rate plots were found to be linear over at least two half-lives. Rate constants for these compounds and for ethyl tosylate, representing the mean values obtained from two runs in each case, are given in Table I.

Table I. Kinetic Data from Solvolysis of Tosyloxyalkyltrimethyltins, $(CH_3)_3Sn(CH_2)_nOTs$, in Acetic Acid–Acetate

n	T, °C	$k_1 \times 10^5$, sec^{-1}	Rel k_1 at 120°	$\Delta H^{\ddagger}$, kcal	$\Delta S^{\ddagger}$, eu
3	25.0	0.388 ± 0.005			
3	45.1	4.73 ± 0.10			
3	65.2	31.0 ± 1.5		21.3	−7.8
3	120.3	3100[a]	585		
4	120.3	3.17 ± 0.15	0.595		
5	120.3	3.41 ± 0.17	0.642		
6	120.3	4.16 ± 0.10	0.783		
EtOTs	120.3	5.31 ± 0.08	1.00	24.4[b]	−16.7[b]

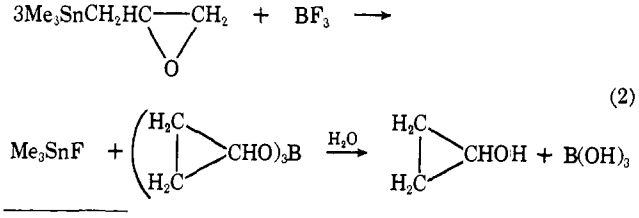
[a] Extrapolated. [b] Reference 12.

A calibration of our data is provided by comparison of our value of 5.31×10^{-5} sec^{-1} at 120.3° for ethyl tosylate with that obtained by extrapolation from the data of Winstein and Marshall[12] of 4.75×10^{-5} sec^{-1}. The rate constant for solvolysis of 3-tosyloxypropyltrimethyltin in trifluoroethanol at 25.0° was 36.0 ± 0.7×10^{-5}, nearly a hundred times the value in acetic acid.

3-Tosyloxypropyltrimethyltin solvolyzes faster than ethyl tosylate by a factor of 585 and faster than the other tosyloxyalkyltrimethyltins by factors approaching a thousand. Since the last four entries in the table probably do not represent limiting unimolecular solvolyses, but have substantial SN2 character,[13] these rate coefficient ratios would be even larger in a less nucleophilic polar solvent. The high reactivity of 3-tosyloxypropyltrimethyltin and the formation of cyclopropane provide strong evidence for σ participation by the electrons of the tin–carbon bond in facilitating departure of the tosylate ion in a concerted 1,3-elimination reaction.

2-Ferrocenylethyl tosylate solvolyzes about 500 times as fast as 2-phenylethyl tosylate.[14] Participation, analogous to that proposed above, involving a pair of electrons of the iron–cyclopentadienide bond has been suggested by Traylor and Ware.[15] Indeed, these authors suggested carbon–metal σ participation as a general phenomenon for the formation of cyclopropanes from γ-metalloalkyl halides.

The use of organotin derivatives has synthetic potential which we are examining. For example, 3,4-epoxybutyltrimethyltin reacts rapidly with boron trifluoride etherate to form cyclopropylcarbinyl borate, which hydrolyzes in moist air to provide a high yield of cyclopropylcarbinol (eq 2).



(2)

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(13) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, p 75.
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Mechanisms of Photochemical Reactions in Solution. LXV.[1] Quenching of Excited Singlet States of Electron-Rich Aromatic Compounds by Methyl Chloroacetate

Sir:

For several years this laboratory has been investigating singlet quenching of aromatic compounds by quenchers having no low-lying singlet states.[2-5] We visualize this phenomenon as involving an interaction between the excited state of the aromatic molecule and the quencher, forming a loosely bound exciplex; the net result of this interaction is an increase of the rates of nonradiative decay processes. A general model of this interaction has been formulated as the following

$$\psi_{\text{exciplex}} = a\psi_{A^*Q} + b\psi_{AQ^*} + c\psi_{A^+Q^-} + d\psi_{A^-Q^+}$$

where A = aromatic compound, Q = quencher, and * denotes the excited state.

