Vinyl Ether Hydrolysis. II. General Acid Catalyzed Hydration of 3-Alkyloxy- and 3-Aryloxycrotonic Acid Derivatives

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Abstract: The hydrolysis of 3-alkyloxy- and 3-aryloxycrotonic acid derivatives, formally vinyl ethers and α,β-unsaturated carbonyl compounds, is general acid catalyzed exhibiting a deuterium solvent isotope effect $k(H_2O)/k(D_2O) > 1$. These results are in accord with those for vinyl ethers, but in contrast to those for 4-methoxy-3-buten-2-one which undergoes specific acid catalyzed hydrolysis characterized by $k(H_2O)/k(D_2O) < 1$. The Brønsted $\alpha = 0.71$ for the reaction of *tert*-butyl 3-ethoxythiolcrotonate with general acids, together with a 130-fold rate enhancement for this thiol ester over the homologous thiolacrylate and $\rho = -0.71$ for hydrolysis of *N*-acetylcysteaminyl 3-(*p*-substituted phenoxy)thiolcrotonates, suggest that hydrolysis of the crotonates proceeds *via* slow proton transfer to the olefin followed by attack of water and breakdown of the hydrolytically labile hemiketal rather than *via* slow proton transfer to the α carbon of the enediol formed by conjugate addition of water to the α,β-unsaturated carbonyl group.

The hydrolysis of vinyl ethers (eq 1) has been shown to be general acid catalyzed, the rate-determining

$$CH_2{=}CHOR \xrightarrow[\text{slow}]{HA} CH_3CH^+OR \xrightarrow[\text{fast}]{H_2O,\ -H^+} CH_3CHO + ROH \quad (1)$$

step being slow proton transfer to the olefin bond.[1-6] This particular reaction is characterized by $k(H_2O)/k(D_2O)$ greater than one, a result in accord with the assigned mechanism. In contrast to these findings, the hydrolysis of 4-methoxy-3-buten-2-one is specific acid catalyzed only with $k(H_2O)/k(D_2O)$ less than one.[7] Noting the reported similarities between ketones and thiol esters regarding certain of their chemical reactions[8,9] we found it of interest to examine the olefin hydration of various β-oxythiolcrotonate esters and congeners (Table I).

Experimental Section

Reagents. Certified ACS grade inorganic salts were purchased from Fisher Scientific Co. Tap distilled water was redistilled through a Corning AG-1a still before use. Organic reagents were purchased from Aldrich Chemical Co. and from Distillation Products Industries (Eastman). Deuterated solvents were obtained from Diaprep, Inc. *N*-Acetylcysteamine was prepared by the procedure of Kuhn and Quadbeck[10] and *N*-acetylcysteaminyl acetoacetate by the procedure of Sheehan and Beck.[11]

3-Alkyloxycrotonates (1–4). All of these esters were prepared from the appropriate trialkyl orthoformate and the appropriate acetoacetate in exactly the same manner as described for ethyl 3-ethoxycrotonate by Dollivar, *et al.*[12] Analytical data for the previously unreported *tert*-butyl 3-ethoxycrotonate are given in Table II.

***tert*-Butyl 3-Ethoxythiolcrotonate (5).** To 12.9 g (0.1 mol) of 3-ethoxycrotonic acid[12] in a 250-ml round-bottomed flask was added 19 ml (0.27 mol) of $SOCl_2$. The reaction flask was immediately fitted with an aspirator and the mixture cooled in an ice bath. The reaction was allowed to proceed 10 min or until the mixture became a brownish color. Benzene (50 ml) was then added to the mixture, and the excess $SOCl_2$ removed by codistillation on the rotary evaporator. This procedure was repeated twice. Distillation of the residue yielded 11.9 g (82.1%) of 3-ethoxycrotonoyl chloride, bp 65–67° (1.9 mm). The acid chloride (0.08 mol) was immediately added dropwise to a cooled solution of 6.4 g (0.07 mol) of *tert*-butylthiol in 200 ml of pyridine contained in a 250-ml three-necked round-bottomed flask fitted with a condenser and a drying tube. The reaction was allowed to proceed at room temperature with stirring for 24 hr after which time enough water was added to the flask to dissolve the pyridinium salt formed. The contents were then transferred to a 1-l. separatory funnel and, following the addition of 300 ml of ether, the pyridine was removed by the careful addition of 1:1 HCl. Upon removal of the pyridine, the ether layer was washed three times with 50-ml portions of saturated $NaHCO_3$ solution and twice with water, and dried over $MgSO_4$. Filtration of the ether, followed by evaporation, left a residue which upon distillation yielded 3.1 g (21.5%) of **5**, bp 65–66° (3.5 mm). The analytical data are given in Table II.

