# THE SPONTANEOUS AND ACID-CATALYSED HYDROLYSIS OF THIOLCARBOXYLIC ACIDS

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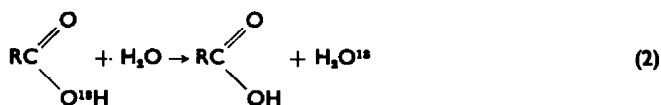
Abstract—The kinetics of the spontaneous and the acid-catalysed hydrolyses of thiolacetic and thiolbenzoic acid have been studied and the data compared with those for the corresponding oxygen exchange processes of their oxygen analogues. The thiol acids appear more susceptible to spontaneous hydrolysis, but less susceptible to the acid-catalysed route, than do their oxygen analogues. These results support our previous generalizations about acylation. Under all conditions thiolbenzoic acid is hydrolysed more slowly than thiolacetic acid and for both compounds the rate of the acid-catalysed reaction is linearly dependent on $[H_3O^+]$. The acid-catalysed route has a bimolecular slow step and for thiolacetic acid $E_a = 16\cdot2$ Kcals mole^{-1} and $\Delta S = -25$ e.u. The spontaneous reaction is subject to a negative, and the acid-catalysed reaction to a positive, salt effect. The latter result is a further point of contrast to the behaviour of the oxygen analogues.

The hydrolysis of a thiolcarboxylic acid leads to the oxygen analogue (1). There has been very little kinetic study of this topic. Extant work refers only to thiolacetic acid (TAA). Sumner and Wadso[1] have shown qualitatively that the reaction of TAA

$$RC\!\!\diagup\!\!\!\diagdown\!\!\!\!\!\!\!\!\!{}^{O}_{SH} + H_2O \rightarrow RC\!\!\diagup\!\!\!\diagdown\!\!\!\!\!\!\!\!\!{}^{O}_{OH} + H_2S \tag{1}$$
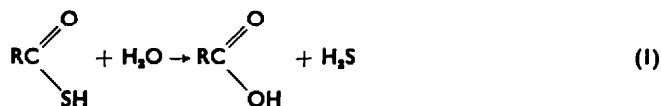
with water is slow at normal temperatures, but that it is catalysed by added mineral acid. The only other available study concerns basic solutions where it is thought[2] that the thiolacetate ion engages in a slow, bimolecular reaction with the hydroxide ion. In this paper we report work on the spontaneous and the acid-catalysed hydrolyses of TAA and thiolbenzoic acid (TBA). The work had two objects: (i) to supplement the few available data, and (ii) to permit a comparison of the reactivities of corresponding sulphur and oxygen compounds towards hydrolysis. Hydrolysis of the oxygen compounds—the common carboxylic acids—is normally called oxygen exchange because it is followed by isotopic labelling (2). Data on the rate of this reaction and/or its susceptibility to acidic catalysis is available[3,4] for the acids acetic,

$$RC\!\!\diagup\!\!\!\diagdown\!\!\!\!\!\!\!\!\!{}^{O}_{O^{18}H} + H_2O \rightarrow RC\!\!\diagup\!\!\!\diagdown\!\!\!\!\!\!\!\!\!{}^{O}_{OH} + H_2O^{18} \tag{2}$$

[1] S. Sumner and I. Wadso, Trans. Farad. Soc. 53, 445 (1957).
[2] M. Cefola, Sr. S. Peter, P. S. Gentile and A. Celiano, Talanta 537 (1960).
[3] D. R. Llewellyn and C. O'Connor, J. Chem. Soc. 545 (1964).
[4] C. A. Bunton, D. H. James and J. B. Senior, J. Chem. Soc. 3364 (1960).

pivalic and benzoic. We have recently argued[5],[6] that in comparisons of the reactivities of sulphur and oxygen compounds—at least in those reactions in which bond-breaking is at all important—the sulphur analogue should react the faster because it contains the better leaving group. For the same reason—the less nucleophilic character of its leaving group—the sulphur compound should be the less susceptible to acidic catalysis.

Spontaneous hydrolysis of TAA

Since TAA hydrolyses comparatively slowly, a reaction temperature of 70° was chosen to provide convenient rates. The initial stoicheiometric concentration of the acid was always kept below 0·1 M to minimize medium effects. A range of initial concentrations below 0·1 M were studied (Table 1) and because the pKa of TAA has

TABLE 1. Spontaneous hydrolysis of TAA at 70°
k_{obs}, k_2 as in text; square brackets represent molarity throughout.

