 4-Methoxy-3-penten-2-one (24), bp 56-58° (8 mm), lit.[16] 54.5-56.5° (8 mm), was prepared by the method of Chang.[16]

Apparatus. Gilford Model 2000 or 2400 and Beckman Model DB-G spectrophotometers were used for the collection of rate data and for scanning reactions. Temperature was maintained in the cuvettes by circulating water of constant temperature from a Tamson T9 bath through thermospacers. pH was measured using a Radiometer PHM22 pH meter with a PHA 630 P scale expander and a GK 2021 B combination electrode. The nmr spectra were taken on a Varian A-60 instrument with tetramethylsilane as internal standard; proton signals are reported in δ values. Melting points were taken in open capillary tubes using a Mel-Temp apparatus and are uncorrected. The infrared spectra were taken on a Perkin-Elmer Model 137 or a Beckman IR-8 spectrophotometer. The titrations were done using a Radiometer Autoburette ABU 11 in combination with pH Meter 26. Calculations were performed on a Hewlett-Packard 9100 A calculator using the Least Squares (09100-70803) and the Mean and Standard Deviation (09100-70801) programs from the program library provided.

Kinetics. The courses of the reactions of β-oxy-α,β-unsaturated ketones were monitored at the following wavelengths (compd, λ nm): acid-catalyzed reactions, 1, 2, 260; 3, 4, 6, 265; 5, 22, 24, 262; 7, 8, 295; 9, 21, 255; 10, 283; 11, 281; 12, 20, 302; 14, 352.5; 16, 300; 17, 18, 247; base-catalyzed reactions, 1, 2, 285; 4, 282; 5, 290; 7, 8, 410. All reactions were carried out in water at $30 \pm 0.1°$. The calculated ionic strength was adjusted with potassium chloride, lithium chloride, potassium chlorate, or ammonium chloride. The pH of each solution was determined before and after all runs and pH remained constant (± 0.02 pH unit) for all runs. Cuvettes (3 ml) were filled to the stopper level with the appropriate solutions, capped, and allowed to come to thermal equilibrium (30-40 min). Reactions were started by adding a known amount of substrate in acetonitrile or methanol (10^{-4}-10^{-5} M) via a micropipet to the appropriate solution in the cuvette. Reactions were carried out under pseudo-first-order conditions and pseudo-first-order rate constants were obtained by multiplying slopes of plots of log ((OD_i − OD_∞)/(OD_i − OD_∞)) or log ((OD_∞ − OD_0)/(OD_∞ − OD_i)) vs. time by 2.303. Reactions were monitored to completion. Pseudo-first-order plots were generally linear to at least 2 to 3 lives. For reactions carried out in dioxane-water 80-20 (v/v), essentially the same conditions were used as for reactions in water solution. Reactions in sodium lauryl sulfate solutions were carried out at a constant pH of 2.70 using 0.02 M formic acid-potassium formate buffer; ionic strength was adjusted to 0.1 M using tetramethylammonium chloride.

The pK_a of p-tert-butylphenol, determined spectrophotometrically,[17] is 10.08. The pK_a of dimethylaminoethanol (DMAE),

(7) L. R. Fedor and J. McLaughlin, ibid., 91, 3594 (1969).

(8) In the interests of conserving journal space, details of the preparations of compounds were deleted in revision. We suggest that those interested in such details consult the doctoral theses which are on microfilm obtainable from University Microfilms, Inc., Ann Arbor, Mich.

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Table II. β-Oxy-α,β-unsaturated Ketones

Compd[a]	Mp or (bp, mm), °C	% yield	Calcd % C	Calcd % H	Found[b] % C	Found[b] % H	Recryst solv
1	90 (1.2)	91.4	74.06	6.21	74.11	6.22	
2	85 (0.1)	86.4	74.97	6.87	74.88	6.88	
3	130 (5)	88.4	77.03	8.31	77.21	8.39	
4	110 (0.8)	92.2	68.73	6.29	68.48	6.31	
5	68–70	72.4	61.08	4.61 (Cl, 18.03)	61.23	4.59 (Cl, 18.23)	THF–hexane
6	79–81	90.8	70.58	4.85 (N, 7.48)	70.72	4.89 (N, 7.45)	MeOH
7	69–71	90.9	57.97	4.38 (N, 6.76)	58.24	4.55 (N, 6.63)	MeOH–H₂O
8	69–71	84	56.59	6.65 (N, 6.60)	56.81	6.44 (N, 6.47)	Ether
10	110 (0.4)	60	75.0	6.82	74.88	6.97	
11	63–64	25	61.0	4.58	60.94	4.61	Hexane
12	160–161 (2.5)	43	68.40	6.18	68.27	6.30	
13	115–116	36	69.11	6.81	69.36	6.88	Ether
14	94–96	80	70.24	7.32	70.38	7.34	H₂O
16	128–131	75	57.97	4.34 (N, 6.76)	57.94	4.68 (N, 6.69)	Hexane
17	40 (0.5)	58	56.25	6.25	56.46	6.42	
18	30–32	80	63.59	8.24	63.78	8.39	MeOH
19	100.5–102.5	35	63.45	5.45	63.36	5.67	Ether
20	50–52	56	67.42	5.62	67.32	5.53	Ether
21	83–86 (10)	60	63.16	8.77	62.93	9.01	

