Concurrent General Acid and General Base Catalysis in the Hydrolysis of an Imidate Ester. 3. Ethyl *N*-*p*-Nitrophenylformimidate[1]

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Abstract: The effects of general acid-base catalysis on the products of the hydrolysis of ethyl *N*-*p*-nitrophenylformimidate have been studied in aqueous solution, at 30 °C, $\mu = 0.5$. General acid catalysts promote the breakdown of a tetrahedral addition intermediate to amine and ester, while monofunctional general bases catalyze the formation of amide and alcohol. Some bifunctional catalysts (phosphate and arsenate dianions, hexafluoroacetone hydrate monoanion) accelerate the expulsion of both amine and alcohol in competing reactions. These conclusions are based on the analysis of the effects of pH variation on the efficiency of the buffer catalysis and on the maximum yields of amine obtained at constant pH with increasing buffer concentration. The observation that buffers may both increase and decrease the amine yield is explained in terms of the combined effects on the amine yield of the several buffer catalytic pathways relative to the solvent-catalyzed pathways.

The hydrolysis of imidate esters derived from *p*-nitroaniline differs from that of more basic imidates in several interesting respects: (a) with most imidates, the yield of amine decreases with increasing pH and follows a sigmoid curve characteristic of the titration of a univalent acid[2]

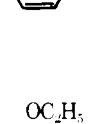
$$\text{amine yield} = [H^+]/([H^+] + K') \qquad (1)$$

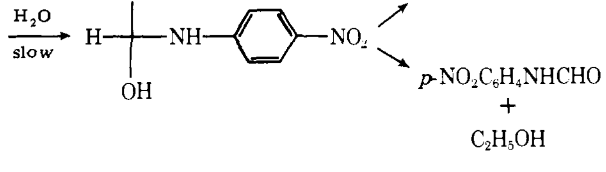
when the resident amine is *p*-nitro- (or *m*-nitro-)aniline, the amine yield is a much steeper function of pH[3]

$$\text{amine yield} = [H^+]^2/([H^+]^2 + K') \qquad (2)$$

(b) with most imidates, increasing the concentration of buffer species at constant pH increases the yield of amine, the latter approaching 100% asymptotically at high buffer concentration; with *N*-*p*-nitrophenylimidates, the maximum amine yields are often much smaller than 100%;[4] (c) increasing concentrations of amine buffers cause a *decrease* in the yield of amine formed from *N*-*p*-nitrophenylimidates, while other buffers (e.g., phosphate, acetate) *increase* the amine yield; with more basic imidates, buffers which affect the amine yield invariably cause an increase in the yield of amine.[4,5a,c,d]

The effects of variation in pH and buffer concentration on the nature of the products of imidate hydrolysis are thought to reflect the influence of specific and general acid-base catalysts on the breakdown of the tetrahedral intermediates formed by hydration of imidate esters.[1-5] Accordingly, the unusual behavior of the *N*-*p*-nitrophenylimidates suggests that the relative importance of the several pathways available for the decomposition of the derived tetrahedral intermediates is markedly different from that which obtains in the hydrolysis of more basic imidates. The experiments described in this paper were undertaken to investigate the mechanisms of acid-base catalysis in the hydrolysis of ethyl *N*-*p*-nitrophenylformimidate (eq 3). It was also desired to explore the hypothesis, suggested by the results of a limited study of this compound,[4] that there exists a fundamental difference in the interaction of the tetrahedral intermediate of eq 3 with bifunctional as compared to monofunctional catalysts, the presence of the former resulting in an increase of amine yield, while the latter cause a decrease in the yield of amine.





(3)

Results

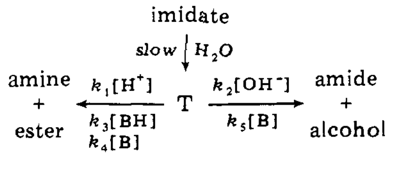
At pH >5 and at zero buffer concentration (30 °C, 2% CH_3CN-H_2O, $\mu = 0.5$ with added KCl), the hydrolysis of the imidate ester obeys the rate law[3]

$$k_{\text{obsd}}(\text{s}^{-1}) = 4.4 \times 10^4[H^+] + 0.51[OH^-] + 1.4 \times 10^{-4} \qquad (4)$$

Spectrophotometric assay for *p*-nitroaniline after 6 or more half-lives of hydrolysis indicates that, at zero buffer concentration, the amine is formed in 100% yield at pH <4 and in <3% yield at pH >7.[6] The sharp decrease in amine yield at intermediate pH conforms well to eq 2, with a midpoint at pH 5.7.[3] As with many other imidates, the change in the products of hydrolysis occurs in a pH range where there is no concomitant change in the rate law (at pH 7, 97% of the reaction still occurs via hydronium ion catalysis), indicating that the product-forming steps are distinct from the rate-determining step.