$10^2[CH_3COSH]_{initial}$	$10^5 k_{obs}$	$10^4[H_3O^+]$	$10^5 k_2$
0·14	1·05	1·1	5·4
0·16	1·1	1·3	5·3
0·69	2·4	3·6	5·5
0·77	3·6	4·1	7·6
5·6	6·6	14	8·8
7·3	6·8	16	8·7
17·0	7·8	26	9·2
60·0	9·8	51	10·7

the value 4·7 it was appreciably dissociated in the reaction mixtures. This meant that there were two species (CH_3COSH and CH_3COS^-) available for hydrolysis. However, the pH of the solutions was, of course, always <7 and examination of the available data[2] for the hydrolysis of CH_3COS^- at 70° shows that its rate of reaction at such a pH is negligible compared with our observed rates. It follows that the undissociated acid is effectively the only species undergoing hydrolysis under our conditions.

The dissociation of the thiol acid in the reaction mixtures leads to complications in the kinetic form of the reaction. This is because the extent of dissociation depends on the hydrogen ion concentration, and this concentration changes (slightly) as the hydrolysis proceeds, since the products (acetic acid and hydrogen sulphide) are

$$CH_3C{\overset{O}{\underset{SH}{\big\langle}}} + H_2O \rightarrow CH_3COOH + H_2S \qquad (3)$$
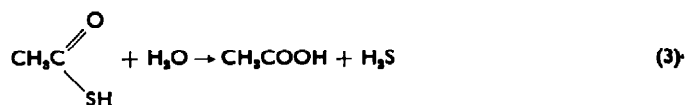
somewhat weaker acids than the thiol acid starting material. As the hydrogen ion concentration falls, the ratio $[CH_3COS^-]/[CH_3COSH]$ will increase, and the observed rate of reaction (which, as noted, occurs via CH_3COSH only) will therefore fall more rapidly than it would have done had this ratio stayed constant. Were the ratio to stay constant throughout the hydrolysis (i.e. were the pH to remain fixed)

[5] D. P. N. Satchell, *Quart. Rev.* **17**, 160 (1963).
[6] J. Hipkin and D. P. N. Satchell, *J. Chem. Soc.* in the press (1965).

then, for a given initial stoicheiometric concentration of thiol acid, the free CH_3COSH would, at any time, be a fixed fraction of the measured quantity (Experimental), the total thio species still present, i.e. of $[CH_3COSH]_{stoich} = ([CH_3COSH] + [CH_3COS^-])$, and a first-order loss of $[CH_3COSH]_{stoich}$ might be expected. In practice it is found that the first-order plots begin to exhibit detectable curvature after about 1·3 half-lives, the curvature being in the direction of slower reaction. The curvature is rather slight—which implies a small change in the pH during reaction—and reasonably accurate first-order constants (k_{obs}) can be calculated from the initial straight portion of the plots. (Values determined this way were reproducible to ±5%.) That the curvature *is* due to the changing nature of the acidic and basic species present during hydrolysis, and not to an other than first-order loss of thiol species, is shown by the accurately first-order nature of the process over several half-lives in buffer solutions, or in the presence of added mineral acid (see below).

Table 1 contains values of k_{obs} obtained at various initial stoicheiometric TAA concentrations. It will be seen that k_{obs} falls as the initial concentration is decreased. One reason for this will already be apparent: the lower the initial stoicheiometric concentration, the smaller the fraction existing as the undissociated thiol acid from the very start of the hydrolysis, and therefore the slower the observed loss of $[CH_3COSH]_{stoich}$. It is possible to correct (approximately) for this effect and to obtain a rate constant which more properly represents the reactivity of the undissociated acid at the particular stoicheiometric concentration used. The correction factor is derived in the following way:

$$H_2O + CH_3COSH \overset{r_a}{\rightleftharpoons} CH_3COS^- + H_3O^+$$

$$H_2O + CH_3COSH \overset{k_2}{\to} CH_3COOH + H_2S$$
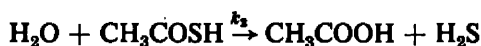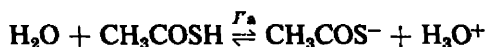
At any time
$$[CH_3COSH]_{stoich} = [CH_3COSH] + [CH_3COS^-]$$

