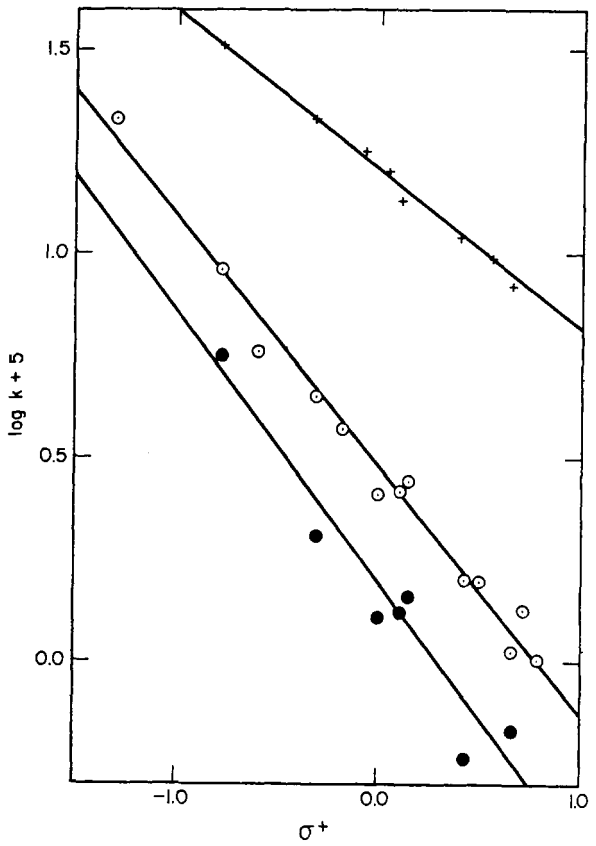
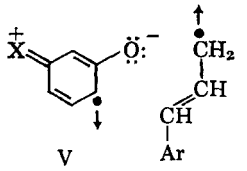


Fig. 1. Hammett plots of rates of rearrangement of substituted allyl aryl ethers: ⊙, allyl *p*-X-phenyl ethers plotted apainst σ_p^+; +, X-cinnamyl *p*-tolyl ethers plotted against σ^+; and ●, rearrangement of allyl *m*-X-phenyl ethers to 2-allyl-5-X-phenols plotted against σ_p^+

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 σ_p^+(*not* σ_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

(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.

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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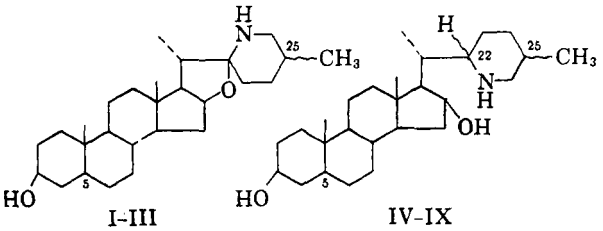
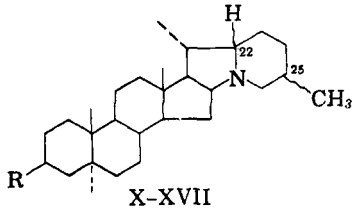
Gas Chromatographic Separation of Steroidal Amines

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.





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

(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).

RETENTION TIME RELATIONSHIPS FOR STEROIDAL AMINES[a]