Increasing buffer concentration at constant pH may result either in an increase or in a decrease in the yield of *p*-nitroaniline (Figure 1). The observation that, depending on pH, hexafluoroacetone hydrate can cause either an increase or a decrease in amine yield (Figure 1B) shows that buffers cannot be simply classified into two groups, i.e., those that increase and those that decrease the yield of amine. The curves that describe the variation of amine yield with increasing buffer concentration are rectangular hyperbolas, which were analyzed with reference to the mechanism of Scheme I. This scheme differs from that previously used[1,5d] with other imidates in two

Scheme I



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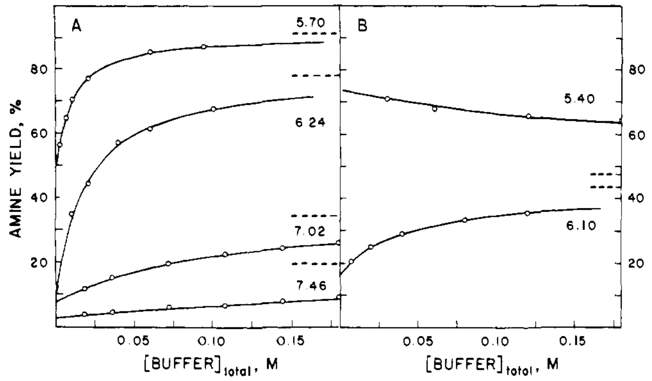


Figure 1. Effect of buffers on yield of *p*-nitroaniline formed on hydrolysis of imidate ester. pH is shown for each set. Dashed lines represent the yield of *p*-nitroaniline extrapolated to infinite buffer concentration. Solid lines are calculated from the equation for a rectangular hyperbola, using values of K_{app} and of amine yield at infinite buffer concentration listed in Table I: A, phosphite (for the experiment at pH 5.70, all solutions contain 0.012 M pyridine buffer); B, hexafluoroacetone hydrate.

aspects: (a) in the absence of buffer, the expulsion of amine from the neutral tetrahedral addition intermediate T requires catalysis by hydronium ion; (b) the breakdown of the neutral intermediate both to amine and to amide products is subject to catalysis by general bases (B). The first provision is required because the transition from amine to amide product depends on $[H^+]^2$, i.e., the compositions of the transition states leading to amine and to amide products differ by two protons. The assumption that general acid-base catalysis may occur in the formation of both products accounts for the observation that the limiting yields of amine obtained at high buffer concentration are frequently much less than 100% (Figure 1).

Application of the steady-state approximation to T gives the equation

mole fraction amine =

$$\frac{\dfrac{([H^+] + K_a)k_1[H^+]}{k_3[H^+] + (k_4 + k_5)K_a} + \dfrac{k_3[H^+] + k_4K_a}{k_3[H^+] + (k_4 + k_5)K_a}[B]_T}{\dfrac{([H^+] + K_a)(k_1[H^+] + k_2[OH^-])}{k_3[H^+] + (k_4 + k_5)K_a} + [B]_T} \tag{5}$$

for the dependence of amine yield on pH and on the total concentration $[B]_T$ of a buffer whose acid dissociation constant is K_a.[7] The constant K_{app}, which is given by the left-hand term in the denominator of eq 5, is equivalent to the buffer concentration which produces half the maximum increase (or decrease) in amine yield and is a direct measure of the relative efficiency of buffers in catalyzing the breakdown of the tetrahedral intermediate. Values of K_{app} for a series of buffers were calculated from data such as those of Figure 1 by a least-squares computer fit to the rectangular hyperbola,[5d,8] and are listed in Table I, where are also given the maximum (or minimum) values of amine yield reached at infinite buffer concentration. At zero buffer concentration, the amine yield follows the equation

$$\text{mole fraction amine} = \frac{[H^+]^2}{[H^+]^2 + (k_2K_w/k_1)} = \frac{[H^+]^2}{[H^+]^2 + K'} \tag{6}$$

where K_w is the ion product of water. The inflection point of the sigmoid curve which relates amine yield to pH occurs at pH 5.7, and yields $K' = 4.0 \times 10^{-12}\ M^2$.[3]

The ability of buffers to catalyze product formation from the tetrahedral intermediate is pH dependent. The expression

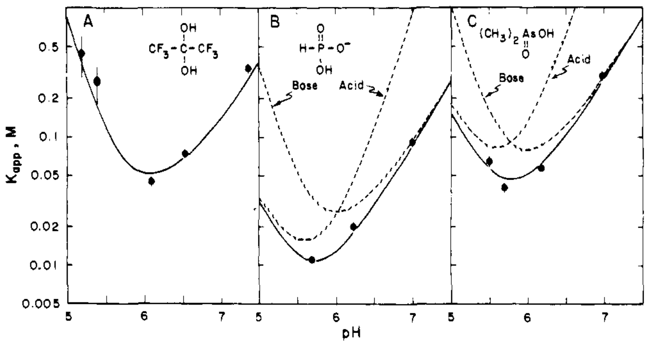


Figure 2. pH dependence of the effectiveness of buffers in catalyzing the formation of *p*-nitroaniline in imidate hydrolysis: A, hexafluoroacetone hydrate; B, phosphite; C, cacodylate. Solid curves are calculated from eq 7, using constants of Table II. Dashed curves are for acid or base catalysis only, and are calculated from eq 7, with k_A and $k_{AH} = 0$, respectively. The solid curve for hexafluoroacetone is for base catalysis only.

