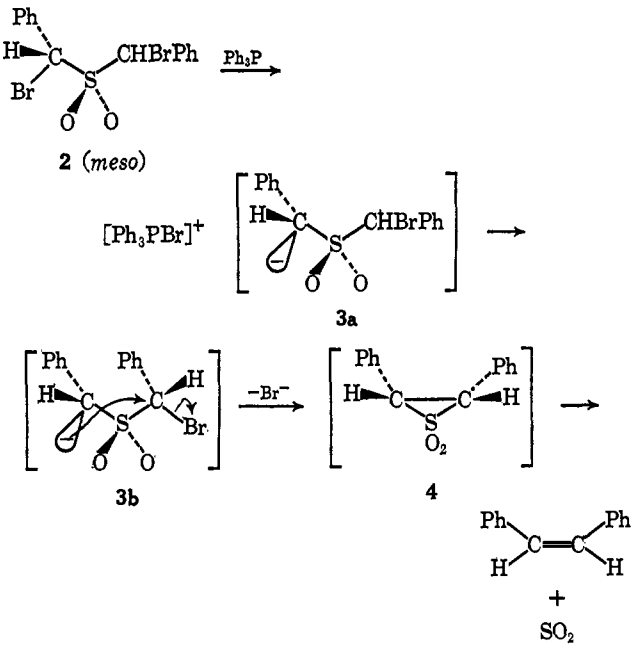
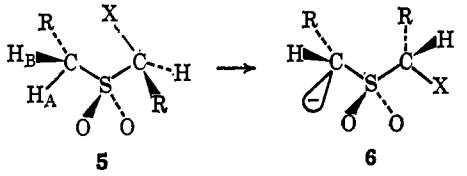


In the 1,3 eliminations initiated by DMF a comparable mechanism (W type in the Nickon–Werstiuk classification[2]) appears reasonable, with proton removal occurring from a conformation in which the proton is *cis* to the sulfone oxygen atoms.

If one further assumption is made, this W-type mechanism can be used to rationalize the observation that base-initiated 1,3 eliminations from RCH_2SO_2CHXR α-halo sulfones give *cis*-alkenes (*via cis*-dialkyl episulfones) in greater amount than *trans*-alkenes.[13] The required assumption is that proton removal occurs from a particular conformation, *e.g.*, **5**, in which the halogen atom is oriented *trans* to the sulfonyl oxygen atoms and in which the alkyl groups are *trans* to one another. The W-type mechanism then requires reaction *via* conformation **6** to give the *cis* episulfone.[14,15]



Acknowledgment. We are grateful to the National Science Foundation (GP 7065) for support of this investigation.

(1966); F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr., and B. B. Jarvis, *J. Am. Chem. Soc.*, **90**, 429 (1968).

(13) See N. P. Neureiter, *ibid.*, **88**, 558 (1966), and references cited therein.

(14) J. M. Williams, Jr., Ph.D. Dissertation, Northwestern University, Aug 1966, pp 53–57.

(15) According to this representation the *cis*:*trans* ratio of episulfones formed will depend principally on the extent to which removal of proton H_A of **5** is preferred to removal of proton H_B (from, *e.g.*, the alternative conformation in which the R groups are *cis*). Since, however, proton removal is reversible,[13] the ratio will also depend on the relative rates of episulfone formation from the two isomeric, asymmetric carbanions. The decrease in *cis*:*trans* ratio for R = Me, Et, Pr[13] can be accommodated by assuming appropriate values for the two equilibrium constants and the two rate constants.

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Substituent Effects in Unimolecular Ion Decompositions. XIII.[1] The Quantitative Effect of Product Ion Stability

Sir:

Since our earlier work describing aromatic systems in which the effect of substituents on mass spectra was related to Hammett σ constants with a high degree of correlation,[2] other systems have been reported that show less or no such correlation.[3] Recently one of us proposed[1] that there are five major factors by which a substituent can affect product ion abundance; we report here the first quantitative study in which one of these factors can be observed independently. The factor studied, the effect of product ion stability, has previously been postulated to be a major driving force in mass spectral reactions, but only qualitative correlative evidence has been available to support this postulate.[4]