***N*-Acetylcysteaminyl 3-Ethoxythiolcrotonate (6).** To a cooled solution of 2 g (0.017 mol) of *N*-acetylcysteamine[10] in 25 ml of pyridine contained in a 100-ml three-necked round-bottomed flask fitted with a condenser and drying tube was added dropwise 2.7 g (0.018 mol) of the previously synthesized 3-ethoxycrotonoyl chloride. The reaction was allowed to proceed at room temperature for 24 hr and the mixture subsequently worked up in exactly the same manner as outlined for **5**. Evaporation of the ether to dryness left yellow crystals which were then recrystallized from CCl_4 to yield 1.7 g (43.3%) of **6**, mp 101°. The analytical data are given in Table II.

***N*-Acetylcysteaminyl 3-Aryloxythiolcrotonates (7–9).** Ethyl 3-chlorocrotonate was allowed to react with the sodium salt of the appropriate phenol in exactly the same manner as described for sodium *p*-nitrophenoxide and ethyl 3-chlorocrotonate by Jones, *et al.*,[13] to yield the corresponding ethyl 3-aryloxycrotonates. Using 0.1-mol quantities of phenoxide and chlorocrotonate the following crude yields were obtained: ethyl 3-phenoxycrotonate, 19.1 g (92.8%); ethyl 3-(*p*-methylphenoxy)crotonate, 19.1 g (88.0%); ethyl 3-(*p*-methoxyphenoxy)crotonate, 23.0 g (97.5%). The crude products were identified by nmr and were used without further purification in the next step. The 3-aryloxy esters were then saponified by the exact procedure used by Dollivar, *et al.*,[12] to obtain 3-ethoxycrotonic acid. Starting with 0.05 mol of the appropriate 3-aryloxycrotonates the following yields were obtained: 3-phen-

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(9) L. R. Fedor, *J. Amer. Chem. Soc.*, **91**, 913 (1969).
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(11) J. C. Sheehan and C. W. Beck, *J. Amer. Chem. Soc.*, 77, 4875 (1955).
(12) M. A. Dollivar, T. L. Gresham, G. B. Kistiakowsky, E. A. Smith, and W. E. Vaughan, *ibid.*, **60**, 440 (1938).
(13) D. E. Jones, R. O. Morris, C. A. Vernon, and R. F. M. White, *J. Chem. Soc.*, 2349 (1960).

Table I. Vinyl Ether with General Structure $CH_3C(OR)=CHCR'(=O)$

Compd	R	R′	Compd	R	R′
1	CH_3	CH_3O	**7**	C_6H_5	$S(CH_2)_2N(-H)COCH_3$
2	CH_3	C_2H_5O	**8**	p-$CH_3C_6H_4$	$S(CH_2)_2N(-H)COCH_3$
3	C_2H_5	C_2H_5O	**9**	p-$CH_3OC_6H_4$	$S(CH_2)_2N(-H)COCH_3$
4	C_2H_5	t-C_4H_9O	**10**	C_2H_5	OH
5	C_2H_5	t-C_4H_9S	**11**	C_2H_5	NH_2
6	C_2H_5	$S(CH_2)_2N(-H)COCH_3$	**12**	Acrylate homolog of **5**	