for K_{app} may be rearranged to

$$K_{\text{app}} = \frac{k_1}{k_3}\left(\frac{[H^+]^2 + K'}{[H^+]}\right)\left(\frac{[H^+] + K_a}{[H^+] + (k_4 + k_5)K_a/k_3}\right)$$

$$= \left(\frac{1}{k_{AH}}\right)\left(\frac{[H^+]^2 + K'}{[H^+]}\right)\left(\frac{[H^+] + K_a}{[H^+] + k_AK_a/k_{AH}}\right) \tag{7}$$

where K' and K_a are known. The values of the constants k_{AH} and k_A for general acid and general base catalysis, respectively, are obtained by fitting data such as shown in Figure 2 to eq 7, and are listed in Table II. These terms express buffer catalytic ability *relative* to the hydronium ion catalyzed expulsion of amine from the tetrahedral intermediate. The dashed lines in Figure 2 represent the contributions of general acid and general base catalysis to product formation, regardless of whether the product is amine or amide. The intersection point of the dashed lines is the pH value where acid and base catalysis contribute equally to product formation, and is given by the expression $pH = pK_a - \log (k_A/k_{AH})$.

With the exception of hexafluoroacetone hydrate, the limiting yields of amine reached at high buffer concentration vary with pH (Table I and Figure 1). Extrapolation of eq 5 to infinite buffer concentration shows that the dependence of the maximum (or minimum) yields on pH should follow a simple sigmoid curve

limiting mole fraction of amine

$$= \frac{[H^+] + k_4K_a/k_3}{[H^+] + (k_4 + k_5)K_a/k_3} \tag{8}$$

with an inflection point at $pH = pK_a - \log (k_A/k_{AH})$, which is identical with the pH value where the conjugate acid and base forms of the catalyst make equal contributions to the formation of the hydrolysis products.

With arsenate buffer, the plot of maximum amine yield vs. pH accurately follows a sigmoid curve (Figure 3A) and approaches a limiting value of 38% amine at high pH. A similar dependence of maximum amine yield on pH was previously reported[4] for phosphate buffer catalysis, in which case the limiting yield at high pH was 27% amine. With some of the other buffers studied, insufficient data were available to rigorously establish the conclusion that the plots of maximum (or minimum) amine yield vs. pH were sigmoid; in these cases, it was assumed that the amine yields were 100 and 0% at low and high pH, respectively, and the sigmoid curve which best correlated the data was constructed between these limits (Figure 3). In the case of phosphite, the agreement is quite good, and offers support for the assumption that the amine yield approaches zero at high pH (i.e., $k_5 \gg k_4$).

Table I. Buffer Catalysis of Amine Formation in Imidate Hydrolysis[a]

buffer	pH[b]	concn range, M	A_{max}, %[c,k] (A_{min})	K_{app}, M[d,k]
pyridine	4.97	0.008-0.16	(64 ± 10)	0.36 ± 0.21
(py)	5.76	0.008-0.16	(35)	0.059 ± 0.008
	5.98	0.008-0.16	24[e]	
acetic acid	5.81	0.016-0.40	88.6 ± 0.6	0.12 ± 0.01
(AA)	6.15	0.03-0.30	75.5 ± 1.1	0.24 ± 0.01
	6.68[f]	0.0-0.40	33 ± 4	0.64 ± 0.13
cacodylic	5.51	0.006-0.30	88.5 ± 0.8	0.063 ± 0.008
acid	5.70	0.008-0.2	73.3 ± 0.5	0.038 ± 0.003
(CD)	6.18	0.004-0.2	61.6 ± 0.6	0.055 ± 0.002
	6.98[g]	0.016-0.4	33 ± 1	0.28 ± 0.03
phosphite	5.70[h]	0.0-0.094	91.3 ± 0.2	0.010 ± 0.001
(PF)	6.24	0.01-0.10	79.3 ± 1.5	0.020 ± 0.001
	7.02	0.018-0.18	35.6 ± 0.4	0.090 ± 0.003
	7.46	0.018-0.18	19.2	0.31
hexafluoroacetone	5.20	0.04-0.40	(46 ± 8)	0.44 ± 0.16
hydrate	5.40	0.02-0.20	(49 ± 4)	0.26 ± 0.06
(HFA)	5.40	0.03-0.30	(48 ± 5)	0.27 ± 0.09
	5.75	0.006-0.10	50[e]	
	6.10	0.008-0.20	43.3 ± 0.5	0.045 ± 0.003
	6.53	0.008-0.20	44.1 ± 0.7	0.072 ± 0.003
	7.37[i]	0.008-0.20	42 ± 3	0.34 ± 0.04
arsenate	6.65	0.003-0.15	78 ± 0.6	0.029 ± 0.001
(ANA)	7.14	0.008-0.20	61 ± 0.6	0.078 ± 0.002
	7.52	0.015-0.30	52 ± 2	0.17 ± 0.01
	7.93	0.04-0.40	49 ± 2	0.36 ± 0.03
phenylphosphonate	5.96[j]	0.0008-0.18	90 ± 1	0.0083 ± 0.0006
(PP)	6.75	0.008-0.20	69 ± 1	0.049 ± 0.003
	7.35[i]	0.008-0.20	49 ± 2	0.19 ± 0.02
selenite	5.90[j]	0.012-0.24	93.3 ± 0.7	0.040 ± 0.002
(SE)	6.04[f]	0.004-0.16	79 ± 1	0.038 ± 0.002
	7.05	0.008-0.16	70 ± 3	0.25 ± 0.02
	7.67	0.02-0.20	43 ± 14	0.57 ± 0.26

