1.26 (C-10 methyl), 1.17 (C-4 methyl), 0.93 d and 0.87 d (J = 7, isopropyl).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.37. Found: C, 72.15; H, 9.25; O, 18.48.

Catalytic hydrogenation of 60 mg of **7** in 10 ml of absolute ethanol (15 psi, 10% Pd-C) for 10 hr gave 60 mg of **10**, mp 161–164°, mmp with authentic material[4] 162–164°, ir and nmr spectra superimposable.

Isomerization of 6.—Treatment of **6** with sodium methoxide–methanol in the usual fashion[4] or chromatography over alumina gave a 1:1 mixture of **11** and **12** which was separated by preparative tlc. The less polar substance **11** was recrystallized from methanol–water and had mp 99–100°; $[\alpha]^{25}D$ +47° ($CHCl_3$, c 0.256); ir 1722, 1225 (ester), and 1658, 1605 cm^{-1} (conjugated enone); uv λ_{max} 238 nm (ϵ 12,500); nmr 5.87 d (J = 2, H-11), 3.60 (methoxyl), 1.22 (C-4 methyl), 1.13 (C-10 methyl), 0.92 and 0.79 d (J = 7.1, isopropyl).

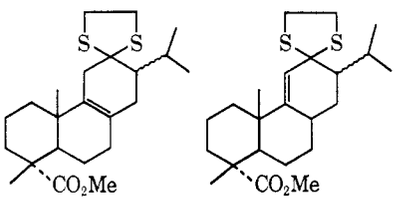
Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70; O, 14.44. Found: C, 75.64; H, 9.69; O, 14.62.

Hydrogenation of 50 mg of **11** in absolute ethanol (10 psi, 5% Pd–C) for 1 hr gave 50 mg of **13**,[4,8] mp 96–97°, mmp 96–97°, ir and nmr spectra superimposable.

The more polar ketone **12** was recrystallized from methanol–water and had mp 103–104°; $[\alpha]^{25}D$ +163° ($CHCl_3$, c 0.33); ir 1719, 1225 (ester), and 1660, 1609 cm^{-1} (conjugated enone); uv λ_{max} 241 nm (ϵ 15,000); nmr 5.70 d (J = 1.8, H-11), 3.60 (methoxyl), 1.22 (C-4 methyl), 1.14 (C-10 methyl), 0.91 d and 0.83 d (J = 6, isopropyl).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70; O, 14.44. Found: C, 75.90; H, 9.71; O, 14.50.

In an attempt to form the thioketal of **11** for the purpose of eventually removing the ketone group, a solution of 130 mg of **11** in 1.5 ml of ethanedithiol was allowed to stand with 0.75 ml of boron trifluoride for 4 hr, poured into water, and extracted with ether. The washed and dried ether extracts were evaporated at reduced pressure. The residue could not be induced to solidify. Preparative tlc afforded separation of the two major components as gums. The major product, *ca.* 70%, appeared to be **19** since the nmr spectrum did not display signals characteristic of vinyl protons, but had signals at 3.63 (methoxyl), 3.22 m (4 protons, $-CH_2S-$), 2.53 (2 protons, 11-methylene group), 1.17 (C-4 methyl), 1.01 (C-10 methyl), and 0.92 d (J = 6.7, isopropyl). The minor product, less than 20%, appeared to be **20**, nmr 5.55 br ($W_{1/2}$ = 2.2, H-11), 3.62 (methoxyl), 3.20 m (4 protons, $-CH_2S-$), 1.19 (C-4 methyl) and 0.92 d (J = 7.5, isopropyl). The nmr spectrum of the crude product also indicated that a small amount, *ca.* 10%, of a third product was present, possibly a C-13 epimer.