Table II. Analytical Data for Various 3-Alkyloxy- and 3-Aryloxycrotonates

			Anal., %							
			Calculated				Found			
Compd	Bp, °C (*P*, mm)	% yield	C	H	N	S	C	H	N	S
4	104–105 (12)	68.0	64.49	9.74			64.73	9.57		
5	65–66 (3.5)	21.5	59.37	8.97		15.85	59.17	8.84		15.72
6	101[c]	43.3[b]	51.93	7.41	6.06	13.86	51.73	7.18	5.86	14.08
7	105[c]	48.4[a]	60.19	6.13	5.01	11.48	60.16	6.13	5.13	11.60
8	88–89[c]	40.0[a]	61.41	6.53	4.77	10.93	61.39	6.65	4.90	11.03
9	79–80[c]	10.0[a]	58.23	6.19	4.53	10.36	58.04	6.10	4.71	10.67
11	114–116[c]	2.6[b]	55.80	8.58	10.84		55.64	8.65	10.62	
12	67 (1.5)	17.0	57.41	8.57		17.03	57.20	8.52		17.25

[a] Recrystallized from ether. [b] Recrystallized from CCl_4. [c] Melting point.

oxycrotonic acid (mp 153–155°), 4.6 g (51.7%); 3-(*p*-methylphenoxy)crotonic acid (mp 152°), 3.4 g (35.6%); 3-(*p*-methoxyphenoxy)-crotonic acid (mp 152–153°), 7.8 g (74.8%). To a solution of 3.2 ml (0.045 mol) of $SOCl_2$ in 50 ml of benzene contained in a 250-ml round-bottomed flask fitted with a condenser and drying tube was added 0.015 mol of the appropriate 3-aryloxycrotonic acid. The mixture was heated with stirring at 50–60° for 1–3 hr until the cessation of gas evolution signaled the completion of the reaction. Excess $SOCl_2$ was removed by codistillation with three 50-ml portions of benzene on the rotary evaporator, and the crude acid chloride obtained was used immediately in the next step without further purification. Condensation of the acid chloride with 1.2 g (0.01 mol) of *N*-acetylcysteamine was carried out as described for **6**. Yields were as follows: **7** (mp 105°), 1.4 g (48.4%); **8** (mp 88–89°), 1.2 g (40.0%); **9** (mp 79–80°), 0.3 g (10.0%). See Table II for additional analytical data.

3-Ethoxycrotonamide (11). To 50 ml of cold, concentrated NH_4OH contained in a three-necked 250-ml round-bottomed flask fitted with a condenser was added dropwise with stirring 20.3 g (0.14 mol) of 3-ethoxycrotonoyl chloride. The crystals formed were filtered off immediately and subsequently recrystallized from CCl_4 to give 0.45 g (2.6%) of the corresponding amide **11**. See Table II for analytical details.

tert-**Butyl 3-Ethoxythiolacrylate (12).** 3-Ethoxyacryloyl chloride,[14] 9.3 g (0.07 mol), was condensed with 6.2 g (0.07 mol) of *tert*-butylthiol in 200 ml of pyridine in the same manner described for **5**. Upon distillation of the flask residue 2.1 g (17.0%) of **12** was obtained, bp 67° (1.5 mm). Additional analytical data are given in Table II.

Apparatus. Gilford Model 2000 and 2400 spectrophotometers were used for the collection of rate data. Ultraviolet scans were taken on a Beckman Model DB-G recording spectrophotometer. Temperature was maintained by circulating water at 30 ± 0.1° from a Tamson Model TE-3 water bath. pH was determined by using a Radiometer Model PHM-22 pH meter equipped with a PHA 630 scale expander using a combined glass–calomel electrode (Radiometer GK2302B).