The abundant $C_7H_7^+$ and $YC_7H_6^+$ ions in the spectra of substituted bibenzyls, $YC_6H_4CH_2CH_2C_6H_5$, were chosen for study because of the continuing interest in the possibility of tropylium *vs.* benzyl structures for such ions.[5] In a recent independent study Brown[6] presents persuasive substituent-effect evidence that $YC_7H_6^+$ ions from $YC_6H_4CH_2OC_6H_5$ have the benzyl structure, despite evidence for the tropylium structure in both decomposing[5,7] and minimum-energy[8] $YC_7H_6^+$ ions. As Brown recognized,[6] a less probable explanation for his evidence involves the effect of substituents on the molecular ion energies. Evidence from our system, in which this effect is eliminated, supports his conclusions fully.

To eliminate this substituent effect on the distribution of the internal energy values of the precursor ions[9] and the substituent effect on bond strength and competitive reactions ("factors 1, 3, and 4"[1]), the abundances of the substituted product ion $YC_7H_6^+$ can be compared directly to that of the reference ion $C_7H_7^+$ in each spectrum. Further decomposition of these ions ("factor 5"[1]) is made negligible by utilizing 15.3-eV ionizing electrons. The results, $[YC_7H_6^+]/[C_7H_7^+]$, which should represent the ratio of the averaged rates of formation of these ions, are plotted *vs.* σ^+ constants in Figure 1.

The observed variation of $[YC_7H_6^+]/[C_7H_7^+]$ is $>10^6$, exceeding the dynamic range of the instrument; $\rho = -3.3$, a much larger absolute value than any previously observed.[10] This provides dramatic quantitative support of the postulation that product ion stability is a major driving force for mass spectral reactions and that the structure of the transition state of this endothermic

(1) Part XII: F. W. McLafferty, submitted for publication.

(2) M. M. Bursey and F. W. McLafferty, *J. Am. Chem. Soc.*, **88**, 529 (1966).

(3) P. Brown and C. Djerassi, *ibid.*, **89**, 2711 (1967); D. G. I. Kingston and H. P. Tannenbaum, *Chem. Commun.*, 444 (1968); F. W. McLafferty and M. M. Bursey, *J. Org. Chem.*, **33**, 124 (1968), and references cited therein.

(4) F. W. McLafferty, "Mass Spectrometry of Organic Ions," Academic Press, New York, N. Y., 1963, p 327; "Interpretation of Mass Spectra," W. A. Benjamin, Inc., New York, N. Y., 1966, p 80.

(5) H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963, Chapter 10, and references cited therein.

(6) P. Brown, *J. Am. Chem. Soc.*, **90**, 2694 (1968).

(7) K. L. Rinehart, A. C. Buchholz, G. E. Van Lear, and H. L. Cantrill, *ibid.*, **90**, 2983 (1968).

(8) J. M. S. Tait, T. W. Shannon, and A. G. Harrison, *ibid.*, **84**, 4 (1962).

(9) To be distinguished from the distribution of the internal energy within a particular ion.

(10) The experimental values correlate with σ approximately as well, yielding $\rho = -5.1$.

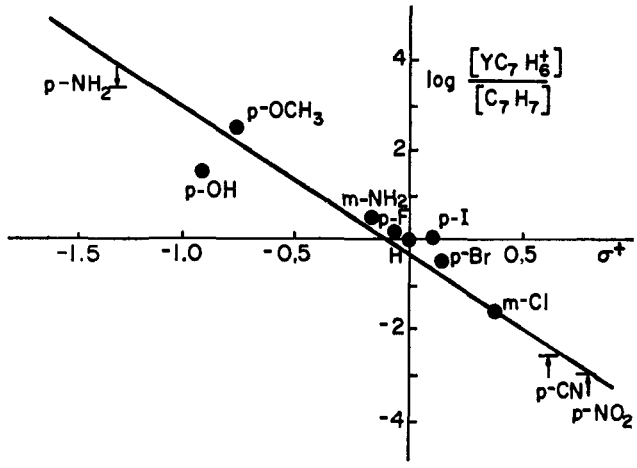

Figure 1. Correlation of the abundance of $YC_7H_6^+$ with that of $C_7H_7^+$ in the spectra of substituted 1,2-diphenylethanes, $YC_6H_4CH_2$-$CH_2C_6H_5$. The values indicated by a line with an arrow are upper or lower limits; in these cases the abundance of one of the conjugate ions was too low for accurate determination. The data were measured at 15.3 eV using a Hitachi RMU-6D mass spectrometer as described previously.[2]