Clearly the importance of each of the terms would be expected to vary depending upon the structure of A or Q. For example, the exciplex involved in singlet quenching of aromatic hydrocarbons by amines seems to approach a true charge-transfer state in which the excited hydrocarbon acts as an electron acceptor.[2,3] Quenching of fluorescence of aromatic compounds by conjugated dienes, however, most likely involves several if not all of the above interactions.[4,5] We were intrigued by the possibility that the intramolecular photocyclizations observed by Witkop and coworkers[6] might be initiated by partial electron transfer in which the excited state of the aromatic compound acted as an electron *donor* to the chlorinated amide. That is, the third term in the above equation would have significant weight. This complex could then undergo rapid radiationless decay to either new products or to the original compounds.

We have found that the fluorescence of many electron-rich aromatics is quenched efficiently by methyl chloroacetate and chloroacetamide.[7] The absorption

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(3) A. Weller, *Fast React. Prim. Processes Chem. Kinet., Proc. Nobel Symp., 5th, 1967*, 413 (1967).
(4) L. M. Stephenson, D. G. Whitten, and G. S. Hammond in "The Chemistry of Ionization and Excitation," Taylor and Francis, London, 1967, pp 35–42.
(5) D. A. Labianca, G. N. Taylor, and G. S. Hammond, manuscript in preparation.
(6) D. Yonemitsu, H. Nakai, Y. Kanaoka, I. Karle, and B. Witkop, *J. Amer. Chem. Soc.*, **91**, 4591 (1969), and references therein.
(7) Recent experiments have indicated that quenchers are not limited to chloro-substituted derivatives of acetic acid. For example, benzyl chloride and allyl chloride quench the fluorescence of 1,4-dimethoxybenzene with high efficiency.

spectra of the quenchers show no transition above 280 nm; thus no low-lying singlet states are available for classical excitation transfer. The absorption spectra of the aromatics in acetonitrile were unchanged by the addition of either methyl chloroacetate or chloroacetamide. The unquenched portion of the fluoroscence has the same spectral distribution as that in solutions without quencher. No new fluorescence was observed. Linear Stern–Volmer plots were obtained and quenching rate constants derived from these plots are listed in Table I. It is of considerable interest that methoxy

Table I. Rate Constants for Quenching of Fluorescence by Methyl Chloroacetate[a,b] (l. sec^{-1} mol^{-1})

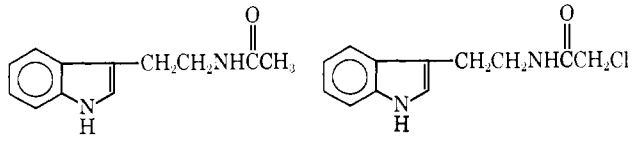
Compound	Solvent: Acetonitrile	Solvent: Hexane	τ_0[c]
Indole	4.2×10^9	1.4×10^{10}	8.5
Anisole	1.1×10^9	1.5×10^9	9.5
1,4-Dimethoxybenzene	5.5×10^9	1.2×10^{10}	2 ± 1
N,*N*-Diethylaniline	8.9×10^9		3 ± 0.5
Naphthalene	4.0×10^6		95
2-Methoxynaphthalene	2.4×10^7		17.5
2,6-Dimethoxynaphthalene	5.6×10^7	1.8×10^7	11.5

[a] Chloroacetamide and methyl chloroacetate exhibit similar quenching efficiencies. However, reliable kinetic data are difficult to obtain with chloroacetamide because of low solubility. [b] Emission spectra from degassed solutions were recorded by an Aminco Bowman spectrophotometer. [c] Lifetime in nanoseconds determined by a TRW Model 31A nanosecond spectral source coupled to a Tektronix Type 556 dual beam oscilloscope.

substitution, which presumably increases electron density of the aromatic nucleus, leads to more efficient quenching. Quenching rate constants appear to be somewhat dependent upon solvent polarity. However, no general trends are observed.

Neither ethyl acetate nor acetamide produced any effect on the fluorescing species. Cyanoacetamide appeared to quench indole fluorescence slightly. However, the rate constant was more than two orders of magnitude lower than that of methyl chloroacetate or chloroacetamide. Very inefficient quenching was also observed with ethyl 3-chloropropionate.

Absorption and emission properties of several compounds whose photochemistry has recently been reported by Witkop[6] have been examined. The absorption spectra of *N*-acetyltryptamine (I) and *N*-chloroacetyltryptamine (II) in EPA are essentially identical. However, the intensity of room temperature fluorescence of I is approximately 15 times that of II.



