using one-electron bonds of the type employed here may well prove to be very useful. For example Shull states that "similar cases are involved in the bridge hydrogen bonds of the boron hydrides or in aromatic compounds where electrons are almost completely delocalized." We have completed calculations for the central ring of diborane[8] and the electrons of the π-system of benzene,[9] and the results show that a description in terms of similar one-electron bonds is more successful than the others when judged by the calculation of energies. For instance, a function using two adjustable constants which places each of the six π-electrons in benzene in a separate two-center bond orbital leads to an energy only 2 kcal./mole greater than that obtained using the equivalent full CI function needing 21 adjustable constants.[10] An MO description would have to employ many configurations before it could do as well, and no analysis in terms of natural orbitals recording high first occupation numbers can alter this fact.

There are, of course, many molecules for which an analysis in terms of pairs (geminals) is almost certainly the best one as was pointed out by Lewis.[11] Molecules for which one Lewis formula may be written would be expected to lend themselves to such an analysis. However there are other molecules for which a single Lewis structure on its own cannot be regarded as satisfactory as was pointed out by Pauling.[12] In such cases an analysis in terms of pairs along the lines advocated by Shull may not provide by any means the best approach.[13]

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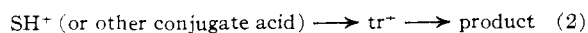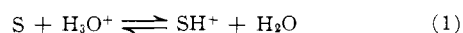OXFORD, ENGLAND

The Effect of Mineral Acid Medium upon f_{SH^+}/f_{tr^+}

Sir:

We are reporting the first instance of the direct measurement of the effect of mineral acid medium upon f_{SH^+}/f_{tr^+}, where f_{SH^+} is the activity coefficient of the conjugate acid of the substrate and f_{tr^-} is that of the transition state in an A-1 reaction. Knowledge of the behavior of such activity coefficient ratios is essential to the proper interpretation of the acidity dependence of reaction rates.

$$S + H_3O^+ \rightleftharpoons SH^+ + H_2O \qquad (1)$$

$$SH^+ \text{ (or other conjugate acid)} \longrightarrow tr^+ \longrightarrow product \quad (2)$$

$$k_{obsd} = \frac{[SH^+]}{[S] + [SH^+]} kf_{SH^-}/f_{tr^-} \qquad (3)$$

when $[SH^+] \gg [S]$

$$k_{obsd} = kf_{SH^+}/f_{tr^+} \qquad (4)$$

Under the usually pertaining condition that $[S] \gg [SH^+]$ the use of eq. 3 as a criterion of mechanism has traditionally involved the application of two assumptions: (1) that the ratio $[SH^+]/[S]$ follows a particular acidity function, i.e., h_0^1; and (2) the ratio f_{SH^-}/f_{tr^+} is relatively insensitive to medium change.[2] The former assumption is not always valid (see ref. 3 and references therein).[2,3] A direct test of the latter assumption is made in the A-1 hydrolysis of the dimethyl acetals of pyridine-2-aldehyde, quinoline-2-aldehyde, and 8-t-butylquinoline-2-aldehyde. In lower acid molarities, the rate-controlling step is the heterolysis of the C–O bond of the oxygen conjugate acid, SH^{*+}, although the ground state is the nitrogen conjugate acid, SH^+. The first term of eq. 5 corresponds to this over-all one-proton A-1 hydrolysis. In higher mineral acid molarities, an over-all two-proton process, involving heterolysis of the C–O bond of the doubly protonated substrate, SH_2^{+2}, may become of increasing importance. This is because of the steep acidity dependence of $[SH_2^{+2}]/[SH^+]$ in the two-proton hydrolysis term, the second term of eq. 5.

$$k_{obsd} = k_1 \frac{K_{SH^+}}{K_{SH^{*+}}} f_{SH^-}/f_{tr^+} + \frac{[SH_2^{+2}]}{[SH^+]} k_2 f_{SH_2^{+2}}/f_{tr^{+2}}$$

$$(5)$$

Consider first the rate results for 2-dimethoxymethylpyridine. In keeping with the mechanistic assignment no catalysis by either molecular acetic acid or acetate ion was observed in acetate buffers at low ionic strength, 0.05 μ (see ref. 4 for accumulated evidence that acetal hydrolysis is A-1). It is evident from the initial decline in k_{obsd}, which goes through a minimum in about 1.6 M $HClO_4$, that one-proton hydrolysis predominates in the lower mineral acid range. The rapid increase in k_{obsd} in the highest acid molarities is indicative of the incursion of the over-all two-proton hydrolysis.[4] These conclusions are confirmed by the solvent isotope effects of Table I.

TABLE I

RATE CONSTANTS AND SOLVENT ISOTOPE EFFECTS IN THE HYDROLYSIS OF 2-DIMETHOXYMETHYLPYRIDINE AT 60°

$HClO_4$; M	$10^4 k_{obsd}$,[a] sec.$^{-1}$	k_{HClO_4}/k_{DClO_4}[b]
0.12	4.86	1.06
0.56	4.42	..
1.60	4.19	1.00
1.96	4.20	..
2.72	4.57	0.97
3.10	5.01	..
3.98	7.03	0.87
5.09	15.40	0.70
5.72	30.9	0.61
6.83	147	0.57

[a] All first-order rate constants in Tables I and II were obtained by an ultraviolet spectrophotometric method and are duplicable to ±2%. [b] Rate in perchloric acid relative to fully deuterated perchloric acid of same molarity.