19 **20**

Methyl 12-Oxo-13β-abietan-18-oate (15).—A solution of 70 mg of **12** in absolute ethanol was hydrogenated (9 psi, 5% Pd-C) for 4 hr, filtered, and evaporated. Recrystallization of the residue from methanol–water afforded 60 mg of **15** which had mp 123–125°; ir 1716, 1230 (ester), and 1710 cm^{-1} (ketone); nmr 3.62 (methoxyl), 1.10 (C-4 methyl), 0.92 (C-10 methyl), 0.97 d and 0.88 d (J = 7, isopropyl); ord curve (c 0.048), $[\alpha]_{400}$ +274°, $[\alpha]_{304}$ +1880°, $[\alpha]_{255}$ −1580°.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; O, 14.35. Found: C, 75.45; H, 9.95; O, 14.34.

A solution of 55 mg of **15** in 20 ml of aqueous methanol containing 250 mg of potassium hydroxide was allowed to stand for 2 hr, acidified, diluted with water, and extracted with ether. The washed and dried ether extracts on evaporation furnished 50 mg of **13** identical in all respects with authentic material.

Registry No.—**4a**, 20104-28-3; **4b**, 20104-29-4; **6**, 20144-61-0; **7**, 20104-30-7; **11**, 20104-31-8; **12**, 20104-32-9; **15**, 20104-33-0; **19**, 20104-34-1; **20**, 20104-35-2.

The Rates of Hydrolysis of Two Thiol Esters in Water[1]

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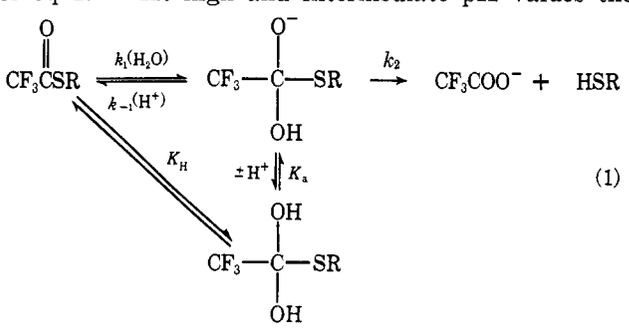
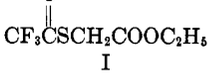
The purpose of this note is to point out that limiting values of the rate constants for decomposition of the tetrahedral addition intermediate in thiol ester hydrolysis to starting materials and products may be calculated from the observed rate constants at a pH value near that at which a change in rate-determining step occurs. In the case of a thiol ester of trifluoroacetic acid the value of these rate constants approach those expected for a diffusion-controlled reaction, reflecting the low stability of the tetrahedral intermediate.

Kinetic evidence for a change in rate-determining step with changing pH, the absolute values of the rate constants required for alternative mechanisms, and a dependence on pH of the exchange of ^{18}O from labeled ester into the solvent that agrees with the behavior predicted from the kinetic data provide convincing evidence that the hydrolysis of ethyl trifluorothiolacetate proceeds with the formation of a kinetically significant intermediate according to the mechanism of eq 1.[2,3] At high and intermediate pH values the



(1)

rate-determining step is the attack of hydroxide ion or the general base catalyzed attack of water on the ester, whereas below pH 2 the breakdown of the anionic tetrahedral addition intermediate becomes rate determining. Calculations of limiting values for the rate constants of eq 1, based upon estimates of the equilibrium constants for formation and ionization of the neutral tetrahedral intermediate, suggested that these rate constants approach the magnitude expected for diffusion-controlled reactions[4] and led us to examine the hydrolysis of ethyl S-trifluoroacetylmercaptoacetate I. This thiol ester has a better leaving group (pK =



I

(1) Contribution No. 653 from the Graduate Department of Biochemistry, Brandeis University, Waltham, Mass. 02154. Supported by grants from the National Science Foundation (GB-5648) and the National Institute of Child Health and Human Development of the National Institutes of Health (HD-1247). R. B. was a National Science Foundation Predoctoral Fellow, 1965–1968.

(2) L. R. Fedor and T. C. Bruice, *J. Amer. Chem. Soc.*, **86**, 5697 (1964); **87**, 4138 (1965).

(3) M. L. Bender and H. d'A. Heck, *ibid.*, **89**, 1211 (1967).

(4) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill Book Co., New York, N. Y., 1969, p 521.