Kinetics. The courses of the reactions were monitored at a specific wavelength (see Table III) by following the loss of absorbance *vs.* time. The reactions of compounds **1–6** and **10** and **11** were carried out in water at 30 ± 0.1° and at a calculated ionic strength of 0.1 *M* with KCl, while those of compounds **7–9** were carried out at a calculated ionic strength of 1.0 *M* with HCl. The pH of each solution was determined before and after all runs and the pH remained constant (±0.02 pH unit) during all runs. 🝢 cuvettes (3 ml) were filled to the stopper level with the appropriate HCl–KCl buffer or carboxylic acid–carboxylate salt buffer, capped, and allowed to come to thermal equilibrium. Reactions were started by adding a known amount of substrate in methanol *via* a micropipet to the appropriate solution in the cuvette. Reactions were carried out under pseudo-first-order conditions (concentration of compound, *ca.* 5×10^{-5} *M*) and pseudo-first-order rate constants were obtained by multiplying slopes of plots of $\log [(OD_0 - OD_\infty)/(OD_t - OD_\infty)]$ *vs.* time by 2.303. Reactions were monitored to completion and pseudo-first-order plots were nearly always linear to at least 2 half-lives. The activity of the hydrogen ion was determined with the glass electrode and pD was determined from the pH meter reading by adding 0.39 to it.[15]

Table III. Rate Constants for the Reaction of Crotonic Acid Derivatives **1–12** with Aqueous Hydrochloric Acid Solution[a]

Compd	λ, nm[d]	k_H, M^{-1} min^{-1}	Total no. of k_{obsd}	pH range
1	238	1.22 ± 0.03	5	1.09–1.78
2	238	1.42 ± 0.02	5	1.07–1.76
3	240	3.41 ± 0.11	5	1.08–1.76
4	240	6.67 ± 0.33	5	1.06–1.75
5	276	2.65 ± 0.06	5	1.08–1.77
6	276	1.08 ± 0.02	5	1.07–1.75
7[b]	276	0.0173 ± 0.0011	3	0.06
8[b]	276	0.0243 ± 0.0011	3	0.07
9[b]	276	0.0265 ± 0.0004	3	0.09
10	238	4.62 ± 0.16	5	0.98–1.70
11	237	11.17 ± 0.31	5	1.07–1.76
12[c]	276	0.0201 ± 0.0006	5	0.04–0.68

[a] Solvent = H_2O, temperature = 30°, μ = 0.1 *M* (KCl). [b] Average of three runs in 1 *N* HCl. [c] μ = 1 *M* (KCl). [d] Wavelength used to monitor the reaction.

Product Analysis. The hydration of compound **6** was followed to completion spectrophotometrically, and the ultraviolet spectrum was found to be identical with that of an authentic sample of *N*-acetylcysteaminyl acetoacetate,[11] ϵ = 4951 ± 187 (three runs) at 235 nm. The ϵ calculated for the hydration of **6** to product was 4529. Based on these figures, the product yield is 91.5 ± 3.6%.

The hydration of **1** was also followed using nmr spectroscopy. The following procedure was used: 0.06 ml of methyl acetoacetate, 0.25 ml of DMSO-*d*, 0.05 ml of D_2O, 0.05 ml of CH_3OD, and 0.02 ml of DCl were placed in one nmr tube, while another tube was charged with 0.06 ml of **1**, 0.25 ml of DMSO-*d*, 0.05 ml of D_2O,

(14) I. I. Kolodkina, K. V. Levshina, S. I. Sergievskaya, and A. I. Kravchenko, *J. Org. Chem. USSR*, **2**, 63 (1966).

(15) T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).

and 0.02 ml of DCl. Repeated scans of the nmr tube containing **1** over 14 hr indicated the loss of the vinyl proton and the appearance of a CH_3OD peak. After 14 hr the spectra for both nmr tubes were identical (4 singlets), except for a downfield shift of 4 Hz for α-methylene protons for the product from **1**. This chemical shift was shown to be dependent on the concentration of added DCl which was slightly different for each tube owing to pipet errors.