[a] At 30 °C, 1% CH_3CN-H_2O, $\mu = 0.5$ (KCl). [b] ±0.02, except where indicated. [c] Maximum or minimum yield of amine obtained by extrapolation to infinite buffer concentration. [d] For definition, see text. [e] No change in yield over concentration range used. [f] In the presence of 0.012 M 3,4-lutidine buffer. [g] ±0.05. [h] In the presence of 0.012 M pyridine buffer. [i] ±0.03. [j] In the presence of 0.006 M 3,4-lutidine buffer. [k] Standard deviation is given.

Table II. Constants for General Acid and General Base Catalysis of Product Formation in Imidate Hydrolysis

buffer	pK_a	10^4k_{AH}[a]	10^4k_A[b]
acetic acid	4.60	2.20	0.22
cacodylic acid	6.18[c]	0.63	1.6
phosphite	6.20[d]	3.4	5.0
hexafluoroacetone hydrate	6.46[c]	*e*	3.6 (1.5 + 2.1)[f]
arsenate	6.60[d]	4.1	8.2 (3.1 + 5.1)[f]
phenyl-phosphonate	6.93[d]	6.4	3.2
selenite	8.02[d]	1.3	8.4
phosphate[g]	6.60[d]	8.2	5.7 (1.5 + 4.2)[f]

[a] $k_{AH} = k_3/k_1$. [b] $k_A = (k_4 + k_5)/k_1$. [c] For conversion of neutral species to monoanion. [d] For conversion of monoanion to dianion. [e] Not observed. [f] The first term in parentheses is k_4/k_1 and the second term is k_5/k_1. [g] Data taken from ref 4.

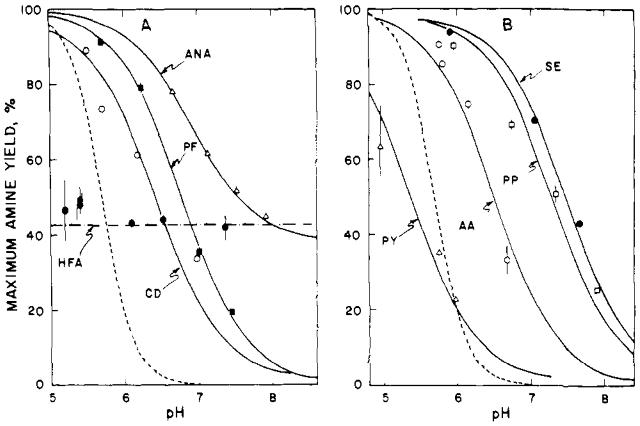


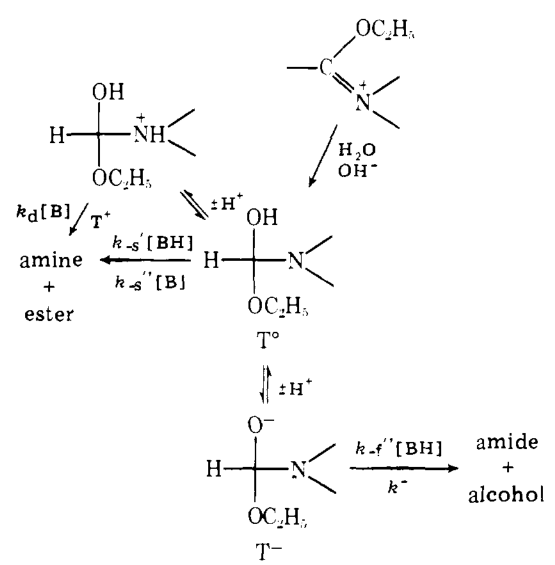
Figure 3. pH dependence of the yield of *p*-nitroaniline, extrapolated to infinite buffer concentration, in imidate hydrolysis. Solid lines are simple sigmoid curves (eq 1) with asymptotes at 100 and 0% amine, except for arsenate (ANA), where the limiting amine yield at high pH is 38%. Dashed sigmoid curves represent the effect of pH on the amine yield at zero buffer concentration (eq 2). Abbreviations are listed in Table I.