[a] Table I. [b] The elemental analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

determined by potentiometeric titrations,[18] is 9.33 ± 0.02; pK_D = 9.84 ± 0.09. pD was obtained by adding 0.39 to the pH meter reading.[19]

Product Analysis. Several workers[20–23] earlier showed that the hydration of alkyl vinyl ethers in acid solution gives alkanols and aldehydes (ketones). Further, the reaction proceeds via oxygen-vinyl carbon bond cleavage.[24] Fedor and McLaughlin[7] using nmr techniques, as well as product isolation, showed that 3-ketobutanal and methanol are the products from the acid-catalyzed hydration of 4-methoxy-3-buten-2-one. By analogy, hydration of β-oxy-α,β-unsaturated ketones gives substituted phenols, alcohols, or carboxylic acids and β-keto aldehydes or β-diketones as was confirmed by uv-spectroscopic comparisons of reaction solutions containing products with solutions containing authentic, presumed products.

Hydration of 4-methoxy-3-buten-2-one in 0.1 M HCl gave methanol and 3-ketobutanal.[7] The molar extinction coefficient (ε) of aldehyde is 980 at λmax 252 nm. For p-methoxyphenol in 0.1 M HCl ε is 144 at 252 nm. The spectrum of the product from hydrolysis of 4-(p-anisoxy)-3-buten-2-one (4) in 0.1 M HCl is in accord with the production of anisole and 3-ketobutanal with ε 1098 at 252 nm. This value may be compared with the theoretical ε 1124 which corresponds to a quantitative product yield of 98%.

Hydration of 4-methoxy-3-buten-2-one in 0.1 M HCl gave methanol and 3-ketobutanal. The molar extinction coefficient (ε) of 3-ketobutanal at 280 nm is 16,583 in 0.1 M KOH. For phenol in 0.1 M KOH ε is 950 at 280 nm. The spectra of the products from hydration of 4-phenoxy-3-buten-2-one (1) in 0.1 M KOH are in accord with the production of phenol and 3-ketobutanal with ε 16,800 at 280 mμ. The ε may be compared with the theoretical ε, 17,533, which corresponds to a quantitative yield of 95.8%.

3-Methoxy-4'-methoxyacrylophenone (12), 0.3389 g (0.0018 mol), was dissolved in 10 ml of dioxane. To the solution was added 5.0 ml of 1.0 M hydrochloric acid and the mixture was left at room temperature for 22 hr. The solution was extracted with ether. The ethereal extract was washed with water, dried (MgSO₄), and concentrated in vacuo to give 0.26 g brownish liquid: nmr CDCl₃ 2.50 (s, impurities), 3.70 (s, dioxane), 3.80 (s, 3, Ar OCH₃), 6.10 (d, 1, J = 4 Hz, COCH), 8.15 (d, 1, J = 4 Hz, HO–CH, 6.85 (d, 2,

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J = 9 Hz, aromatic), 7.85 (d, 2, J = 9 Hz, aromatic), no OH band; ir (neat) 1600 cm⁻¹ (broad); uv max (water) 281 nm. The spectral data are identical with those for p-methoxybenzoylacetaldehyde. From a calibrated capillary tube 1 drop of 3-methoxy-4'-methoxyacrylophenone (12) in methanol was added to 3.0 ml of 1.0 M HCl solution, final concentration of 12 = 3.8 × 10⁻⁵ M, and scanned three times at 10-min intervals in the DB-G spectrophotometer using 1.0 M HCl solution as a reference. The final absorbance maximum was not changed after 4 hr. The yield of 4-methoxybenzoylacetaldehyde (ε 7842, 281.5 nm) formed on hydrolysis of 12 was 92 ± 5%.

Results

In dilute acid solutions the hydrations of β-oxy-α,β-unsaturated ketones obey the rate law of eq 2. The

$$\text{rate} = k_{obsd}[\text{S}] \qquad k_{obsd} = k_H a_H \qquad (2)$$

second-order rate constants, k_H, were obtained from slopes of plots (not shown) of k_{obsd} vs. a_H (Table III). For 14 rate constants for hydration of the neutral and protonated form of the compound were determined using eq 3. Thus, a plot of $k_{obsd} f$ values wherein

$$k_{obsd} f = k_H^+ a_H + k_H K_a \qquad (3)$$

$f = (K_a + a_H)/a_H$ vs. a_H values gave as slope the second-order rate constant for acid-catalyzed hydration of 14H⁺ and intercept the product of the second-order rate constant for acid-catalyzed hydration of 14 and K_a. The kinetically determined pK_a = 2.3 was used to evaluate the rate constant for hydration of 14.[25] Hydrations of 4, 10, 16, 18, 20, and 24 catalyzed by DCl–D₂O are about 2.5 times faster than the analogous reactions in HCl–H₂O (Table III). Hydration of 4 in formate buffer ((HA)/(A⁻) = 10, pH 2.41, six concentrations, 0.01–0.10 M) gave k_{obsd} = 0.069 ± 0.001 min⁻¹; the calculated value ($k_H a_H$) is 0.069 min⁻¹. Compounds 12 and 24 were similarly indifferent toward formate buffers at pH 3.5. The influence of para substituents on the

(25) Acid-catalyzed hydration of 5 was favored over the kinetically equivalent spontaneous hydration of 5H⁺ because spontaneous reactions were not detected for the other compounds of this study.