Results

The various crotonic acid derivatives **1–11** undergo general acid catalyzed hydration to yield the corresponding 3-oxobutyric acid derivative and alcohol or the appropriate phenol. Kinetically the reactions obey the rate law of eq 2 and in aqueous solutions of acidic buf-

$$CH_3C(OR)=CHCY + H_2O \longrightarrow CH_3CCH_2CY + ROH$$

$$\frac{-d[S]}{dt} = [\sum k_2[\text{acid}]][S] \qquad (2)$$

fers at constant pH they are described by eq 3. For re-

$$\frac{-d[S]}{dt[S]} = k_{obsd} = k_2'[\text{acid}]_{total} + k_H a_H \qquad (3)$$

actions run in carboxylic acid buffers, plots of k_{obsd} *vs.* the concentration of total acid gave as the slope the apparent second-order rate constant k_2' and as the intercept the concentration-dependent rate constant $k_H a_H$. The true second-order rate constant k_2 was determined by dividing k_2' by $a_H/(K_a + a_H)$, the mole fraction of total acid present as a free acid (Table IV). The rate constant k_H was determined from the slope of plots of intercept values *vs.* a_H or from k_{obsd}/a_H for reactions run in hydrochloric acid solutions (Table III).

Table IV. Rate Constants[a] for the Reactions of *tert*-Butyl 3-Ethoxythiolcrotonate with (A) Methoxyacetic Acid, (B) Chloroacetic Acid, (C) Dichloroacetic Acid, (D) Trifluoroacetic Acid, (E) H_3O^+[d]

Catalyst	pK_a	pH range (no. of pH's)	k_2, M^{-1} min^{-1}	No. of k_{obsd}
A	3.53[b,e]	2.55–3.62 (3)	0.0145 ± 0.0022	16
B	2.86[b,e]	2.34–3.17 (3)	0.0513 ± 0.0058	17
C	1.29[c]	1.67–2.22 (3)	0.881 ± 0.094	17
D	0.23[b]	1.41 (1)	2.85 ± 0.69	5
E	−1.74		2.65 ± 0.06[d]	5

[a] Solvent = H_2O, temp = 30°, μ = 0.1 M (KCl). [b] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., London, 1962, p 124. [c] C. Moreau, *Bull. Soc. Chim. Fr.*, 31 (1968). [d] Rate constant k_H not used in evaluation of Brønsted α. [e] No term first order in carboxylate ion, indicative of a Michael reaction, was found when the data were appropriately treated.

The hydration of several crotonic acid derivatives exhibits a deuterium solvent isotope effect $k_H(H_2O)/k_D(D_2O) > 1$ (Table V). A Brønsted type plot of log k_2 *vs.* pK_a for the reactions of **5** with carboxylic acids gave as slope $\alpha = 0.71 \pm 0.05$. A Hammett-type plot of log k_H *vs.* σ for the hydration of **7–9** gave as slope $\rho = -0.71 \pm 0.13$.

Discussion

The hydration of compounds **1–12**, formally vinyl ethers and α,β-unsaturated carbonyl compounds, is general acid catalyzed, as is the case for simple vinyl ethers.[1–6] As noted in the introductory statement, the hydration of 4-methoxy-3-buten-2-one, formally a vinyl ether and an α,β-unsaturated ketone, is specific acid catalyzed only, and it was proposed that hydration proceeds *via* fast protonation of the carbonyl oxygen followed by rate-determining attack of water on the conjugate acid (eq 4).[7]

Table V. Deuterium Solvent Isotope Effects for Hydration of Acid Derivatives[a]

Compd	k_H, M^{-1} min^{-1}	k_D, M^{-1} min^{-1} [b]	pD range	k_H/k_D
3	3.41 ± 0.11	1.27 ± 0.03	1.09–1.75	2.69
4	6.67 ± 0.33	2.90 ± 0.08	1.08–1.75	2.30
5	2.65 ± 0.06	1.05 ± 0.14	1.12–1.72	2.53
10	4.62 ± 0.16	1.96 ± 0.02	1.06–1.68	2.36