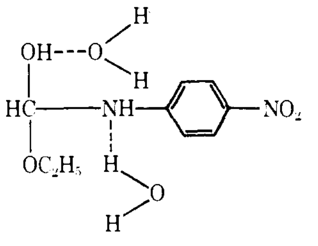
For those buffers where the limiting amine yield at high buffer concentration and high pH is significantly greater than zero, the term k_A for general base catalysis can be separated into its components k_4/k_1 and k_5/k_1, which describe respectively general base catalysis of amine expulsion and general base catalysis of alcohol expulsion from the tetrahedral intermediate (Table II).

Discussion

It is well established that general acid-base catalysts influence the breakdown of the tetrahedral intermediates generated either by the hydration of imidate esters[1,2,4,5] or in related acyl transfer reactions, such as the aminolysis of esters[9] and the alcoholysis of amides.[10] These effects manifest themselves as changes in the product distribution in imidate hydrolysis, and as rate increases in acyl transfer reactions. In most instances, general acids and bases mainly catalyze the expulsion of amine from the tetrahedral intermediate, so that at high buffer concentration the imidate ester is completely converted to amine (and ester); in the related acyl transfer reaction, predominant or exclusive expulsion of the amine leads

Scheme II





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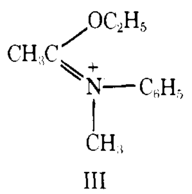
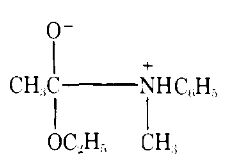


III

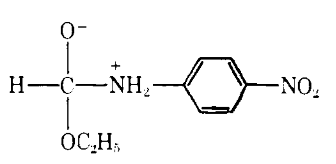
to hyperbolic plots of observed rate constant vs. buffer concentration, i.e., the reaction rate becomes independent of buffer concentration as the rate of expulsion (and of addition) of the amine becomes faster than some other (uncatalyzed) step on the reaction pathway. Evidence that *both* formation and breakdown of a tetrahedral intermediate may be subject to general acid-base catalysis has been reported in a few cases of ester aminolysis or amide alcoholysis.[9a,10b] It would be expected, then, that, at least for some imidate esters, buffers would catalyze the departure of both amine and alcohol from the tetrahedral intermediate, so that the hydrolysis product reached asymptotically at high buffer concentration would consist of a mixture of amine (ester) and amide (alcohol). Though detailed studies of the mechanism of general acid-base catalysis in the hydrolysis of imidate esters have been reported, these were limited to reactions where buffer catalysis of the breakdown of the tetrahedral intermediates occurred with essentially quantitative expulsion of amine.[1,5c,d]

The principal features of the mechanism (Scheme II) proposed to account for the effects of acid-base catalysis on the products of the hydrolysis of ethyl *N*-*p*-nitrophenylformimidate are as follows. Rate-determining hydration of the protonated imidate yields a neutral tetrahedral intermediate T^0 which is in acid-base equilibrium with cationic [T^+] and anionic [T^-] species. In the absence of buffer species, the sole precursor of amine is T^+, while the cleavage of T^- yields exclusively the amide. Monofunctional general acids catalyze the conversion of the tetrahedral intermediate to amine (step k_d),[19] while monofunctional general bases catalyze the breakdown of the intermediate to alcohol and amide (step k_{-f}''). Bifunctional general acids accelerate the expulsion of amine from the intermediate (k_{-s}') while bifunctional general bases catalyze the expulsion of both amine and alcohol in competing reactions (k_{-s}'', k_{-f}'').

In the absence of buffers, the dependence of amine yield on the square of the hydrogen ion concentration (eq 6) reflects the fact that the decomposition of T^0 to products cannot compete with the lower energy pathways via T^+ and T^-. Arguments have been presented to the effect that the zwitterionic intermediate Ia may be too unstable to exist;[1] owing to its much better leaving group, the zwitterionic species Ib would be even less likely to have a finite lifetime. Considering a possible concerted water-catalyzed breakdown of T^0 to amine (transition state II), the lowered basicity of the nitrogen atom of T^0 should be offset in part by the better leaving ability of *p*-nitroaniline (as compared to *N*-methylaniline) and by the somewhat higher acidity of the hydroxyl proton. The same reasoning applies to the pathway for amine formation via T^+: the effect of the much lower concentration of T^+ (pK_a for the process $T^+ \rightleftharpoons T^0 + H^+$ is estimated to be −3.6,[11] as compared to pK_a = 1.1[17] for T^+ derived from imidate III) should be partly compensated by the greater reactivity of T^+. It is not clear how the interplay of these various factors results in the choice of T^+ (or of some kinetic equivalent) as the favored pathway for amine formation from the *p*-nitrophenylimidate.