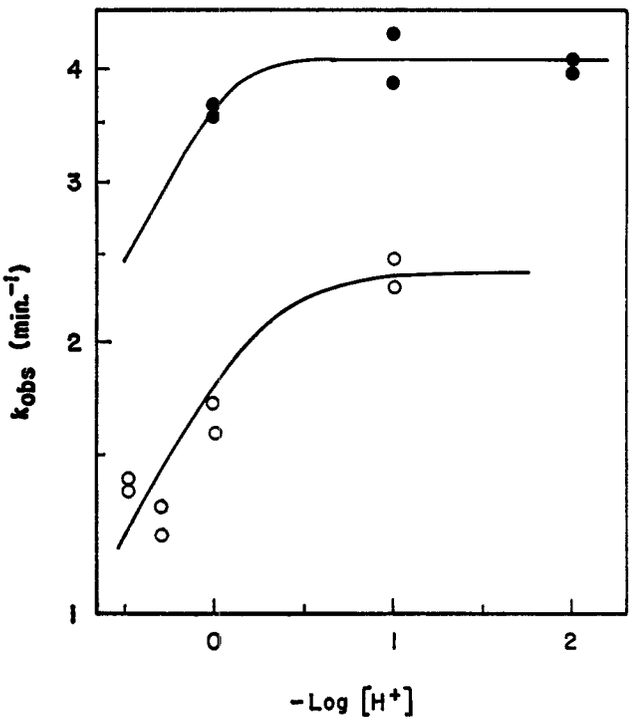


Figure 1.—Hydrolysis of ethyl S-trifluoroacetylmercaptoacetate (I) in hydrochloric acid solutions at 25°, followed at 244 mμ: upper curve, ionic strength maintained at 1.0 M with potassium chloride; lower curve, ionic strength maintained at 3.0 M with lithium chloride.

7.8) than that of ethyl trifluorothiolacetate (pK = 10.3) and might be expected to exhibit even larger absolute rate constants.

The pH–rate profiles for the hydrolysis of the thiol ester bond of I are shown in Figure 1. At an ionic strength of 1.0 M, maintained with potassium chloride (upper curve), there is an indication of a decrease in rate in the most acidic solution. This small rate decrease is probably not an activity coefficient effect, because it is observed even more clearly in solutions maintained at an ionic strength of 3.0 M with lithium chloride (lower curve). In contrast, the pseudo-first-order rate constants for the hydrolysis of phenyl thioformate increase with increasing acidity and follow the rate law of eq 2, with values of k_w and k_a of 3.3 ×

$$\text{rate} = k_w[\text{ester}] + k_a a_{H^+}[\text{ester}] \quad (2)$$

10^{-3} min^{-1} and 9.2 × 10^{-2} M^{-1} min^{-1}, respectively (Table I).

The rate constant for the pH-independent hydrolysis of I is 4.1 min^{-1}, compared with a value of 0.42 min^{-1} for the corresponding reaction of ethyl trifluorothiolacetate.[2] This corresponds to a Brønsted β value of 0.4 for the sensitivity of water-catalyzed thiol ester hydrolysis to the pK_a of the leaving group.

The acid inhibition of the hydrolysis of I is similar to that observed with ethyl trifluorothiolacetate[2] and suggests that the hydrolysis of I also proceeds according to the mechanism of eq 1, with a change from rate-determining attack of water to rate-determining breakdown of the anionic addition intermediate as the pH is decreased. The alternative mechanism of rate-determining hydroxide ion attack at low pH would require a rate constant of 4 × 10^{13} M^{-1} sec^{-1}. This value is above the rate of diffusion-controlled encounter of the

TABLE I
HYDROLYSIS OF PHENYL THIOFORMATE AT 25° IONIC STRENGTH 1.0 M[a]

pH	k_{obsd}, min^{-1}
0.09	0.072
0.10	0.076
0.49	0.027
0.50	0.027
1.07	0.012
1.07	0.012
1.46	0.0072
1.46	0.0066
2.06	0.0058
2.06	0.0057
3.10[b]	0.0039[c]
4.99[d]	0.0033[c]