Table III. Second-Order Rate Constants for Acid-Catalyzed Hydration of β-Oxy-α,β-unsaturated Ketones[a]

Compd	k_H, M^{-1} min^{-1}	No. of k_{obsd}	pH (pD) range	k_D/k_H
1	13.80 ± 0.28[b]	5	1.20–2.09	
1	1.44 ± 0.04[e]	3	1.13–1.65	
2	17.08 ± 0.24[b]	5	1.20–2.09	
2	1.48 ± 0.07[e]	3	1.13–1.65	
3	13.53 ± 1.83[b]	5	1.01–2.03	
4	17.61 ± 0.39[b]	5	1.20–2.09	
4	48.17 ± 0.65[d]	4	1.09–2.14	2.7
4	1.93 ± 0.07[e]	3	1.13–1.65	
5	12.43 ± 0.27[b]	5	1.20–2.09	
5	1.12 ± 0.05[e]	3	1.13–1.65	
6	5.95 ± 0.28[b]	6	1.20–2.09	
7	4.74 ± 0.16[b]	6	1.20–2.09	
7	0.83 ± 0.04[e]	3	1.13–1.65	
8	5.56 ± 0.17[b]	6	1.06–2.04	
9	28.4 ± 0.67	6	1.38–2.37	
10	24.6 ± 2.4	4	1.73–2.32	2.4
10	58.7 ± 2.7[c]	4	1.80–2.34	
11	27.2 ± 1.9	9	1.91–2.13	
12	14.8 ± 1.3	13	1.60–2.46	
14	8.3	10	2.08–2.82	
14H$^+$	27.1 ± 1.5	10	2.08–2.82	
16	35.3 ± 5.8	7	2.08–3.11	
16	96.4 ± 5.6[c]	5	2.08–2.62	2.7
17	1.16 ± 0.09	9	0.92–1.67	
18	1.78 ± 0.12	9	1.15–1.78	2.6
18	4.66 ± 0.09[c]	2	2.26	
20	0.31 ± 0.02	6	0.03–1	2.6
20	0.79 ± 0.07[c]	2	1.1	
23	38.7 ± 2.98	6	2.25–2.68	
22	19.9 ± 0.68	5	1.75–2.10	
21	10.94 ± 1.72	8	1.42–2.30	
24	11.12 ± 0.72	9	1.30–3.06	
24	29[c]	1	2.95	2.6
25	43.5[7]			

[a] Solvent = H$_2$O, μ = 1.0 M with KCl, t = 30° unless otherwise specified. Values for second-order rate constants and their standard deviations were calculated using a Hewlett-Packard Calculator and the Least Squares Program in the Program Library. [b] Solvent = H$_2$O, μ = 0.1 M (KCl), t = 30°. [c] Solvent = D$_2$O, μ = 1.0 M (KCl), t = 30°. [d] Solvent = D$_2$O, μ = 0.1 M (KCl), t = 30°. [e] Solvent = dioxane–H$_2$O (80:20 v/v), μ = 0.1 M (KCl), t = 30°.

rates of acid-catalyzed hydration of **9, 10, 11, 12, 14, 14H$^+$**, and **16** is given by ρ^+ = 0.26 ± 0.05 based on the σ^+ values of Brown and Okamoto.[26] The value of σ for $(CH_3)_3N^+$ was used for $(CH_3)_2NH^+$. For **1–7**, ρ^+ = −0.18 + 0.01 using ρ^* values derived in the usual way from ionization constants of phenols.[27] For **22, 23**, and 4-methoxy-3-buten-2-one (**25**) log k_H values are related to the aliphatic electronic and steric substituent constants by eq 4.

$$\log k_H = -0.54\sigma^* + 0.33E_s + 1.64 \, (r = 1.00) \quad (4)$$

Rates of acid catalyzed hydration of **1, 2, 4, 5,** and **7** are depressed *ca.* tenfold in dioxane–water (80:20 v/v) (Table III).

Reactions of **1** and **4** in dilute acidic solution are virtually unaffected by changes in ionic strength to ~0.4 M salt concentrations using LiCl, KCl, KClO$_4$, and NH$_4$Cl. At pH 1.47, tetramethylammonium chloride "catalyzed" hydration of **1** with a second-order rate constant of 0.19 M^{-1} min^{-1}. Reactions of **1, 4,** and **7** in 0.02 M formate buffer containing sodium lauryl sulfate obeyed the rate law of eq 5. The constants evaluated

(26) H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).

