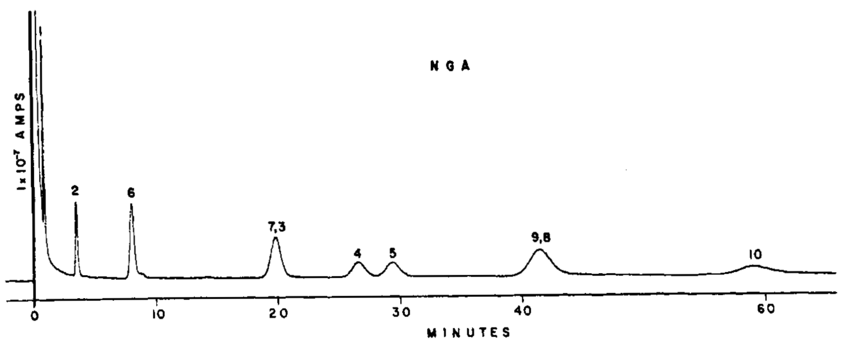

Fig. 1. Separation of steroids with a neopentyl glycol adipate (0.75%) phase on Gas-Chrom P. The conditions and compounds are described in Table I

these may prove to be particularly useful in separation and identification work. Packings with phase concentrations ranging from 0.01 to 10% have been prepared by the filtration technique[3] with these polyesters.

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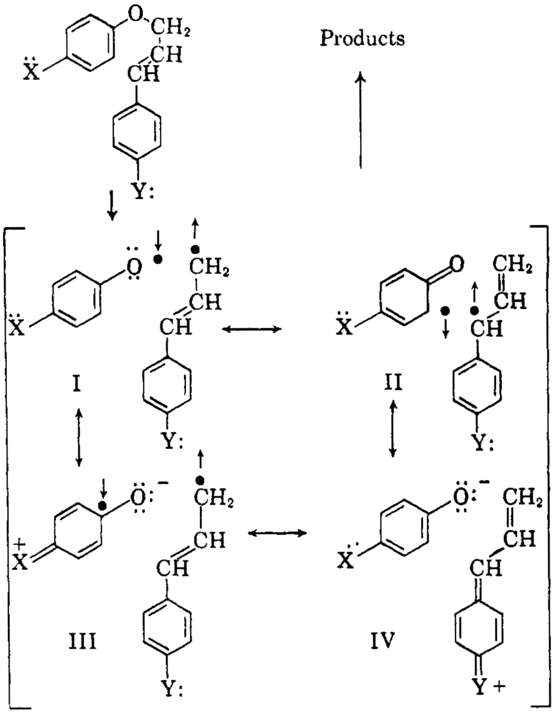
The Electronic Nature of the Transition State of the Claisen Rearrangement

Sir:

Although the Claisen rearrangement has been extensively investigated, the electronic nature of the transition state has not been adequately delineated. For this reason we have made a detailed study of substituent effects on this reaction. The following representation[1,2] is consistent with our experimental findings:



Transition State

It has been shown[3] that the rearrangement rates of allyl *p*-X-phenyl ethers are correlated by Hammett's equation using $\sigma_p{}^+$ constants and a ρ of -0.61 ($r = 0.99$). The isomerization rates of eleven Y-cinnamyl *p*-tolyl ethers were determined spectrophotometrically and are correlated using σ^+ constants and a ρ of -0.40 ($r = 0.99$).

The negative *rhos* indicate that electron depletion occurs in both the cinnamyl chain and the aryloxy portion of the molecule as the reactant changes to transition state. The need for σ^+ constants shows that this electron deficiency interacts directly with the substituent by resonance.

These deductions are accommodated by the proposed transition state. The quasi-radical bond-breaking and bond-forming involves an oxygen atom formally having seven electrons (I). This electron-deficient, electronegative oxygen atom will withdraw electrons from the aryloxy ring (*cf.* III) and the cinnamyl group (*cf.* IV). The electron deficits created in this way would require σ^+ for correlation of substituent effects.[4,5]

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(1) These structures do not imply that actual scission of the molecule into radicals occurs. Structure I is simply the cinnamyl aryl ether with a stretched C—O bond and the γ-carbon in a position to form a long bond to the *ortho* position as indicated in II. Many other contributors of the types shown are possible.

(2) The aryloxy portion of contributing structures I, II, III, and IV are similar to the structures postulated to account for the stability of semiquinones (see G. W. Wheland, *Advanced Organic Chemistry*, 3rd Ed., Wiley, New York, 1960, pp. 802, 803, and 811).

(3) (a) W. N. White, D. Gwynn, R. Schlitt, C. Girard, and W. Fife, *J. Am. Chem. Soc.*, **80**, 3271 (3958); (b) H. L. Goering and R. R. Jacobson, *J. Am. Chem. Soc.*, **80**, 3277 (1958).

(4) Similarly thermal cleavage of *t*-butyl X-phenylperacetates (P. D. Bartlett and C. Rüchardt, *J. Am. Chem. Soc.*, **82**, 3756 (3960)) required σ^+ constants for correlation probably because of the electronegativity of the oxygen of the *t*-butoxy radical.