[a] Maintained with potassium chloride. [b] Methoxyacetate buffer, 0.017–0.100 M, 30% base. [c] Extrapolated to zero buffer concentration. [d] Acetate buffer, 0.017–0.100 M, 70% base.

reactants and serves to rule out this mechanism, as shown previously for ethyl trifluorothiolacetate.[2] In the case of phenyl thioformate, there is no indication of a change in rate-determining step and acid catalysis of the rate-determining attack of water becomes apparent with increasing acidity. The change in rate-determining step for I occurs approximately one pH unit below that for ethyl trifluoroacetate, as might be expected in view of the better leaving group of the former compound; it must occur at a still lower pH with phenyl thioformate.

The rate constant for breakdown of the anionic tetrahedral addition intermediate of eq 1 is given by eq 3, in which k_{obsd} is the observed pseudo-first-order rate

$$k_2 \geq \frac{k_{obsd} a_{H^+}}{K_H K_a} \quad (3)$$

constant for hydrolysis at a given acidity, K_H is the equilibrium constant for formation of the uncharged tetrahedral intermediate from the ester, and K_a is the acid dissociation constant of this intermediate. No evidence for accumulation of an addition compound was obtained by comparison of the ultraviolet (uv) absorbance of I (or phenyl thioformate) in hexane and water. The value of the pK_a of the addition intermediate was estimated to be approximately 9 from a plot of pK_a against $\Sigma\sigma_I$ for a series of alcohols.[5] The pK_a of trifluoroacetaldehyde hydrate, $CF_3CH(OH)_2$, is 10.2.[6] If the value of K_H is assumed to be $\leq$0.1 and K_a is taken as 10^{-9}, the value of k_2 for the anionic addition intermediate formed from I is $\geq 4 \times 10^9$ sec^{-1}.[7] The magnitude of this first-order rate constant suggests that as the pH is increased the rate of diffusion-controlled protonation of the anionic intermediate will become slower than its rate of breakdown to products; *i.e.*, it will not be in equilibrium with its conjugate acid.

A change in rate-determining step occurs with increasing acidity when the addition intermediate undergoes acid-catalyzed breakdown to starting materials faster than it decomposes to products, *i.e.*,

(5) R. W. Taft, Jr., and I. C. Lewis, *J. Amer. Chem. Soc.*, **81**, 5343 (1959); P. R. Wells, *Chem. Rev.*, **63**, 171 (1963); M. Charton, *J. Org. Chem.*, **29**, 1222 (1964); R. Barnett, Ph.D. Thesis, Brandeis University, 1968.

(6) R. Stewart and M. M. Mocek, *Can. J. Chem.*, **41**, 1160 (1963).

(7) This rate constant may be calculated more exactly from the steady-state rate equation, $k_{obsd} = K_A K_H k_2 (1 + k_2/k_{-1})$ and the data of Figure 1. Note that a low value for the experimental rate constant in acid solution will give too low a value for k_2.

$k_{-1}[H^+] > k_2$. Thus, the value of k_{-1} must also be large; from the pH at which the change in rate-determining step occurs this rate constant may be estimated to be on the order of $10^9\ M^{-1}\ sec^{-1}$. These rate constants are of the magnitude expected for diffusion-controlled reactions[8] and raise the possibility that the $k_{-1} - k_1$ step might represent a diffusion-controlled proton transfer. A rate-determining proton-transfer step of this kind should exhibit general acid–base catalysis with Bronsted β values of 0 or 1.0 when the acidities of the proton donors and acceptors are sufficiently different.[8,9] The value of β for the hydrolysis of ethyl trifluorothiolacetate[2] is approximately 0.3, which means either that this hypothesis does not hold for this ester or that the observed catalytic constants represent a curved portion of the Bronsted plot. In any case, the calculations serve to emphasize the high reactivity, low stability, and short lifetime of the addition intermediate even for the hydrolysis of thiol esters of trifluoroacetate; the line between the usual type of intermediate and a series of incompletely defined way stations along the reaction coordinate at which proton transfer may occur becomes increasingly hard to draw for these reactions.