and
$$-d[CH_3COSH]_{stoich}/dt = -d[CH_3COSH]/dt = k_2[CH_3COSH]$$

but
$$[CH_3COS^-] = K_a[CH_3COSH]/[H_3O^+]$$

$$\therefore \quad [CH_3COSH] = [H_3O^+][CH_3COSH]_{stoich}/(K_a + [H_3O^+])$$

$$\therefore \quad -d[CH_3COSH]_{stoich}/dt = \frac{k_2[H_3O^+]}{(K_a + [H_3O^+])} \cdot [CH_3COSH]_{stoich}$$

$$= k_{obs}[CH_3COSH]_{stoich}$$

Thus $k_2 = \{(K_a + [H_3O^+])/[H_3O^+]\}k_{obs}$

A knowledge of K_a and the initial $[CH_3COSH]_{stoich}$ permits the calculation of the initial $[H_3O^+]$ and hence of k_2 from k_{obs}. Previous[7] data concerning K_a refer to 25°. We have checked these data and have shown also (Experimental) that the value of K_a changes negligibly with temperature, at least in the range between 25–40°. In our calculation of k_2 we have assumed that K_a has the same value at 70°. This perhaps makes our calculation approximate, but very similar data, with the same *trend*, are

[7] A. Hantzch and W. Bucerius, *Ber. Dtsch. Chem. Ges.* **59**, 793 (1926).

obtained with arbitrarily* modified values of K_a, and it is the trend which is important for the subsequent arguments. The calculated values of k_2 at the different initial stoicheiometric concentrations are in Table 1. It is apparent that k_2 is not constant, although it approaches constancy for the lowest concentrations. The rate of reaction of the TAA molecules increases as the initial concentration increases. This implies that in addition to the spontaneous hydrolysis, one (or more) catalysed paths are operative, these accounting for the increase in rate with increase in the total concentration of acidic and basic species in the system. The study of the hydrolysis in buffer solutions and in the presence of mineral acid shows that both acid and base-catalysed paths are available.

Hydrolysis of TAA in buffer solutions

Our data are in Table 2. As noted above, in buffer mixtures the first-order plots yielding k_{obs} were linear over several half-lives. The hydrogen ion concentrations in

TABLE 2. HYDROLYSIS OF TAA IN THE PRESENCE OF SALTS AT 70°
$[CH_3COSH]_{initial} \sim 1 \cdot 1 \times 10^{-2}$

$[CH_3CO_2H]$	$[CH_3CO_2Na]$	$[KCl]$	$10^5 k_{obs}$	$10^5 k_2$
—	—	—	7·7	9·0
0·08	0·08	—	0·46	9·9
0·08	0·08	0·04	0·34	7·3
0·12	0·08	0·04	0·48	7·0
0·08	0·12	—	0·32	10·2

the various buffers were measured directly at 25°. The few data in Table 2, some of which refer to solutions of constant ionic strength, are sufficient to show (i) that the hydrolysis is subject to a substantial negative salt effect, (ii) that catalysis by molecular acetic acid is negligible and (iii) that catalysis by acetate ion is appreciable. These results, taken in conjunction with those for the magnitude of the catalysis by hydrogen ions detailed below, imply (a) that in the spontaneous hydrolysis in water the upward trend in k_2 with stoicheiometric concentration (Table 1) is probably due partly to basic catalysis by acetate and thiolacetate ions† and partly to catalysis by hydrogen ions, and (b) that this trend would be more marked if it were not opposed by the negative salt effect which must also be attendant on the increase in solute concentration.

Acid-catalysed hydrolysis of TAA

Data covering a range of acid concentrations from 0·1 M to 4·8 M are in Table 3. The effect of added salt and of change in temperature are also noted. An appreciable acidic catalysis was found and consequently most of the data refer to 40°, rather than 70°. In these hydrogen chloride solutions very little of the thiol acid will be dissociated. No correction to the observed rate is therfore necessary. The first-order plots were rectilinear over several half-lives. The experiments with added potassium

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* By considering available data for the temp dependence of the dissociation constants of similar acids. In fact the error will not be large ($<10\%$) even if K_a^{AcSH} alters as much[s] as does K_a^{AcOH} between 40° and 70°. In view of its invariant nature between 25° and 40°, K_a^{AcSH} probably alters less than this.