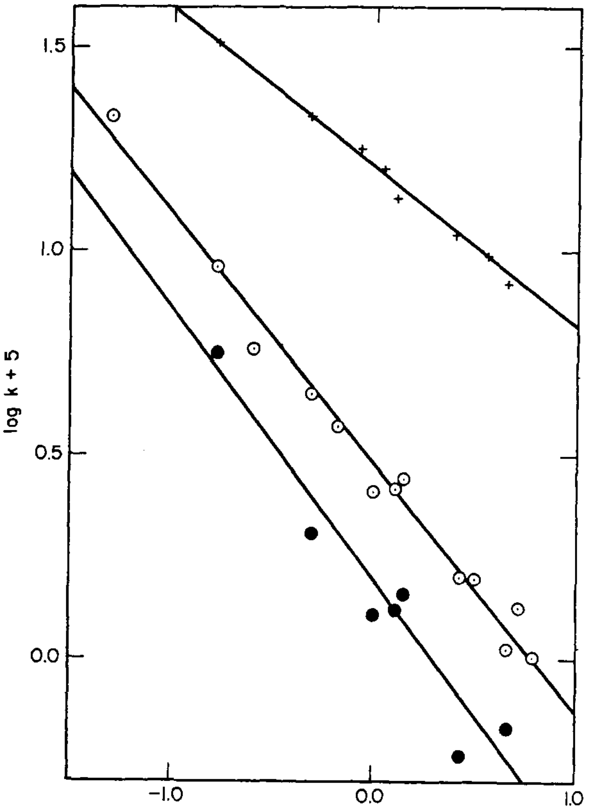
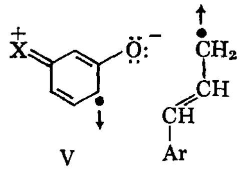


Fig. 1. Hammett plots of rates of rearrangement of substituted allyl aryl ethers: ⊙, allyl *p*-X-phenyl ethers plotted apainst $\sigma_p{}^+$; +, X-cinnamyl *p*-tolyl ethers plotted against σ^+; and ●, rearrangement of allyl *m*-X-phenyl ethers to 2-allyl-5-X-phenols plotted against $\sigma_p{}^+$

This picture of the activated complex also explains the unusual substituent effect in the rearrangement of allyl *m*-X-phenyl ethers (determined spectrophotometrically[2a]). The rates of rearrangement to the unhindered 2-allyl-5-X-phenols were obtained by multiplying the overall rates by the fraction of this isomer formed (ascertained by isotope dilution analysis). These rates were correlated using $\sigma_p{}^+$(*not* $\sigma_m{}^+$) and a ρ of -0.66 ($r = 0.96$), which is similar to that used for the *para* isomers. This result is explicable if structures such as V contribute to the transition state.[6]



V

The proposed transition state also accounts for the accelerating effects of alkyl and aryl substitution at the α and γ-positions in the allyl side chain.

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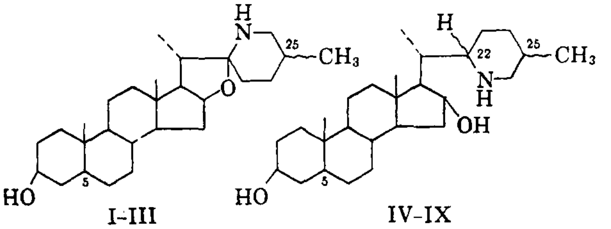
[5] It is reported that inhibition of autoxidation by substituted phenols is correlated by σ^+ constants and a negative ρ (C. D. Cook, D. C. Lane, and R. S. Stone, private communication).

[6] There is no *a priori* reason for expecting a difference in energy between structures III and V. Simple LCAO-MO calculations indicate that the change from reactant to this transition state involves nearly equal energy increments for both *meta* and *para* substituted isomers.

Gas Chromatographic Separation of Steroidal Amines

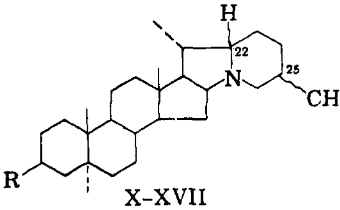
Sir:

Recent studies in this laboratory have established that gas chromatographic methods may be used to separate naturally occurring compounds of complex structure in the steroid[1-5] and alkaloid[6] fields. The sensitivity and resolving power of these methods is now well established; however, it is not known in these fields if structural correlations can be made from retention time interrelationships.



I-III

IV-IX



X-XVII

In order to investigate this point, a study was made of the gas chromatographic behavior of a series of steroidal amines derived from tomatidine

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(1) W. J. A. VandenHeuvel, C. C. Sweeley, and E. C. Horning, *J. Am. Chem. Soc.*, **82**, 3481 (1960) (steroids).

(2) W. J. A. VandenHeuvel, C. C. Sweeley, and E. C. Horning, *Biochem. Biophys. Res. Comm.*, **3**, 33 (1960) (sex hormones and bile acids).

(3) W. J. A. VandenHeuvel and E. C. Horning, *Biochem. Biophys. Res. Comm.*, in press (adrenal cortical steroid hormones).

(4) W. J. A. VandenHeuvel, C. C. Sweeley, and E. C. Horning, "Separation of Steroids by Gas Chromatography," Symposium on Drugs Affecting Lipid Metabolism, Milan, Italy, June 2–4, 1960 (sterols and sterol esters).

(5) C. C. Sweeley and E. C. Horning, *Nature*, **187**, 144 (1960) (steroids).

(6) H. A. Lloyd, H. M. Fales, P. F. Highet, W. J. A. VandenHeuvel, and W. C. Wildman, *J. Am. Chem. Soc.*, **82**, 3791 (1960).