As regards the ratio f_{SH^-}/f_{tr^+}, the conclusion is plain that it suffers an initial steady decline as perchloric acid molarity is increased. Whether or not this decline

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(3) R. W. Taft, Jr., ibid., **82**, 2695, (1960).

(4) M. W. Fuller and W. M. Schubert, ibid., **85**, 108 (1963).

continues beyond 1.6 M HClO$_4$ is obscured by the incursion of the two-proton process. A similar situation prevails in the hydrolysis of 2-dimethoxymethylquinoline. The initial decline in k_{obsd}, and hence in f_{SH^+}/f_{tr^+}, is somewhat steeper and persists into higher acid molarities. One can rationalize these decreases in f_{SH^+}/f_{tr^+} with increasing HClO$_4$ molarity in terms of stronger solvation of the transition state than the ground state through solvation by the oxygen atoms of water molecules (cf. ref. 2 and 3). However, the decline in f_{SH^-}/f_{tr^+} is not spectacular, especially when viewed on a logarithmic scale. In effect then, the assumption applied first by Hammett, that a ratio such as f_{SH^+}/f_{tr^+} suffers relatively little medium effect, is reasonably good in the instances of the hydrolyses of the dimethyl acetals of pyridine-2-aldehyde and quinoline-2-aldehyde.

It was expected that an 8-t-butyl substituent on the 2-dimethoxymethylquinoline would substantially alter matters. According to molecular models, the N–H proton of the nitrogen conjugate acid (i.e., the ground state) is very effectively shielded from solvation. On the other hand, the main sites of developing charge in the transition state are only remotely shielded. On this basis two predictions are made: (1) In any particular medium, $f_{SH^+}K_{SH^+}/f_{tr^+}K_{SH^+}$ should be greater for the 8-t-butyl than the unsubstituted quinoline. (2) The quantity f_{SH^-}/f_{tr^+} for the t-butyl derivative should decrease more than the corresponding ratio for the unsubstituted compound as mineral acid molarity is increased. In other words, in the t-butyl compound, the ground state (i.e., SH$^+$) would have less to lose in free energy of solvation, relative to the transition state, as the activity of water is decreased. These predictions have been realized in full. Thus k_{obsd} is appreciably greater in any particular medium for the 8-t-butyl derivative (note that the rate results are at 40° for the t-butyl compound and at 60° for the unsubstituted one). Furthermore, k_{obsd}, and hence f_{SH^+}/f_{tr^+}, declines by a factor of about 12-fold between 0.6 and 6 M HClO$_4$. It is of interest to note that a Hammett plot (somewhat scattered) has a slope of about 0.65 in this instance.

TABLE II

RATE CONSTANTS FOR THE HYDROLYSIS OF
2-DIMETHOXYMETHYLQUINOLINE (A) AND
8-t-BUTYL-2-DIMETHOXYMETHYLQUINOLINE (B)

HClO$_4$, M	$10^4 k_{obsd}$ Compd. A	Compd. B
0.10	4.67	a
0.58	3.72	12.41
0.95	3.51	10.01
1.27	. . .	9.13
1.60	3.32	7.36
1.96	3.21	. . .
2.33	3.19	5.25
2.71	3.21	4.80
3.11	3.33	4.11
3.54	3.74	3.44
3.99	4.36	3.20
4.60	5.74	1.91
5.09	9.13	1.60
5.72	18.0	1.36
6.51	46.5	1.11
7.60	. . .	2.03
9.42	. . .	106.8

^{a} Compound insoluble.

For the 8-t-butyl compound the one-proton process predominates over a much wider range of perchloric acid strength; i.e., the rate does not begin to turn up until about 7 M HClO$_4$. This is to be expected since the two-proton hydrolysis should be less effected by the substituent, i.e., solvation of the NH proton should be roughly equal in the ground state and transition state of the two-proton process.

While the situation just described is a contrived one it nevertheless allows the conclusion that the assumption that f_{SH^+}/f_{tr^-} for an A-1 process suffers little change with medium should be applied with care. Unfortunately, the results also demonstrate again that one cannot base mechanistic conclusions on merely the acidity dependence of a rate constant. They further saliently point out that considerably more must be learned about the effect of medium upon the free energies of the ground and transition states of reactions catalyzed in strong acids before the interpretation of the acidity dependence of rate constants can once again be considered to be firmly based.

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The Possibility of a Cyclic Mechanism for Acid-Catalyzed Ester Hydrolysis

Sir:

The observation of Bell[1] that the rate of hydrolysis of ethyl acetate does not increase with acidity as rapidly as expected for a Hammett indicator[2] has raised questions about the pK_a of ethyl acetate[3] and the involvement of water in the reaction.[4] Recently Long has concluded that solvent deuterium isotope effects for ester hydrolysis are best fitted by five or more exchangeable hydrogens in the transition state,[5] whereas the accepted tetrahedral mechanism has only three such hydrogens.[6] We now wish to report evidence for a transition state involving protonated ester and two water molecules in a six-membered ring. This transition state has five exchangeable hydrogens, and quantitatively accounts for the water and acidity dependence that we observe.

We have studied the rate of hydrolysis of ethyl acetate at 25° in 11–79% sulfuric acid by the spectrophotometric and dilatometric techniques. The rate reaches a maximum at 50–60% acid and decreases rapidly at higher concentrations. To interpret this maximum, it is necessary to know the pK_a of ethyl acetate, but none has been reported for an aliphatic ester.[7]

The concentration of protonated ethyl acetate as a function of sulfuric acid concentration was determined

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