I II

Fluorescence from *N*-chloroacetyl-3,4-dimethoxyphenethylamine has also been found to be significantly less than that from *N*-acetyl-3,4-dimethoxyphenethylamine. This behavior is most certainly due to intramolecular singlet quenching by the chloro-substituted amide.

Preliminary experiments have shown that one major and several minor products are formed after irradiation of a methanol solution of 1,4-dimethoxybenzene and methyl chloroacetate. The major product was separated by chromatography on silica gel and identified as the methyl ester of (2,5-dimethoxyphenyl)acetic acid by comparison with an authentic sample. In a similar reaction Yonemitsu and Naruto[8] have reported that irradiation of solutions of anisole and chloroacetamide leads to the formation of methoxyphenylacetamides.

The following kinetic scheme is consistent with the results.

$$A \xrightarrow{h\nu} A^{*1}$$

$$A^{*1} \xrightarrow{k_f} A + h\nu'$$

$$A^{*1} \xrightarrow{k_{isc}} A^{*3}$$

$$A^{*1} \xrightarrow{k_d} A$$

$$A^{*1} + Q \xrightarrow{k_q} [AQ]^*$$

$$[AQ]^* \xrightarrow{k_d'} A + Q$$

$$[AQ]^* \xrightarrow{k_p} \text{products}$$

A step involving decay of the complex to the aromatic species and quencher (k_d') is included since the quantum yield for disappearance of 2-methoxynaphthalene in methanol solution containing methyl chloroacetate is insufficient to account for the number of fluorescent molecules quenched. Apparently the exciplex does not decay to the triplet state of the aromatic species since sensitized cis–trans isomerization of *cis*-piperylene[9] by 1,4-dimethoxybenzene or *N*,*N*-diethylaniline is strongly inhibited by addition of methylchloroacetate.

Our original intuitive notion that charge transfer from aromatic to quencher would contribute to exciplex binding may be correct. However, the specificity associated with the requirement for an α-chlorine substituent indicates that other factors are involved. We are inclined to believe that the carbon–chlorine bonds in the quenchers are involved in the internal conversion process in which electronic excitation of the exciplex is converted to vibrational energy. This process could be directly related to bond breaking which leads ultimately to the observed photoreactions. The general line of reasoning is the same as was adopted in discussion of the very high reactivity of quadricyclene as a quencher for aromatic hydrocarbons, a process which also leads to a chemical change in the quencher.[10] The fairly obvious connection between low fluorescence efficiency and photoreactivity in the Witkop photocyclization reactions is consistent with the intermolecular cases reported here.

The solvent effects shown in Table I are not very informative. With the first three the rates are high enough to be diffusion limited so solvent viscosity would be expected to be more important than any effect on the exciplex binding energy. The fact that the rate of quenching of 2,6-dimethoxynaphthalene is slower in hexane than in acetonitrile could be attributed to a polar medium effect. This would then be the kind of effect expected, but not observed by Solomon,

(8) O. Yonemitsu and S. Naruto, *Tetrahedron Lett.*, 2387 (1969).
(9) A. A. Lamola and G. S. Hammond, *J. Chem. Phys.*, 43, 2129 (1965).
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Steel, and Weller[11] on the basis of their views of the quenching of fluorescence of aromatic hydrocarbons by quadricyclene. The solvent effects in this example are significantly larger than those observed in the quenching of naphthalene by conjugated dienes.[12]

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(13) National Institutes of Health Postdoctoral Fellow, 1969 to present.

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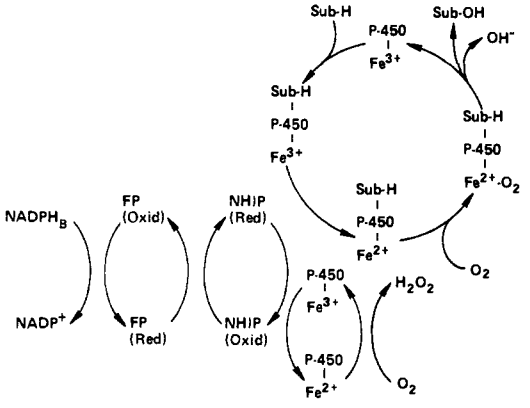
The Effect of 4,4-Dideuteration of Nicotinamide Adenine Dinucleotide Phosphate on Steroid Hydroxylation