Experimental Section

Ethyl S-trifluoroacetylmercaptoacetate [bp 106–107° (60–65 mm); ir 1709, 1739 cm^{-1} in acetonitrile, λ_{max} 242 mμ in water] was synthesized[2] from ethyl mercaptoacetate and trifluoroacetic anhydride at 0°. Phenyl thioformate[10] [bp 73–75° (1.5 mm); ir 1682, 782, 728 cm^{-1} in acetonitrile; λ_{max} 230 mμ in water, 236 mμ in hexane] was prepared from benzenethiol and the mixed anhydride formed from formic acid and ethyl chloroformate.[11] Pseudo-first-order rate constants for the hydrolysis of these esters were determined spectrophotometrically as described previously.[12] Good first-order kinetics were observed for at least two half times and the total change in absorbance was approximately the same at all pH values.

Registry No.—I, 20104-50-1; phenyl thioformate, 20104-51-2.

(8) M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, **3**, 1 (1964).
(9) R. Barnett and W. P. Jencks, *J. Amer. Chem. Soc.*, **90**, 4199 (1968); **91**, 2358 (1969).
(10) G. A. Olah and S. J. Kuhn, *ibid.*, **82**, 2380 (1960).
(11) T. Wieland and H. Köppe, *Ann. Chem.*, **581**, 1 (1953).
(12) W. P. Jencks and J. Carriuolo, *J. Amer. Chem. Soc.*, **82**, 675 (1960).

Ionic and Radical Reactions in the Bromination of Butadiene

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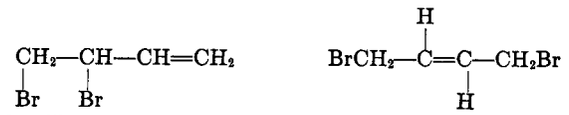
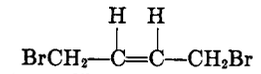
While continuing our studies on the bromination of dienes,[1] we became concerned that previous reports[1,2] which proposed ionic mechanisms in the bromination of dienes may have overlooked a possible radical component to these reactions. This concern was intensified by a report by Poutsma[3] confirming a radical route in the chlorination of butadiene at high diene concentrations. Therefore, we decided to reinvestigate the bromination of butadiene. The structures of the three possible dibromide products in this reaction are shown.





Results and Discussion

Treatment of butadiene at various concentrations in carbon tetrachloride with bromine gave **1**, **2**, and **3** in the quantities indicated in Table I. The formation of **3** was not previously reported in the bromination of butadiene. The percentages of the dibromides were determined by vpc analysis. The material balances were obtained by the internal standard method using *p*-dichlorobenzene.

TABLE I
ADDITION OF BROMINE TO BUTADIENE UNDER VARIOUS CONDITIONS

Mole fraction of butadiene	% of 1	Yield, %
Nitrogen, Safelight, − 15°		
0.020	60	
0.032	60	
0.045	56	100
0.067	51	100
0.11	45[a]	
0.39	21	100
1.0	21	
Nitrogen, Illuminated, −15°		
0.020	58	
0.045	52	80
0.067	45[a]	
0.10	34	
0.14	21	85
1.0	23	
Nitrogen, Safelight, 25°		
0.045	56	
0.10	45[a]	
0.18	37	
0.30	24	
Nitrogen, Illuminated, 25°		
0.032	41[a]	
0.045	31	
0.10	21	85

[a] Dibromide **3** first appears here in trace amounts and increases with increasing concentration of butadiene until it becomes approximately 4% at complete radical conditions.

The results in Table I show that at −15° the percentages of **1** vary from approximately 60% at low concentrations of butadiene to approximately 20% at

(1) For previous paper, see. V. L. Heasley, C. L. Frye, R. T. Gore, Jr., and P. S. Wilday, *J. Org. Chem.*, **33**, 2342 (1968).
(2) L. F. Hatch, P. D. Gardner, and R. E. Gilbert, *J. Amer. Chem. Soc.*, **81**, 5943 (1956).
(3) M. L. Poutsma, *J. Org. Chem.*, **31**, 4167 (1966).