(27) Reference 17, p 133.

$$\text{rate}/[\textbf{1, 4, 7,}] = k_{obsd} = k_H a_H + k_1[\text{SLS}]^2/$$
$$(K + [\text{SLS}]^2) \quad (5)$$

from double reciprocal plots are (compound, k_1 (min^{-1}), $K(M)$, r): **1**, 0.216, 1.4 × 10^{-5}, 0.997; **4**, 0.221, 1.1 × 10^{-5}, 0.991; **7**, 0.074, 3.8 × 10^{-5}, 0.997. For these reactions, ρ^* (k_1) = −0.16 ± 0.01; the coefficient of π, the lipophilicity constant,[28] is 0.87 ± 0.00 and was obtained by plotting log K *vs* π.

Hydrations of **1, 2, 4, 5, 7,** and **8** in dilute potassium hydroxide solutions are first order in hydroxide ion concentration. Second-order rate constants (Table IV) were obtained from slopes of plots of k_{obsd} *vs.* a_{OH}. For these reactions ρ^* = 0.1 ± 0.02.

Table IV. Second-Order Rate Constants for Base-Catalyzed Hydration of 4-(Para-substituted phenoxy)-3-buten-2-ones in Aqueous Potassium Hydroxide Solution[a]

Compd	K_{OH}, M^{-1} min^{-1}	No. of k_{obsd}	pH (pD) range[b] ±0.02
1	14.57 ± 0.71	6	11.72–12.65
2	14.19 ± 0.75	6	11.72–12.65
4	14.04 ± 0.28	5	11.72–12.65
5	19.39 ± 0.60	5	11.72–12.65
7	28.12 ± 1.12	5	11.72–12.65
8	39.48 ± 2.17	5	11.72–12.55
7	29.86 ± 2.51[c]	3	12.34–12.71

[a] μ = 0.1 M (KCl), t = 30.0 ± 0.1°. [b] Saturated solution of Ca(OH)$_2$ (pH 12.29) was used to standardize the pH meter, KOH = 0.01–0.1 M. [c] Reaction carried out in NaOD–D$_2$O to give k_{OD} M^{-1} min^{-1}.

Hydration of **7** is catalyzed by N,N-dimethylaminoethanol (DMAE). Slopes of linear plots of k_{obsd} *vs.* [DMAE]$_{total}$ were divided by $K_a/(K_a + a_H)$ to give the second-order rate constant 0.22 ± 0.03 M^{-1} min^{-1} for DMAE catalysis (0.01–0.1 M DMAE, 18 k_{obsd}, pH 9.15, 9.32, 10.27). In D$_2$O, k_2 = 0.26 M^{-1} min^{-1} (3 k_{obsd}, pD = 9.97). Hydration of **8** (pentadeuterated **7**) in H$_2$O catalyzed by DMAE gave k_2 = 0.66 M^{-1} min^{-1} (6 k_{obsd}, pH 9.18) from which k_2 (**8**)/k_2 (**7**) = 3. Potassium hydroxide catalyzed hydration of butynone monitored at 280 nm is first-order in hydroxide ion concentration and gave k_{OH} = 2.66 ± 0.21 M^{-1} min^{-1} (6 k_{obsd}, 0.01–0.1 M KOH, pOH 1.06–2.04, μ = 0.1 M (KCl).
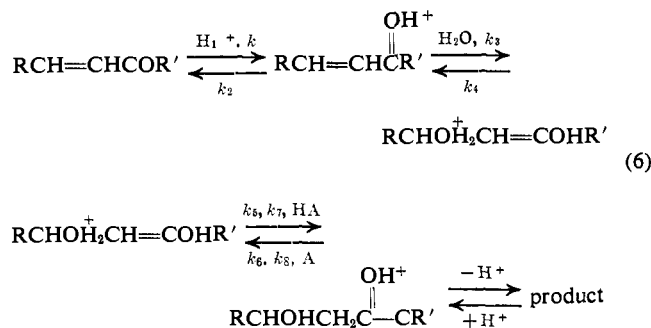
Discussion

Acid catalyzed hydrations of β-oxy-α,β-unsaturated ketones to β-keto aldehydes (β-diketones) are characterized by (1) a deuterium solvent isotope effect, k_D/k_H ~ 2.5, (2) specific acid catalysis, (3) insensitivity toward para substituents in aryl substituted derivatives, (4) a fourfold *decrease* in reactivity on β-CH$_3$ substitution, and (5) a tenfold decrease in reactivity when the solvent is changed from water to dioxane–water (4:1 v/v). Three readily identifiable reaction mechanisms which may be examined in the light of these results are (1) rate determining protonation of the olefin bond followed by reaction of the β-carbonium ion with water, etc., as occurs with vinyl ethers,[6] (2) preequilibrium protonation of the olefin bond followed by rate-determining reaction of the β-carbonium ion with water, etc.,[29] and

(28) T. Fujita, J. Iwasa, and C. Hansch, *J. Amer. Chem. Soc.*, **86**, 5157 (1964).

(29) A. J. Kresge and H. J. Chen, *ibid.*, **94**, 2818 (1972).