† Catalysis by OH⁻ is not implicated because as $[CH_3COSH]_{stoich}$ increases the pH decreases.

[s] R. H. Robinson and R. H. Stokes, *Electrolyte Solutions*. Butterworths, London (1959).

chloride indicate that the acid-catalysed, in contrast to the spontaneous, hydrolysis is subject to a small, positive salt effect. Columns 3 and 5 of Table 3 show that the acid-catalysed reaction (first-order rate constant k) is very much more closely dependent on $[H_3O^+]$ than on H_0. The true catalytic constants [i.e. those which would

TABLE 3. ACID-CATALYSED HYDROLYSIS OF TAA

k as in text; H_0 from reference 10; $[CH_3COSH]_{initial} \sim 7 \times 10^{-3}$

(a) At 40°

[HCl]	$10^4 k$	$10^4 k/[H_3O^+]$	H_0	$\log k + H_0 + 4$
0·12	0·55	4·6	0·92	0·66
0·48	1·80	3·8	0·22	0·48
0·96	3·71	3·9	−0·16	0·41
1·44	5·51	3·9	−0·45	0·29
1·90	8·00	4·2	−0·65	0·26
2·40	10·6	4·5	−0·83	0·21
2·88	14·5	5·0	−1·01	0·15
3·36	14·8	4·4	−1·06	0·11
3·84	17·9	4·7	−1·34	−0·09
4·32	23·4	5·4	−1·51	−0·14
4·80	24·0	5·0	−1·68	−0·30

(b) At 70°

[HCl]	$10^4 k$	$10^4 k/[H_3O^+]$
0·12	5·10	42·5

(c) At 40° in the presence of added KCl

[HCl]	[KCl]	$10^4 k$
2·40	—	10·6
2·40	0·51	11·4
2·40	0·85	11·8

be found in the absence of the (unknown) *salt* effect no doubt produced by the hydrogen chloride] are probably slightly smaller than the $k/[H_3O^+]$ values quoted, especially at the higher acid concentrations. This is the probable reason for the slightly greater than first-order dependance on $[H_3O^+]$ observed.

The hydrolysis of TBA

Data for this acid are in Table 4. They are not as numerous as those for TAA but show similar effects. Analogous considerations and arguments apply, and there are probably no fundamental differences between the behaviour of the aliphatic and aromatic thiol acids towards hydrolysis. No value for pKa for TBA was available and we have determined this quantity to be $3·3 \times 10^{-3}$ at 25°. It was used, without temperature correction, to calculate k_2 from k_{obs}. In this case a net downward trend in k_2 with concentration is found and presumably implies a dominant negative salt effect. The first-order plots for the spontaneous rates were again slightly curved and initial slopes were taken. Plots for the acid-catalysed reactions were accurately rectilinear.

TABLE 4. SPONTANEOUS AND ACID-CATALYSED HYDROLYSIS OF TBA AT 70°

(a) Spontaneous reaction

$10^4[C_6H_5COSH]_{init.}$	$10^4 k_{obs}$	$10^4[H_3O^+]$	$10^5 k_2$
1·2	1·1	1·15	3·3
5·4	2·2	4·7	1·6
12·0	2·7	9·4	1·2

(b) Acid-catalysed reactions ($[C_6H_5COSH]_{initial} \sim 1 \times 10^{-4}$)

[HCl]	$10^4 k$	$10^4 k/[H_3O^+]$	H_0	$H_0 + \log k + 4$
0·58	1·07	1·8	0·12	0·15
1·44	2·20	1·6	−0·44	−0·10
2·40	4·10	1·7	−0·83	−0·22
3·12	5·40	1·7	−1·08	−0·35
3·80	7·10	1·9	−1·34	−0·49
4·80	10·4	2·2	−1·70	−0·68

A comparison of the data for TBA and TAA reveals the following facts:

(i) The aromatic acid is hydrolysed spontaneously about twice as slowly. (At 70° $k_2 \sim 3 \times 10^{-5}$ sec^{-1} compared with $k_2 \sim 5 \times 10^{-5}$ sec^{-1}.)