Ia

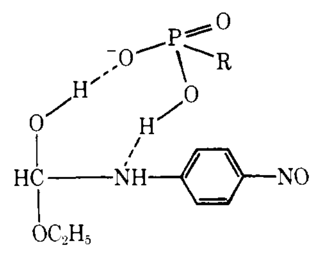


Ib

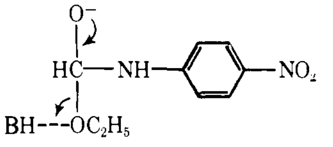
Use was made of Scheme I and the derived eq 7 to separate the observed buffer catalysis into its general acid and general base components (expressed formally in terms of the reaction of the catalyst with the neutral tetrahedral intermediate). Scheme I predicts that the dependence of K_{app} on pH will exhibit a minimum, i.e., a pH range of maximum buffer catalysis. Put another way, the neutral intermediate which is the species susceptible to buffer catalysis is diverted into hydronium and hydroxide ion catalyzed reactions, at low and high pH, respectively. In contrast, K_{app} for buffer catalysis in the hydrolysis of III generally approaches a low and constant value at acidic pH, owing to the absence of a competing specific-acid-catalyzed process.[5d] The anticipated minimum in K_{app} is shown by hexafluoroacetone hydrate and cacodylic acid (Figures 2A and 2C). Other buffers could not readily be studied at pH values low enough for K_{app} to reach a minimum value, owing largely to the high amine yields formed in the absence of buffer at pH ≤5.5; with pyridine and imidazole,[4] K_{app} *decreases* with increasing pH, so that the expected minimum value of K_{app} probably occurs at somewhat higher pH than studied.

The general-acid-catalyzed reaction (expressed in terms of the neutral intermediate) appears to proceed predominantly or exclusively with formation of amine and ester. For several of the catalysts studied, the extrapolated maximum yields at low pH are 90–95%, and fall well on plots of maximum yield vs. pH which reach 100% in the limit at acidic pH (Figure 3). This apparent general acid catalysis is proposed in Scheme II to consist of the kinetically indistinguishable general-base-catalyzed breakdown of T^+. Evidence for such a pathway has been obtained in the hydrolysis of other imidate esters.[5c,d] That proton abstraction from T^+ is concerted with the cleavage of the C–N bond is supported by the considerations cited above concerning the nonexistence of the zwitterion $T^{\pm}$ as a discrete species.

With the exception of pyridine and hexafluoroacetone, the conjugate acid forms of the buffers used are bifunctional and could conceivably act on T^0 via a mechanism (IV) involving concerted proton donation and abstraction, though insufficient data with monofunctional catalysts are available to establish whether bifunctional catalysts are more reactive than mono-



IV



V

functional catalysts of the same pK_a.

The (formal) reaction of general bases with the neutral intermediate results mainly in the formation of amide and alcohol. With the exceptions of phosphate[4] and arsenate dianions and of the monoanion of hexafluoroacetone hydrate (which are discussed below), the plots in Figure 3 show that the maximum amine yields decrease steadily with increasing pH and appear to approach a limiting value of zero at high pH. General-acid-catalyzed cleavage of T^- represents a kinetically equivalent possible mechanism for the general-base-catalyzed breakdown of the neutral intermediate (V).

It has been suggested in Scheme II that general acid catalysis leads solely to expulsion of amine while (monofunctional) general base catalysis results in the departure of the alcohol. If this view is correct, then it follows from eq 7 and 8 that the inflection point of the sigmoid curves of Figure 3 should occur precisely at the pH where the contributions of the general acid and the general base pathways to the overall buffer catalysis are equal. The latter pH value is shown in Figure 2 as the intersection of the dashed lines which represent the separate contributions of general acid and general base catalysis. In some cases (phosphite, phenylphosphonate, selenite) the agreement is quite good, the difference between the two pH values being less than 0.3 pH units, which is well within the estimated experimental error. Though the agreement is less satisfactory with the other buffers used (e.g., cacodylic acid shows a difference of 0.6 units between the two pH values), it is probable that this imprecision reflects the well-known difficulties in calculating a "pK" value using three or four scattered points, rather than the operation of some other mechanism.