(3) preequilibrium protonation of the carbonyl oxygen atom followed by rate-determining reaction of the cation at the β-carbon atom with water, etc. The latter mechanism is a modification of one proposed by Noyce[5] (eq 6) for hydration of certain α,β-unsaturated

$$RCH=CHCOR' \underset{k_2}{\overset{H_1^+,\ k}{\rightleftharpoons}} RCH=CH\overset{OH^+}{\overset{\|}{C}}R' \underset{k_4}{\overset{H_2O,\ k_3}{\rightleftharpoons}}$$

$$RCHO\overset{+}{H}_2CH=COHR' \tag{6}$$

$$RCHO\overset{+}{H}_2CH=COHR' \underset{k_6,\ k_8,\ A}{\overset{k_5,\ k_7,\ HA}{\rightleftharpoons}}$$

$$RCHOHCH_2\overset{OH^+}{\overset{\|}{C}}-CR' \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} product$$

ketones. For this mechanism, general-acid-catalyzed ketonization of the enediol, k_7, is rate determining. For the β-oxy-α,β-unsaturated ketones a change in the rate-determining step from k_7 to k_3 accommodates the kinetics results, and the change in rate-determining step from one of ketonization to one of conjugate addition of water becomes a consequence of the fact that enols of β-dicarbonyl compounds are stable relative to enols,[30,31] and/or β elimination of the leaving group from the enediol is a more facile process than ketonization. These three mechanistic possibilities will be discussed in turn; the discussion will attempt to show that the modified Noyce mechanism is reasonable and likely correct for acid-catalyzed hydration of β-oxy-α,β-unsaturated ketones.

Considering rate-determining protonation of the olefin bond, we direct attention to solvent isotope effects and the specific acid nature of the catalysis which indicate that proton transfer is rapid with respect to a subsequent event leading to products. Against rate-determining protonation of the olefin bond occurring late along the reaction coordinate between initial state and β-carbonium ion (Brønsted $\alpha \rightarrow 1$) is the result that 4-methoxy-3-penten-2-one (24) undergoes hydration ca. one-fourth as fast as 4-methoxy-3-buten-2-one (25); β-methyl substitution thus decreases reactivity rather than increasing it as the A-SE2 mechanism predicts. In this regard ethyl isopropenyl ether undergoes acid-catalyzed hydration 270 times faster than ethyl vinyl ether via the A-SE2 mechanism.[6,23] Finally, ρ^+ for 9-12, 14, and 16 has the incorrect sign for the A-SE2 mechanism[32] and $\rho^* = -0.18$ for 1-7, although it has the correct sign, is quite small for this mechanism (cf. $\rho^* = -1.1$[33] for hydration of para-substituted phenyl vinyl ethers via the A-SE2 mechanism).

The second mechanism, featuring fast protonation of the olefin bond and subsequent slow hydration, etc., is incorrect because the α-vinyl H of 25 does not exchange with D during hydration in D_2O. Thus reaction of 25 in DCl–D_2O to $\sim$75% completion followed by isolation of unreacted 25 and examination of its nmr spectrum showed a 1:3 ratio of α-vinyl H to

methoxy H signals;[34] a smaller ratio is anticipated for preequilibrium olefin bond protonation. Further, successive integrations of the α-vinyl H and the methoxy H signals for hydration of 25 (0.04 ml in 0.4 ml of 0.0004 M DCl) showed that the relative intensity of these signals remained constant during $\sim$50% reaction; for more extensive reaction, integration of the α-vinyl H signal was unreliable.

We consider now the reaction mechanism of eq 6, k_3 rate determining, which in our view best accommodates the data. Just as for similar A1 and A2 reactions involving low pK_a oxy acids the intermediacy of the cation is assumed in the absence of experimental evidence (e.g., kinetic pK_a) for its existence. Necessarily, analogies must be used in estimating such parameters as ρ for the protonation step. Rates of hydration of 4'-substituted acrylophenones (ρ^+ 0.26) and of 4-(para-substituted phenoxy)-3-buten-2-ones (ρ^* -0.18) are rather insensitive to electronic effects, suggestive of a multistep reaction having opposing electronic requirements. For these reactions, $k_H = k_1 k_3/k_2$ ($k_2/k_1 > a_H$ in the acidity range of the experiments), and ρ (exptl) $= \rho (k_3) - \rho (k_2/k_1)$. For acrylophenones, $\rho^+ (k_2/k_1) = 2.3$, calculated from the pK_a values for para-substituted acetophenones,[35] was assumed and accordingly, $\rho^+ (k_3) = 2.56$. Similarly $\rho^* (k_3) = -0.18$ to 0.8 was calculated for 4-(para-substituted phenoxy)-3-buten-2-ones assuming a minimum value for ρ^* (k_2/k_1) = 0 and a maximum value for ρ^* (k_2/k_1) = 1 (based on $\rho^* = 1$ for the same pK_a values for acetophenones); likely $\rho^* (k_3)$ has a small, positive value on this σ^* scale. The results suggest that reaction of water at the β-carbon atom of protonated β-oxy-α,β-unsaturated ketones is facilitated by low electron density, that β-carbonium ion formation is not involved in the k_3 step, and that appreciable β-C–O bond formation has occurred in the transition state. The greater sensitivity toward electronic effects of k_3 for acrylophenones vs. 4-(para-substituted phenoxy)-3-buten-2-ones suggests that in the transition state for hydration, electrons are delocalized primarily over the α,β-unsaturated carbonyl group and para substituents of the butenones play a minor role in transition state stabilization. Similar small ρ (exptl) values characterize multistep reactions such as semicarbazone formation in para-substituted benzaldehydes (ρ 0.07),[36] acid-catalyzed hydrolysis of ethyl benzoates (ρ 0.14),[37] acid-catalyzed hydrolysis of benzamides (ρ 0.12),[38] and acid-catalyzed hydrolysis of phenyl acetates (ρ -0.22).[39]