(ii) The aromatic acid is also hydrolysed the more slowly under acidic catalysis. (At 70° $10^4 k/[H_3O^+] \sim 1 \cdot 8$ l. mole^{-1} sec^{-1} compared with $10^4 k/[H_3O^+] \sim 42$ l. mole^{-1} sec^{-1}.)

(iii) The aromatic acid is less *susceptible* to acidic catalysis, i.e. the rate enhancement produced relative to the spontaneous rate is less by a factor of ca. 13.

Comparative behaviour of the sulphur and oxygen analogues towards hydrolysis

(a) *Spontaneous rates.* Exchange data are only available for acetic acid. Interpolation between values given by Llewellyn and O'Connor[3] indicates that TAA is hydrolysed at least 20-fold more rapidly ($k_2 \sim 5 \times 10^{-5}$ sec^{-1} compared with $k_2 \sim 2 \cdot 5 \times 10^{-6}$ sec^{-1} or less). That the spontaneous reaction is faster for the sulphur compound is understandable. In the hydrolysis of acids the leaving group, be it OH or SH, cannot be classed as good. It is likely therefore that, no matter what the attacking reagent, the departure of the leaving group will influence the rate to some extent, i.e. bond-breaking will be significant. Under such circumstances compounds with the best leaving groups may react the fastest. Since H_2S is a stronger acid than H_2O, SH will be a better leaving group than OH, and the thiol acid would therefore be expected to undergo hydrolysis the faster, as found. Our present results fit satisfactorily into our previous rationalizations concerning such reactions, which should be consulted for more detailed arguments.[5,6] It may be significant that, in chlorobenzene, TBA acylates aniline more readily than does benzoic acid, though the mechanism (and hence the interpretation) of acylation in such a solvent could be more complicated.[9]

(b) *Acid-catalysed rates.* Here exchange data are available for both acetic and benzoic acids.[3,4] For acetic acid at 70°, in the absence of added salt, $10^4 k/[H_3O^+] \sim 385$ l. mole^{-1} sec^{-1}. This compares with the value of ca. 42 l. mole^{-1} sec^{-1} noted above for TAA. For benzoic acid at 70°, $10^4 k/[H_3O^+] \sim 2 \cdot 5$ l. mole^{-1} sec^{-1}

⁹ P. J. Hawkins, D. S. Tarbell and P. Noble, *J. Amer. Chem. Soc.* 75, 4462 (1953).

while for TBA the value is ca. 1.8 l. mole^{-1} sec^{-1}. It is noteworthy that the acid-catalysed oxygen exchange shows a negative salt effect whereas the thiol acid hydrolysis displays a positive effect. Because in each case the acid catalyst will produce a salt effect (in addition to its catalytic role—see p. 839) the above figures represent minimum differences between the susceptibilities of the oxygen and sulphur compounds towards acid catalysis. It is clear therefore that the sulphur compounds can be said to be less susceptible than their oxygen analogues. This is a sensible result: it agrees with our theoretical predictions (p. 836) and is in keeping with our experimental findings for the hydrolyses of carboxylic anhydrides.[6]

That the acid-catalysed rates are proportional to $[H_3O^+]$ and that the activation energy and entropy of activation for the acid-catalysed path have values 16.2 Kcals. mole^{-1} and -25 e.u. respectively is compatible with the following bimolecular mechanism for the catalysed hydrolysis.

$$RCOSH + H_3O^+ \rightleftharpoons RCOSH_2^+ + H_2O \quad \text{Fast}$$

$$RCOSH_2^+ + H_2O \rightarrow RCO_2H_2^+ + H_2S \quad \text{Slow}$$

$$RCO_2H_2^+ + H_2O \rightarrow RCO_2H + H_3O^+ \quad \text{Fast.}$$

The same route has been proposed[3,4] for the acid-catalysed oxygen exchange for which the Arrhenius parameters are rather similar, and, at this level of sophistication, the two reactions doubtless have the same mechanism. However, their finer details cannot be identical because added salt produces effects in opposite senses in the two cases. This may be understood in the following way. Added salt increases the tendency of the medium to protonate either substrate (H_0 decreases[10]) but renders molecular water less available for hydrogen bonding to the leaving group and for nucleophilic attack on the protonated substrate.[11] Once protonated (on sulphur) the thiol acid possesses a good leaving group and the second (slow) step could be rather insensitive to the availability of hydrogen bonding for the leaving group and of the attacking nucleophilic. This is less likely to be true for the oxygen analogues where the effect of salt on the second step may outweigh its effect on the protonation equilibrium. Thus salt can aid the reaction of the sulphur compounds but hinder that of the oxygen compounds, as found.