[a] Temperature = 30°, μ = 0.1 M(KCl). [b] Average and standard deviation for five k_{obsd} values for each compound.

$$CH_3OCH=CHCCH_3 \underset{\text{fast}}{\overset{+H_3O^+}{\rightleftharpoons}} CH_3OCH=CH=CCH_3 \xrightarrow[\text{slow}]{H_2O,\ -H^+} CH_3OCHCH=CCH_3 \xrightarrow{\text{fast}} \text{products} \qquad (4)$$

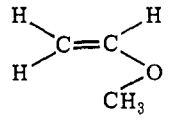
The result that compounds **1–12** undergo general acid catalysis of hydration rules out the mechanism of eq 4 and suggests two reasonable alternatives: (1) rate-determining olefin protonation as occurs for vinyl ethers; (2) rate-determining "ketonization" of the "enediol," or its hydrolysis product, eq 4, as proposed by Noyce and Reed[16] for the acid-catalyzed hydration of certain α,β-unsaturated ketones.

The results of this study favor the vinyl ether mechanism of hydration. (1) Hydration is *ca.* 2.3 times faster in water than in deuterium oxide (Table V), results in accord with those for simple vinyl ethers.[1,2] (2) The Brønsted α of 0.71 for general acid catalyzed hydration of *tert*-butyl 3-ethoxythiolcrotonate (**5**) falls within the range observed for vinyl ethers.[5,6] Furthermore, as observed previously,[5,6] the rate constant for hydronium ion catalysis shows a negative deviation from the Brønsted equation. The pK_a value for water calculated from the Brønsted equation is 0.3, a value within the range 0.2 ± 0.1 previously calculated for hydration of various vinyl ethers.[6] (3) The Hammet ρ of −0.71 for **7–9** indicates that electron-releasing groups increase the rate of reaction.[17] This value, although considerably larger than that of −2.21 obtained for hydration of para-substituted phenyl vinyl ethers[4] in dioxane–water, is in accord with the vinyl ether mechanism (eq 1) and its magnitude reasonably reflects the contribution the β-methyl group makes, together with para substituents, toward the stabilization of the crotonate carbonium ion. (4) Compound **5** hydrolyzes 130-fold faster than the homologous *tert*-butyl 3-

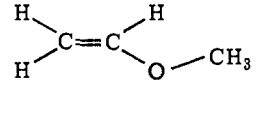
(16) D. S. Noyce and W. L. Reed, *J. Amer. Chem. Soc.*, 80, 5539 (1958).

(17) In attempting to expand the Hammett plot, we synthesized the *p*-chloro and *p*-nitrophenoxy analogs of **7–9** but we could not obtain reliable kinetics for these new compounds. The reported ρ value and its standard deviation were determined from the data; for an extended series of compounds covering a larger range in σ, the ρ value could well be different.

ethoxythiolacrylate. The rate increase is analogous to the 270[2,6]-fold rate enhancement observed for hydration of ethyl isopropenyl ether *vs.* ethyl vinyl ether, and most simply reflects the greater stability of the methyl-substituted carbonium ion. Should compounds **1–12** hydrolyze *via* the mechanism of eq 4 (ketonization slow) a rate decrease from compound **5** as compared to the acrylate could result from steric hindrance to protonation in the transition state. Certainly, there appears to be no reason to expect a rate enhancement of the magnitude observed for the reaction *via* the mechanism of eq 4. (5) The magnitude of the rate constants (Table II) for this study is approximately that predicted for vinyl ether hydrolysis. Ethoxycyclopentene (k_H = 27,240 M^{-1} min^{-1} at 25°)[6] hydrolyzes 2060 times faster than 2-ethoxycyclopentene-2-carboxylic acid (k_H = 13.2 M^{-1} min^{-1} at 30°);[3] 2-ethoxypropene (k_H = 34,740 M^{-1} min^{-1} at 25°)[6] hydrolyzes 7620 times faster than *cis*-3-ethoxycrotonic acid (k_H = 4.6 M^{-1} min^{-1} at 30°).[18] The 3.7-fold difference between the rate ratios is accountable on the basis that the ethoxy group of 2-ethoxycyclopentene-2-carboxylic acid is cis to the carboxyl group; in the acyclic derivative, the ethoxy group is trans to the carboxyl group. It has been demonstrated that *cis*-vinyl ethers are more reactive by about fourfold than the trans isomers.[21] This reactivity difference could be attributed to a higher ground-state energy for the cis compounds due to less favorable orbital overlap between the oxygen p electrons and the olefin π electrons.[22] The degree of overlap is itself a function of the dihedral angle between the C–C–O and C–O–C planes which has been estimated at about 65° for the presumed more stable syn conformer *vs.* the anti conformer.[23,24] The conclusion of geometry is