Compound[b]	C-22 Config.[b]	C-25 Config.[c]		Time[d]
Tomatidine (I)		25 normal(L)	C5α	4.26
5α-Solasodan-3β-ol (II)		25 iso(D)	C5α	4.10
Solasodine (III)		25 iso(D)	Δ[b]	3.95
Dihydrotomatidine A (IV)	22α	25L	C5α	7.33
Dihydrotomatidine B (V)	22β	25L	C5α	7.65
Dihydrosolasodine A (VI)	22α	25D	Δ[b]	7.20
Dihydrosolasodine B (VII)	22β	25D	Δ[b]	7.85
Tetrahydrosolasodine A (VIII)	22α	25D	C5α	7.27
Tetrahydrosolasodine B (IX)	22β	25D	C5α	7.95
C-25L,22-isosolanidan-3-one (X)	22α	25α(L)	R,=O	3.32
C-25D,22-isosolanidan-3-one (XI)	22α	25β(D)	R,=O	3.37
C-25D,solanidan-3-one (XII)	22β	25β(D)	R,=O	2.33
Solanidan-3-one (XIII)	22β	25α(L)	R,=O	2.41
C-25L,22-isosolanidan-3β-ol (XIV)	22α	25α(L)	R,—OH	3.05
C-25D,22-isosolanidan-3β-ol (XV)	22α	25β(D)	R,—OH	3.09
C-25D,solanidan-3β-ol (XVI)	22β	25β(D)	R,—OH	2.13
Solanidan-3β-ol (XVII)	22β	25α(L)	R,—OH	2.24
Cholestane[e]				1.00[d]

[a] Argon ionization detector, 6 ft. × 4 mm. i.d. column, pressure 20 p.s.i., temperature 222°, 0.75% SE-30 phase on Chromosorb W, 80–100 mesh. [b] The notation follows Sato *et al.* [c] The normal configuration corresponds to an axial 25-methyl; the iso configuration to an equatorial 25-methyl. [d] Relative retention time, with cholestane as reference compound. [e] Time, 3.9 min.

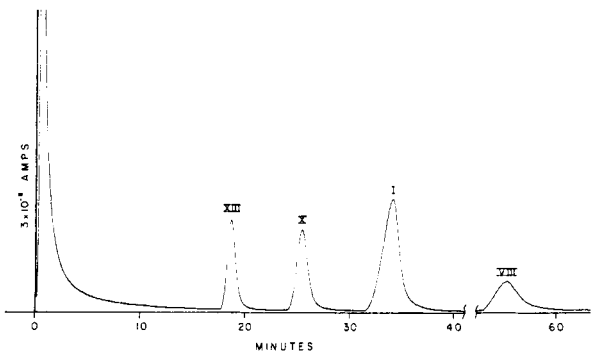


Fig. 1. Gas chromatographic behavior of steroidal amines. Suitable phases are silicones SE-30, SE-52, and SF-96 (General Electric Co.); this separation was carried out at 222°, 18 p.s.i., with 1% SF-96 on Gas-Chrom P, 100–140 mesh, in a 6 ft. × 4 mm. i.d. column. The compounds are identified in the Table.

and solasodine. The Table of relative retention times shows the values obtained in each instance for pairs of compounds which were identical except for the configuration of substituents at C-22 and C-25 carbon atoms. In compounds IV–IX, those having the 22a configuration (Diol A series of Sato and Latham[7]) had a uniformly lower retention time than that observed for the corresponding compounds having the 22β configuration (Diol B series).

For solanidane derivatives, the E,F ring relationship was found to be of major importance in determining the relative retention times. Compounds of the 22β-H series had uniformly much lower retention times than compounds of the 22α-H series. The configuration of the methyl group at C-25 had a smaller effect on the retention time; for each pair of compounds the lower retention time was found when the 22-H and 25-methyl had a *cis*-relationship.

The fact that these compounds may be separated readily by gas chromatographic techniques at 222° is a further illustration of the value of these methods for studying compounds and reactions in the steroid and alkaloid fields. In this instance the stereochemical assignments were made on the basis of relationships established by classical chemical procedures (footnote or references), but it is evident that for groups of compounds correlations may be made between structural features and retention times.

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(7) Y. Sato and H. G. Latham, *J. Am. Chem. Soc.*, **78**, 3150, 3146 (1956); Y. Sato and N. Ikekawa, *J. Org. Chem.*, in press.

Reaction of Benzyne with Organophosphorus Esters[1]

Sir:

Extensive investigations of the reactions of benzyne with nucleophiles have been conducted in recent years[2]; a number of these reactions have employed heteroatom nucleophiles leading to the

(1) Phosphonic Acids and Esters V. Part IV, C. E. Griffin, *Chem. & Ind.*, 1058 (1960).

(2) For a recent review of the chemistry of benzyne, see R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960).