EXPERIMENTAL

Materials. TAA was the B.D.H. reagent, purified by fractionation in a stream of N_2. A cut, b.p. 87–88°, was taken. Acid-base and iodometric titration showed the purity to be >98%. TBA was prepared by Noble and Tarbell's method.[12] A cut, b.p. 85–87° at 10 mm, was taken. Titration showed the purity to be 96%. The other reagents were the purest available commercial samples.

Kinetic arrangements. Undissociated TAA has in water an absorption maximum at 2225 Å and the thiol acetate ion a maximum close to 2470 Å. In the absence of added mineral or other acids, the intensity of these bands does not show a linear dependence on $[CH_3COSH]_{stoich}$. This is because as the stoicheiometric concentration is decreased the extent of dissociation increases. However, either in the presence of sufficient added acetic acid to maintain the quantity ($[CH_3COSH]_{stoich}$ + $[CH_3COOH]_{stoich}$) constant (i.e. to simulate the conditions during hydrolysis) or in the presence of added mineral acid (when effectively all the TAA exists as the undissociated species) the bands show a linear dependence on $[CH_3COSH]_{stoich}$. Hence for the spontaneous reactions the fall in the 2470 Å

[10] F. A. Long and M. A. Paul, *Chem. Revs.* **57**, 1 (1957).

[11] C. A. Bunton, N. A. Fuller, S. G. Perry and I. H. Pitman, *J. Chem. Soc.* 4478 (1962).

[12] P. Noble and D. S. Tarbell, *Organic Syntheses* **32**, 101 (1952).

band was followed and for the acid-catalysed reactions the fall in that at 2225 Å. Similar circumstances apply for TBA. In this case the anion absorbs at 2800 Å and the undissociated acid at 2440 Å. In the acid catalysed reactions measurements were actually made at 2500 Å, because there is serious overlap from the absorption of the benzoic acid product at 2440 Å.

Initial stoicheiometric thiol acid concentrations were determined either by direct weighing or from the initial optical densities. Spectral measurements were made at 25° and, for solutions containing added mineral acid, at low $[H_3O^+]$ concentrations, when the hydrolysis is slow enough to permit accurate measurements.

Reaction was initiated by adding the thiol acid to a known volume of water (or buffer or aqueous acid) contained in a volumetric flask immersed in a bath maintained at the appropriate temp. Aliquot portions were removed at intervals and the optical measurments made either directly (when the initial stoicheiometric concentration was small) or on suitably diluted solutions. In this way the loss of $[RCOSH]_{stoich}$ was followed. In runs in buffer solutions, or in aqueous acid, the first-order plots of log $[RCOSH]_{stoich}$ against time were accurately rectilinear over several half-lives. In the spontaneous hydrolyses in pure water, however, the plots were only straight for ca. 1·3 half-lives, whereafter a slight and smooth fall in the rate was apparent (p. 837). For these runs the first-order constants were calculated from the data for the first half-life.

In every case the final optical density had a value which indicated effectively complete hydrolysis. Water, of course, was in vast excess in the reaction mixtures.

Dissociation Constants. These were determined by a spectroscopic method based on the different absorptions of the anions and undissociated acids noted above. Measurements were made of [PhCOSH] and [PhCOS⁻] (or [CH₃COSH] and [CH₃COS⁻]) in aqueous solutions of different stoicheiometric concentrations and/or in various acetate buffers of measured pH. The pH measurements were made with a Cambridge pH meter, calibrated against standard buffers, using a glass electrode in conjunction with a standard calomel reference electrode.

At 25°, $K_a = (3·3 \pm 0·2) \times 10^{-3}$ for TBA and $(4·7 \pm 0·2) \times 10^{-4}$ for TAA. Raising the temp to 40° has a negligible effect (within our limits of error) on the value for TAA. (The temp cannot profitably be raised too far because of the attendant hydrolysis.)