4-Acetoxy-3-buten-2-one (17) and 4-pivaloyloxy-3-buten-2-one (18) react ca. 40-fold more slowly than 25 but ca. 100-fold faster than vinyl acetate, which under comparable conditions hydrolyzes via the $A_{Ac}2$ mechanism.[40] The latter rate difference coupled with the

(30) J. U. Lowe, Jr., and L. N. Ferguson, J. Org. Chem., 30, 3000 (1965).

(31) (a) A. Gero, ibid., 19, 469 (1954); (b) ibid., 21, 1960 (1956).

(32) T. Okuyama, T. Fueno, and J. Furukawa, Bull. Chem. Soc. Jap., 43, 3256 (1970).

(33) T. Fueno, I. Matsumura, T. Okuyama, and J. Furukawa, ibid., 41, 818 (1968).

(34) 25 (0.5 g) was dissolved in 4.2 ml of 0.0042 M DCl in D_2O. After about 2 half-lives, the reaction mixture was basified to pH 6, $MgSO_4$ was added, and the residue was extracted with ether. The nmr spectrum ($CDCl_3$) of the residue obtained on evaporation of the dried ether solution was taken.

(35) G. S. Levy, J. D. Cargioli, and W. Racela, J. Amer. Chem. Soc., 92, 6238 (1970).

(36) B. M. Anderson and W. P. Jencks, ibid., 82, 1773 (1960).

(37) H. H. Jaffé, Chem. Rev., 53, 191 (1953).

(38) J. A. Leisten, J. Chem. Soc., 765 (1959).

(39) T. C. Bruice and M. F. Mayahi, J. Amer. Chem. Soc., 82, 3067 (1960).

(40) (a) D. S. Noyce and R. M. Pollack, J. Amer. Chem. Soc., 91, 119 (1969); (b) ibid., 91, 7158 (1969).

result that $A_{Ac}2$ ester hydrolysis is subject to steric and electronic effects such that ethyl acetate is *ca.* 90 times more reactive than ethyl pivalate,[41] while **18** is slightly more reactive than **17**, indicates **17** and **18** undergo hydration *via* the modified mechanism of eq 6. The relative reactivities of **17**, **18**, and **25** suggest that electron donation assists the reaction so that the effect of β-oxy substituents on pK_a is more important than their effects on k_3. In this regard, the rates of hydration of **22**, **23**, and **25** are predicted, within experimental error, by eq 4. In terms of the modified mechanism of eq 6, the E_s parameter reflects the influence of bulk on the equilibrium constant k_2/k_1; the substituents are too far removed from the β-carbon atom to sterically influence k_3. The positive ρ^* value reasonably reflects inductive electronic effects on k_3 as well as on k_2/k_1. For k_3, the contribution of electronic effects to the experimentally determined ρ^* should be positive; for k_2/k_1 the contribution should be negative. The experimental result, $\rho^* = -0.54$, suggests that for aliphatic compounds electronic effects influencing pK_a are more important than such effects influencing k_3.

α- and β-CH$_3$ substituents (**21** and **24**) decrease reactivity fourfold. While both substituents should increase the fraction of cation *via* inductive effects, compensatory inductive electron release to the β-carbon atom as well as steric effects result in a net decrease in reactivity. The effect of α-CH$_3$ on the planarity of the conjugated π system may also be a factor influencing reactivity of **21**.

The second-order rate constants for the acid-catalyzed hydration of **1–7** in dioxane–water (80% (v/v); Table III) are 6–11-fold smaller than in water. This decreased reactivity in dioxane–water with decreased dielectric of the medium[42] may be compared with the 40-fold rate decrease attending hydration of ethyl vinyl ether under comparable conditions *via* the A-S$_E$2 mechanism.[20,23] Reasonably, the latter rate decrease is due to carbonium ion destabilization in dioxane–water solution. In the case of compounds **1–7**, both ground states and transition states are charged (eq 6) with the likelihood that transition states are destabilized more than ground states by the solvent of low dielectric with a resulting rate decrease of only 6–11-fold. Regarding this latter point, the catalytic role of sodium lauryl sulfate in the hydration of **1**, **4**, and **7** may be one of increasing the pK_a of the cations (ground-state destabilization) primarily.[43,44] The virtually identical ρ^* (−0.16 *vs.* − 0.18) value for hydration in the presence and absence of micelles indicates that reaction pathways are the same (eq 6).