The maximum amine yields obtained with arsenate and phosphate buffers exhibit a sigmoid dependence on pH, but do not decrease to zero at the high pH limit. The conjugate bases of both these buffers are bifunctional, and may interact with the intermediates via two competing transition states. A cyclic proton transfer similar to IV would lead to amine formation, while a process such as V would result in the expulsion of the alcohol. The observation that phosphate and arsenate dianions are nearly as effective as the corresponding monoanions in catalyzing the cleavage of the intermediate to amine suggests that these dianions, and probably also all the bifunctional general acids listed in Table II, act via cyclic, bifunctional mechanisms. Previous studies[1,18] have shown that bifunctional catalysis of similar reactions exhibits little dependence on the pK of the catalyst, while simple general acid catalysis, especially with weakly acidic buffers (pK_a for HPO_4^{2-} acting as an acid is 12.5), is steeply dependent on catalyst pK.[5c,d,12,18]

Hexafluoroacetone hydrate monoanion has been found to be an effective bifunctional catalyst,[1] and in the present case appears to behave with equal facility as a bifunctional acid and as a monofunctional base. The resulting maximum amine yield is essentially constant at 46 ± 3% over the pH range studied. This invariance in the maximum yield of amine (Figure 3) is in accord with the finding that the sole reactive species of this catalyst is the conjugate base form (Figure 2A); a change in the maximum amine yield with changing pH is expected only if there occurs a change in the mechanism of buffer catalysis over that pH range.

The observation that some buffers cause an increase in the yield of amine produced in the hydrolysis of the imidate ester while others decrease the amine yield is not the result of some fundamental difference in catalytic mechanism, such as between bifunctional and monofunctional catalysis. Rather, it reflects the interplay of the buffer catalytic constants *relative* to the solvent-catalyzed reactions. The case of hexafluoroacetone is particularly illuminating. As the result of an invariant mechanism in the range of pH 5.2–7.4, the maximum yield of amine remains constant at about 46%. In the same pH range, the amine yield at zero buffer concentration varies from 90 to about 0% (Figure 3A, dashed line), the two lines intersecting at pH 5.7. Clearly, at pH <5.7, the addition of hexafluoroacetone buffer will cause a decrease in amine yield, while an increase in amine will occur at higher pH. At pH 5.7, there will be no observable buffer effect on the amine yield, not because the buffer has suddenly lost its catalytic properties, but simply because the rates of formation of the two products in the buffer-catalyzed reaction are in the same ratio as in the solvent-catalyzed reaction.

The position along the x axis of the sigmoid curve which describes the dependence of the maximum amine yield on pH (Figure 3) is determined by the pK_a and the ratio of the values of k_{AH} and k_A for the given buffer. It is this position relative to the line which relates yield of amine to pH in the absence of buffer (Figure 3, dashed lines) that determines whether a given buffer will cause an increase or decrease in amine yield. Buffers whose sigmoid curve is located entirely to the left of the dashed curve will cause exclusively a decrease in amine yield with increasing buffer concentration, while the converse holds for buffers whose variance in maximum amine yield occurs completely to the right of the dashed line. Both decreases and increases in amine yield will be seen with buffers whose maximum yield curve crosses the dashed line. A probable example of the latter behavior is found with pyridine (Figure 3B), which causes decreases in amine yield at pH 4.97 and 5.76, but has no effect at pH 6, where the two curves intersect. Small increases in amine yield were observed at higher pH, but were not analyzed quantitatively since they could not be easily corrected for possible nonspecific solvent effects. It should be noted that, even if the sigmoid maximum yield curve for a buffer crosses the solvent curve (dashed line) precisely at the midpoint of the latter (pH 5.7), the two curves will not be superimposable, since the buffer curve is a simple sigmoid function of pH (eq 8) while the pH dependence of the amine yield in the absence of buffer obeys the steeper pH function of eq 6.

Experimental Section

Ethyl *N*-*p*-nitrophenylformimidate[3] was recrystallized from benzene and had mp 68–69 °C; UV max (CH_3CN) 311 nm (ϵ_{max} 13 300). Other chemicals were obtained from commercial sources and were purified as previously described.[1,5d]

Product Analysis. The yield of *p*-nitroaniline produced on hydrolysis of the imidate (1% CH_3CN-H_2O, 30 °C, ionic strength 0.5, maintained with added KCl) was determined at completion of reaction from the absorbance at 380 nm (*p*-nitroaniline, ϵ 13 000; *p*-nitroformanilide, ϵ 840). With each buffer, standard solutions containing known concentrations of *p*-nitroaniline were used.

In early experiments, it was noted that stock solutions of the imidate in acetonitrile underwent slow decomposition, with the formation of up to 5–10% of *p*-nitroaniline after a period of 1 week. When care was taken to rinse glassware (previously exposed to sulfuric acid-potassium dichromate cleaning solution) with dilute aqueous sodium bicarbonate solution, the appearance of *p*-nitroaniline in the stock solution was greatly reduced.