Sir:

The 11β-hydroxylase reaction of adrenal mitochrondria involves the transfer of two reducing equivalents from reduced nicotinamide adenine dinucleotide phosphate (NADPH) to a molecule of oxygen which is in a complex with cytochrome P-450 and deoxycorticosterone (DOC), resulting in the formation of corticosterone (CORT) and OH^-. Omura, *et al.*,[1] have purified a flavo protein and a nonheme iron protein, which together form a cytochrome P-450 reductase. Further, they prepared a particle-bound cytochrome P-450, almost devoid of reductase activity, which in the presence of NADPH and reductase was able to hydroxylate DOC to CORT. On the basis of these studies, they postulated that the transfer of reducing equivalents was through the reductase and cytochrome P-450 to the molecular oxygen (Scheme I).

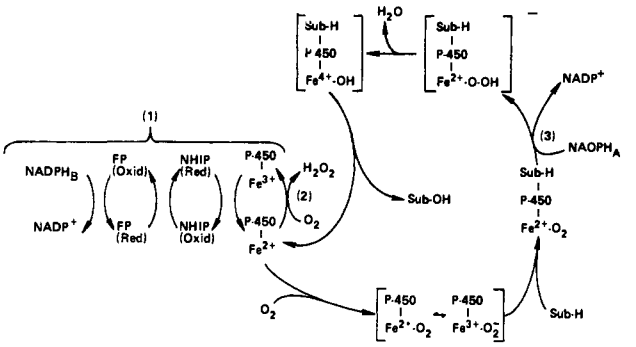
Scheme I



(1) T. Omura, E. Sanders, R. W. Estabrook, D. Y. Cooper, and O. Rosenthal, *Arch. Biochem. Biophys.*, **117**, 660 (1966).

Sih, *et al.*,[2,3] have suggested that the reductase merely serves to keep the cytochrome in the reduced or active form. Subsequently, hydrogen is transferred from a second NADPH to form a hydroperoxide which then decomposes to CORT and OH^- (Scheme II).

Scheme II



They based their suggestion on the fact that (1) although by manipulations of the proportions of the enzymes, NADH can serve to reduce cytochrome P-450, it does not serve in the hydroxylation reaction; (2) Scheme I should have ping-pong kinetics and yet does not; and (3) the stereochemistry of the dehydrogenation of the dihydronicotinamide ring of NADPH is different for the reduction of the cytochrome and the overall reaction. These observations could be explained on the basis of there being an alternative electron chain and in no way require, as suggested by Sih, *et al.*,[2,3] the existence of an intermediate hydroperoxide. Therefore, the question as to the existence of such a species remains unanswered.

It is well known that the maximal rate of hydroxylations is determined by the rate of reduction of the cytochrome P-450 (reaction 1, Scheme II).[1,4] Yet the actual rate in either scheme will be determined by a competition between the autoxidation of the reduced heme[5] to give an ineffective reaction (reaction 2) and the reduction of the O–O bond to give the hydroxylating species in the effective reaction (reaction 3). These latter two reactions appear to have comparable fluxes of reducing equivalents. Substitution of deuterium for the 4 H's of NADPH (NADP(D)D) would affect neither the rate of reduction nor the rate of autoxidation of the heme, while it would probably slow two–threefold the transhydrogenation involved in the formation of the hydroperoxide and therefore in Scheme II give a two–threefold reduction in the rate of formation of product.[4] No similar isotope effect would be expected in Scheme I. In examining an analogous system, the hydroxylation of ethylmorphine and aniline by hepatic microsomes, I have found that NADP(D)D was nearly as effective in supporting hydroxylation as NADPH.[4] I therefore have examined the 11β-hydroxylase of adrenal mitochondria to see if it behaves similarly.

NADP(D) and tritiated NADP (NADP(T)) were prepared by the method of San Pietro[6] and purified by

(2) C. J. Sih, Y. Y. Tsong, and B. Stein, *J. Amer. Chem. Soc.*, **90**, 5300 (1968).
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(6) A. San Pietro, *J. Biol. Chem.*, **217**, 579 (1955).