Noteworthy is the insensitivity of β-oxy-α,β-unsaturated ketones toward structural changes and, as well, the magnitude of the rate constants. With respect to relative rates, we have attempted to show that reactivity is a function of pK_a of the ketones and their capability to undergo Michael addition. Generally, factors favoring protonation disfavor Michael reaction and a leveling of reactivity results. With respect to the

magnitude of the rates, they are greater by *ca.* 10^3–10^4 than those for acid-catalyzed hydrations of mesityl oxide and crotonaldehyde.[45] The reactivity difference in terms of the mechanism for acid-catalyzed ketonization (mesityl oxide, and crotonaldehyde) and that of eq 6 is due to a presumed larger pK_a of β-oxy-α,β-unsaturated ketones[35] and as well to the presumed relative ease of mobilizing π electrons with attending hydration *vs.* carbon acid prototropy. Concerning the latter, facility of Michael-type reactions is known,[46] as is the difficulty of breaking C–H bonds using water as the proton acceptor.[47]

The data are shown to be in agreement with the mechanism of eq 6, although more complex mechanisms may be written to explain the results. The chemical events following k_3 can only be a matter for speculation; product formation in acidic solutions could result from the usual hemiacetal[48] decomposition or from a ketonization–elimination reaction.

Base-catalyzed hydrations of **1–7** gave 3-ketobutanal and para-substituted phenols. Products may arise either by hydration of butynone formed by β elimination of para-substituted phenoxides or by Michael addition of hydroxide ion to **1–7** followed by hemiacetal decomposition or β elimination concerted with ketonization of the enolate ion. Two results of this study rule out the E2 pathway. (1) Hydration of butynone to give 3-ketobutanal is slower than hydration of **1–7** ($k_{OH} = 2.7$ *vs.* 14–28 M^{-1} min^{-1}). Thus butynone accumulation would be detectable at the analytical wavelengths for **1**, **2**, **4**, and **5** during their hydrations; unstable "infinity" absorbance with $k_{OH} = 2.66$ M^{-1} min^{-1} would serve to identify butynone as an intermediate. No butynone was so detected. (2) The second-order rate constant for base-catalyzed hydration of 4-(p-nitrophenoxy)-3-buten-2-one-d_5 (**8**) is *greater* than that for nondeuterated compound (**7**), $k_{OH}(8)/k_{OH}(7) = 1.4$. In this regard, α-CH bond breaking is rate determining for hydroxide ion catalyzed elimination of 4-(para-substituted phenoxy)-2-butanones.[51] Therefore for isotopically substituted **8**, slow α-CD bond breaking should give rise to a sizable primary isotope effect, $k_{OH}(8)/k_{OH}(7) < 1$, as is the case for base catalyzed elimination of acetate from 9-acetoxy-10-methyl-*cis*-decalone-2 (1-d_2) for which $k_{OH}(D)/k_{OH}(H) = 0.109$.[52] The larger rate of hydration of **8** *vs.* **7** may be due to relative hyperconjugative ground state stabilization of **7** *vs.* **8**.[53]

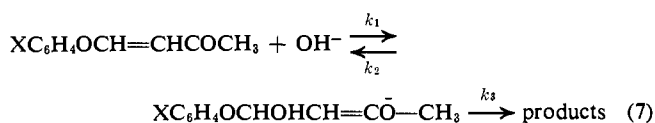Turning now to the Michael addition mechanism

(41) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt, New York, N. Y., 1960, p 314.

(42) F. E. Critchfield, J. A. Gibson, Jr., and J. L. Hall, *J. Amer. Chem. Soc.*, **75**, 1991 (1953).

(43) T. C. Bruice, J. Katzhendler, and L. R. Fedor, *ibid.*, **90**, 1333 (1968).

(44) E. J. Fendler and J. H. Fendler, *Advan. Phys. Org. Chem.*, **8**, 271 (1970).

(45) R. P. Bell, J. Preston, and R. B. Whitney, *J. Chem. Soc.*, 1166 (1962).

(46) C. E. Lough, D. J. Currie, and H. L. Hommes, *Can. J. Chem.*, **46**, 771 (1968).

(47) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964).

(48) Hemiacetal decomposition, shown to be fast with respect to carbonium ion formation in the acid-catalyzed hydrolysis of acetals and ketals,[49,50] is assumed to be fast in contrast to reaction of cations with water at β-C. Acid-catalyzed hydrolysis of acetone diethyl ketal is *ca.* 10^3 greater than is acid-catalyzed hydration of **24**; the rate discrepancy between unimolecular hemiacetal decomposition and Michael addition is likely much greater than 10^3 considering the weaker acidity of protonated β-oxy-α,β-unsaturated ketones *vs.* protonated acetals.

(49) A. M. Wenthe and E. H. Cordes, *J. Amer. Chem. Soc.*, **87**, 3173 (1965).

(50) E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967).

(51) L. R. Fedor and W. R. Glave, *J. Amer. Chem. Soc.*, **93**, 985 (1971).

(52) D. J. Hupe, M. C. R. Kendell, and T. A. Spencer, *ibid.*, **94**, 1254 (1972).

(53) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, p 255, and references therein.