syn



anti

supported by the result that for hydrolysis of *cis*-styryl ethyl ethers, $\rho = -1.07$; for hydrolysis of *trans*-styryl ethers, $\rho = -0.70$.[4] The greater sensitivity of the cis isomers to electronic effects could then be a reflection of the lessened oxygen p electron overlap with the incipient carbonium ion in the transition state.

Of interest to us was the difference in mechanisms of hydration of β-oxy α,β-unsaturated ketones (specific acid catalysis) and β-oxy α,β-unsaturated carboxyl derivatives (general acid catalysis) of this study. For the acid-catalyzed hydration of para-substituted cinnamic acids[25–27] Noyce, *et al.*, argued convincingly for a mechanism involving rate-determining protonation of the olefin bond as has been reported for acid-catalyzed hydration of para-substituted styrenes[28] and isobutylene.[29] Noyce and Reed[16,27] further postulated that hydration of 4-phenyl-3-buten-2-one and 4-(*p*-nitrophenyl)-3-buten-2-one proceeds *via* the mechanism of eq 4 with *ketonization of the enediol* (last step) rate determining. Thus, for α,β-unsaturated ketones for which enolization is energetically favorable, as appears to be the case for β-oxy α,β-unsaturated ketones, hydration may occur *via* the mechanism of eq 4, or by some variation of it; otherwise rate-determing protonation of the olefin bond occurs, as for **1–12**, and carbonium ion stability plays a prominent role in hydration.

A measure of the presumed greater ease of enolization of ketones *vs.* esters is provided by a comparison of the rate constants for hydration of 4-methoxy-3-buten-2-one (k_H = 43.5 M^{-1} min^{-1}) and **12** (k_H = 0.0201 M^{-1} min^{-1}). This rate difference represents *ca.* 4.6 kcal/mol in activation energy favoring ketone hydration *via* the mechanism of eq 4. Hydration of the thiolacrylate **12** *via* enolization is then disfavored by more than 4.6 kcal/mol; otherwise there would be no mechanism change. However, a similar comparison of rate constants for 4-methoxy-3-penten-2-one (k_H = 11.12 M^{-1})[30] and **5** (k_H = 2.65 M^{-1} min^{-1}) reveals only a 4.2-fold rate difference equivalent to *ca.* 0.86 kcal/mol in activation energy favoring hydration of the ketone *via* enolization. Increased carbonium ion stabilization for **5** has markedly narrowed the rate gap and it could be predicted that for a suitable ketone, high carbonium ion stabilization coupled with unfavorable enolization of the protonated ketone could lead to hydration *via* rate-determining protonation of the olefin bond. This possibility is being investigated in our laboratory.

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(18) The compounds synthesized for this study were obtained as single geometric isomers as determined by nmr and thin-layer chromatography. Since these compounds appear to exist in only one form no comparison between the properties of the isomers can be made, and, therefore, it remains impossible to unequivocally designate the compounds as either cis or trans. We favor the cis geometry (methyl and ester function in a cis relation) since this would put the presumably bulkier oxygen functions in a trans attitude. See the other references[19,20] listed below for further information, particularly that of Theron and Vessiere.

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