The procedure used in a typical experiment is as follows. A 5-mL sample of aqueous buffer solution was placed in a capped test tube and kept in a constant-temperature water bath at 30 °C. After temperature equilibration, 50 μL of the stock solution of the imidate ester (0.01 M) in acetonitrile was added to the buffer solution by means of a Gilson Pipetman adjustable pipet (delivery range 0-200 μL). The reaction mixture was thoroughly stirred and kept at 30 °C for at least 10 half-lives of reaction before assay.

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(6) In an earlier study,[3] hydrolysis at acid pH gave *p*-nitroaniline in about 90% yield, possibly owing to partial decomposition of this fairly unstable imidate ester in the solid state or in the acetonitrile stock solution.
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C-C Bond Homolysis in $(CF_3S)_3C-C(SCF_3)_3$ at Room Temperature. Thermodynamic, Kinetic, and Electron Spin Resonance Results[1]

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Abstract: In benzene solution at 10-60 °C $(CF_3S)_3C-C(SCF_3)_3$ undergoes a reversible homolytic C-C cleavage reaction to yield $(CF_3S)_3\dot{C}$ radicals which were identified by ESR. From the dependence of the stationary concentration of $(CF_3S)_3C$ on temperature the C-C bond dissociation energy is determined to be 13.7 kcal/mol. At 30 °C the equilibrium constant for C-C homolysis is 7.5×10^{-10} M. The change in free entropy occurring on C-C homolysis corresponds to 3.6 eu. The activation energy and entropy for C-C bond cleavage are 21.0 kcal/mol and 7.5 eu, respectively. The experimental results concerning the facile C-C homolysis are interpreted essentially in terms of sterically induced destabilization of the C-C bond in $(CF_3S)_3C-C(SCF_3)_3$.

Since the discovery by Lankamp, Nauta, and MacLean in 1968 that the triphenylmethyl radical on dimerization does not yield hexaphenylethane but a cyclohexadiene-type compound,[4] attempts have been made[5-9] to produce true ethanes that—by virtue of their voluminous or radical-stabilizing substituents—tend to undergo facile C-C homolysis at relatively low temperatures. As shown by Seebach et al.[6,7] with hexakis(aryl- or alkylthio)ethanes, homolytic dissociation of the C- C bond is detectable in the temperature range 55-110 °C.[10]

During systematic investigations of the photochemistry of perfluorothioketones, $(CF_3S)_2CS$ was also irradiated. During this photolysis, besides 1,1,3,3-tetrakis(trifluoromethylmercapto)thiirane and $CF_3S_nCF_3$, $(CF_3S)_3CC(SCF_3)_3$[11] was also formed. The present paper describes thermodynamic and kinetic results concerning the homolysis of hexakis(trifluoromethylmercapto)ethane in solutions near room temperature.

Experimental Section

A. Materials. Hexakis(trifluoromethylmercapto)ethane. In a quartz vessel equipped with stirrer and condenser, a solution of 9.8 g (0.04 mol) of $(CF_3S)_2CS$[12] in 400 mL of hexane was irradiated for 10 h at reflux temperature in a Rayonet photoreactor with UV light of 300 nm. The photolysis reaction was controlled by analyzing samples for the amount of unreacted starting material using the 500-nm band of $(CF_3S)_2CS$ for detection. The reaction was stopped at 90% conversion of $(CF_3S)_2CS$. On cooling to −70 to −80 °C white crystals of $(CF_3S)_2CC(SCF_3)_3$ deposited. After filtration the crystals were washed with hexane and recrystallized from ether: yield 1.6 g (18%); mp 129-130 °C (sealed tube); sublimation at 90 °C; IR (RbBr pellet) 1210 (s), 1170 (vs), 1085 (vs), 761 (s), 747 (m), 620 (w), 560 (w), 556 (m), 546 (m), 468 (m), 445 (w), 425 (m), 355 (m), 335 cm^{-1} (vw); ^{19}F NMR (in 90% CCl_3F) (CF_3) 36.9 ppm. Anal. Calcd for $C_8F_{18}S_6$: C, 15.13; S, 30.34. Found: C, 15.24; S, 30.51.

Benzene (Uvasol, Merck) was dried with sodium and used without further purification. Nitrogen and argon (99.997%) were purified with Oxisorb filters (Messer-Griesheim) (after purification O_2 content <0.1 vpm; H_2O content 0.5 vpm). Galvinoxyl (Aldrich) was recrystallized from carbon tetrachloride and stored at −30 °C under nitrogen. 2-Phenylbis(biphenylene)allyl[13] was recrystallized from benzene and isolated as a 1:1 adduct with benzene. For galvinoxyl and 2-phenylbis(biphenylene)allyl the free-radical content was determined spectrophotometrically using previously reported extinction coefficients.[13,14]

B. ESR Measurements. The ESR measurements were performed using a Varian E-9 ESR spectrometer with a variable-temperature unit. For double integration of the spectra the ESR spectrometer was connected to a DEC PDP 10 computer. The doubly integrated spectra of $C(SCF_3)_3$ in benzene[15] were compared with corresponding data

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