(eq 7), we note that kinetically the concentration of

$$XC_6H_4OCH{=}CHCOCH_3 + OH^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}}$$

$$XC_6H_4OCHOHCH{=}\overset{-}{C}O{-}CH_3 \overset{k_3}{\longrightarrow} \text{products} \quad (7)$$

enolate anion is low under our experimental conditions; thus no rate saturation effects as a function of hydroxide ion concentration were observed. For this mechanism either k_1 or k_3 is rate determining. The latter possibility which requires that $k_2 > k_3$ was rejected for the following reason. For this case, $k_{OH} = k_1k_3/k_2$. Experimentally ρ^* $(k_{OH}) = \rho^*$ $(k_3) - \rho^*$ (k_2/k_1). A reasonable value for ρ^* (k_3) is 0.6, previously calculated for loss of para-substituted phenoxides from 4-(para-substituted phenoxy)-2-butanone enolate anions;[51] similar decomposition of enolate anion via hemiacetal decomposition could be expected to exhibit a positive ρ^* of the same approximate magnitude. Accepting this value for ρ^* (k_3), we calculate that ρ^* $(k_2/k_1) = +0.5$. In fact, ρ^* (k_2/k_1) should be a negative quantity and accordingly we reject the mechanism of eq 7 wherein $k_2 > k_3$. On the other hand, the experimentally determined ρ^* value is in accord with rate-determining attack of hydroxide ion on 1–7 so that $k_{OH} = k_1$.

Comparison of ρ^* values for 1–7 and para-substituted phenyl acetates reveals that phenyl acetates are three times more sensitive than 1–7 toward electronic effects.[39] Assuming hydroxide ion attack is rate determining in both cases, the smaller ρ^* for 1–7 reflects the contribution of the conjugated π system to transition state stabilization. The lesser reactivity of 1–7 would then be attributed to greater ground-state stabilization of 1–7 vs. phenyl acetates. The transition state could then be viewed as enolate anion-like with appreciable β-O–C bond formation.

We have speculated on the nature of the k_3 step (eq 7) which involves decomposition of enolate anion via (i) β elimination of para-substituted phenoxides or (ii) hemiacetal decomposition. Such speculation, although not productive for hydroxide ion catalyzed hydration, may be productive for reaction of 7 with N,N-dimethylaminoethanol (DMAE) which is also viewed as a Michael reaction rather than as one of general base catalysis of hydration or elimination for the following reasons.[54] The deuterium solvent kinetic isotope

effect for this reaction is $k(D_2O)/k(H_2O) = 1.2$, a result which renders unlikely the involvement of DMAE as a general base which catalyzes the reaction of 7 with water. In this regard there are no examples known to us of general base catalysis of aminolysis or hydrolysis of p-nitrophenyl acetate of which 7 is a vinylog. For reactions of this ester with imidazole, $k(D_2O)/k(H_2O) = 1.$[56,57] Further, the imidazole catalyzed *hydrolysis* of ethyl trifluorothiolacetate[58] and ethyl dichloroacetate[59] has $k(D_2O)/k(H_2O) = 0.3$; similarly, for solvolysis of 4-(2'-acetoxyphenyl)imidazole.[60] Thus for those cases where general base catalysis of hydrolysis occurs, deuterium solvent isotope effects are rather large. Also related to the question of nucleophilic vs. general base catalysis of hydration by DMAE is the result that reaction of aniline with 25 in aqueous methanol at room temperature gives high yields of 4-anilino-3-buten-2-one. Finally, with respect to the possibility that DMAE catalyzes an E2 reaction, we note that hydration of 8 catalyzed by DMAE proceeds 2.9-fold *faster* than the analogous reaction with 7 rendering unlikely an elimination reaction mechanism.

Considering now the k_3 step (eq 7) for nucleophilic reaction of 7 with DMAE it can be shown that if the hemiacetal mechanism operates, and if hydroxide ion and DMAE do indeed react via the same mechanism as appears likely, then DMAE should *inhibit* the overall reaction since reaction of 7 with DMAE would yield a "dead end" complex (a quaternized zwitterion). Since DMAE is a catalyst for the reaction we suggest that DMAE, and also hydroxide ion, reacts via Michael addition to the olefin bond in a slow step, subsequently yielding product via β elimination from the generated enolate anion. Studies previously reported[51] suggest that β elimination from 4-(para-substituted phenoxy)-2-butanones catalyzed by hydroxide ion, which acts as a general base, must proceed with rate constants in excess of 300–500 M^{-1} min^{-1}, since this range in rate constants represents rate determining α hydrogen atom removal from these compounds. β elimination from the enolates of 1–7 is compatible with this result.

to association of amine molecules in the nonprotic solvent such that amines react in pairs.

(54) Addition of primary and secondary amines to p-tolyl vinyl sulfone in ethanol solution is kinetically first order in amine; in benzene solution, the reaction is second order in amine, suggesting general-base catalysis of amine addition.[55] However, the latter result may be due

(55) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. B*, 343 (1967).

(56) M. L. Bender, E. J. Pollack, and M. C. Neveu, *J. Amer. Chem. Soc.*, **84**, 595 (1962).

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(58) L. R. Fedor and T. C. Bruice, *J. Amer. Chem. Soc.*, **87**, 4138 (1965).

(59) W. P. Jencks and J. Carriuolo, *ibid.*, **83**, 1743 (1961).

(60) S. M. Felton and T. C. Bruice, *Chem. Commun.*, 907 (1968).