reaction resembles that of the product.[4,11] Further, the substituent effect on the stability of the ion product far exceeds that on the radical product; *e.g.*, in *p*-NH_2-$C_6H_4CH_2CH_2C_6H_5$, although the electron-donating group should stabilize the benzyl radical, the abundance of the conjugate $C_7H_7^+$ ion is still negligible because of the competitive stabilization of the *p*-$NH_2C_6H_4CH_2^+$ ion. This is similar to polar effects observed in free-radical reactions.[12]

Following the reasoning of Brown,[6] the difference of a factor of nearly 1000 in $[NH_2C_7H_6^+]/[C_7H_7^+]$ for the *meta* and *para* isomers can only be explained by different transition states for the respective decompositions. With the strong evidence for the close similarity of the transition state and product ion structures, this is consistent with a benzylic structure for the ground-state $NH_2C_7H_6^+$ products, and not the tropylium structure. Any effect of differences in the distributions of energy values in the molecular ions of the isomers should be eliminated.[1,6]

The correlation of σ^+ with log Z/Z_0, where $Z = [YC_7H_6^+][YC_6H_4CH_2CH_2C_6H_5^+]$, is poor, as expected because the distribution of the energy values of the molecular ions is changing with Y. However, it appears that the ionization potential is an approximate measure of this effect, so that the results are much better correlated by a two-term equation. Such techniques for the quantitative measurement of the basic factors yielding substituent effects[1] will be discussed in the full paper.[13]

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(13) We thank the National Institutes of Health, Grants GM12755 and FR00354, for generous support of this work.

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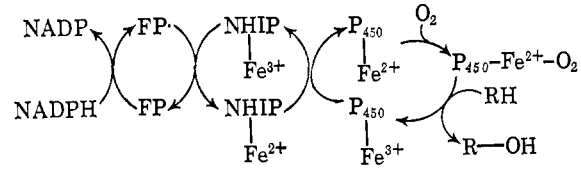
The Roles of Reduced Nicotinamide–Adenine Dinucleotide Phosphate in Steroid Hydroxylation

Sir:

The C-11β hydroxylation of deoxycorticosterone (DOC) by adrenal cortex mitochondria requires reduced nicotinamide–adenine dinucleotide phosphate (NADPH)[1] as the electron donor and incorporates ^{18}O from molecular oxygen into DOC.[2] Since there is nearly a 1:1 correlation between oxygen consumed and DOC hydroxylated,[3] the steroid 11β-hydroxylase of adrenocortical mitochondria falls within the external mixed-function oxidase classification of Mason[4] or the monooxygenase terminology of Hayaishi.[5] Since enzymatic hydroxylation of steroids has been found to proceed with retention of configuration[6-8] and appear to follow the rule of Bloom and Shull,[9] it is likely that enzymatic hydroxylations occur by stereospecific displacement of hydrogen by an electrophilic species such as OH^+. Largely due to the elegant studies of Cooper, *et al.*,[10-12] on the one hand and Kimura's group[13-15] on the other, the mitochondrial steroid 11β-hydroxylase has been resolved into three components: adrenodoxin reductase or flavoprotein (FP), adrenodoxin or nonheme iron protein (NHIP), and cytochrome P_{450} (P_{450}) or hemoprotein. On the basis of reconstitution experiments, Scheme I was proposed[12] for the roles of these components in electron transfer and steroid hydroxylation.

Scheme I



According to Scheme I, reduced cytochrome P_{450} reacts with substrate and molecular oxygen; one atom of the "activated" oxygen molecule is utilized to oxidize the hemoprotein (P_{450}) while the other atom of oxygen reacts with the substrate molecule and results in the introduction of one oxygen atom as a hydroxyl group into the steroid molecule. The function of NADPH is *solely* to provide the reducing equivalents for $P_{450}(Fe^{2+})$ *via* the NADPH–cytochrome P_{450} reductase electron-

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(5) O. Hayaishi, *Proc. Intern. Congr. Biochem., 6th, New York, N. Y.*, 33, 31 (1964).
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