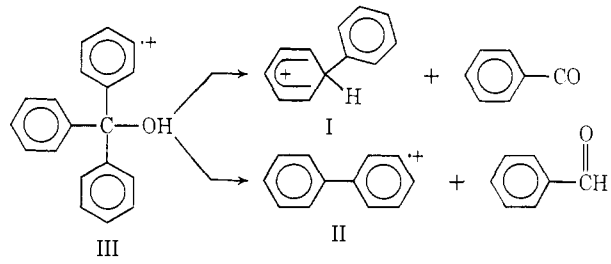
Skeletal Rearrangements in Mass Spectra. II. Evidence for the Radical Site Mechanism[1]

Sir:

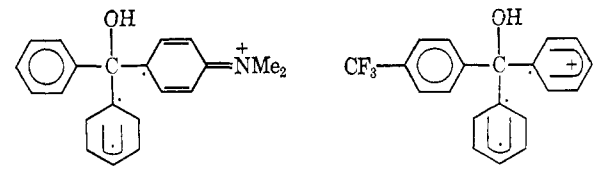
Recently a surprising number of examples of mass spectral rearrangements have been cited which involve the migration of atoms other than hydrogen.[1,2] Obviously, failure to recognize such a skeletal rearrangement in the spectrum of an unknown could lead to erroneous conclusions as to the structure of the unknown. Conversely, an understanding of such rearrangements could make them useful for structure determination, paralleling the usefulness found for many reactions involving the rearrangement of hydrogen atoms.[3] We have recently pointed out[1] that a wide variety of bisunsaturated compounds commonly undergo skeletal rearrangements in which part or all of the bridging moiety is eliminated. We postulated[1] a reaction mechanism involving attack of a radical site of one unsaturated group on the polarizable π electrons of the other group, although mechanisms involving the site of the positive charge should also be considered.[1-4] We present here substituent effect[5] evidence in support of the radical site mechanism.

A system containing three aryl groups, substituted triphenylcarbinols, was chosen for study in order that the reference reactivity of the phenyl group could be compared to those of the aryl groups in the same compound; this minimizes reactivity differences due to the effect of the substituent on the energy values of the precursor ions.[6] Ions chosen for study were $C_{12}H_{11}^+$ and $C_{12}H_{10}\cdot^+$, for which I and II, respectively, are possible structures.[7] The relative abundances using 30-eV electrons are I, 0.46; II, 0.76; $M\cdot^+$ (III), 1.00; $(M - C_6H_5)^+$, 2.41; and C_7H_5O (base peak), 2.86. Table I shows the effects of a strongly electron-donating group, p-$N(CH_3)_2$, and a strongly electron-withdrawing group, p-CF_3, on the formation of these ions.



III I II

Electron-withdrawing groups should weaken the aryl–C_α bond which is cleaved in forming the rearranged ions; despite this, in all cases formation of the rearranged ion containing the most strongly electron-donating aryl group is favored. Although such an aryl group should be the favored site for ionizations, as illustrated in IV and V, the site of highest *net* positive charge (such as the nitrogen atom in IV) cannot be involved in the reaction center on steric grounds. However, the radical character[8] of the molecular ion should also be concentrated on the ring of lowest ionization potential. Thus in IV the sterically favorable position *para* to the $-NMe_2$ group (as well as on the *ortho* positions) should be a reactive site. The substituents can also affect these abundances by influencing other factors such as bond energies or the rates of competing reactions;[11] these factors do not appear to be sufficiently



IV V

Table I. The Effect of Substituents on Skeletal Rearrangements in Triphenylcarbinols, $C_6H_5(C_6H_4Y)(C_6H_4Y')COH$[a]

	$(M - Me_2NC_7H_4O)/(M - C_7H_5O)$[b]	$(M - CF_3C_7H_4O)/(M - C_7H_5O)$	$(M - Me_2NC_7H_5O)/(M - C_7H_6O)$	$(M - CF_3C_7H_5O)/(M - C_7H_6O)$
Y = p-NMe_2, Y' = H	0.11		0.79	
Y = Y' = p-NMe_2	0.35		0.72	
Y = p-CF_3, Y' = H		19		1.6
Y = Y' = p-CF_3		98		11
Y = p-NMe_2, Y' = p-CF_3	0.05	0.94	0.35	1.7

[a] Measurements were made as described previously[6] at ten values of electron energy from 10 to 70 eV. Only the 30-eV values are reported, as the others support the same conclusions. [b] Abundance per phenyl group of each type; thus if Y' = H the reported values are twice the observed values, and if Y = Y' they are half.

(1) Part I: P. C. Wszolek, F. W. McLafferty, and J. H. Brewster, *Org. Mass Spectrom.*, **1**, 127 (1968).

(2) For a comprehensive review see P. Brown and C. Djerassi, *Angew. Chem. Intern. Ed. Engl.*, **6**, 477 (1967).

(3) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967; F. W. McLafferty, "Interpretation of Mass Spectra," W. A. Benjamin, Inc., New York, N. Y., 1966.

(4) P. Brown and C. Djerassi, *J. Am. Chem. Soc.*, **89**, 2711 (1967).

(5) M. M. Bursey and F. W. McLafferty, *ibid.*, **89**, 1 (1967), and references cited therein.

(6) T. W. Wachs and F. W. McLafferty, *ibid.*, **89**, 5044 (1967); F. W. McLafferty and M. M. Bursey, *J. Org. Chem.*, **33**, 124 (1968); F. W. McLafferty, *Chem. Commun.*, 956 (1968).

(7) These postulations are supported by a more extensive study to be reported in the full paper, which includes examination of the spectra of several isotopically labeled triphenylcarbinols.

(8) Which we equate to the charge density in the highest filled molecular orbital (HFMO), in contrast to the net charge on the molecule.[9] Although we feel that sites of high charge density in the HFMO also account for reactivities in certain other mass spectral and photochemical reactions,[9] it does not mean that these reactions parallel all radical reactions. For example, in certain radical rearrangement reactions in solution a nitrophenyl group migrates in preference to a phenyl group.[10]

(9) F. P. Boer, T. W. Shannon, and F. W. McLafferty, *J. Am. Chem. Soc.*, in press.

(10) P. D. Bartlett and J. D. Cotman, *ibid.*, **72**, 3095 (1950).

(11) For example, the substituent effects on the formation of $(M - YC_7H_5O)\cdot^+$ appear to be less important than those on $(M - YC_7H_4O)^+$. The former reaction probably involves rearrangement of the extra H lost to the departing phenyl group; an electron-donating group on the departing phenyl should thus increase the tendency for this step in the formation of $(M - YC_7H_5O)\cdot^+$.

important to affect our qualitative conclusions concerning the role of the radical site.[12]

(12) We gratefully acknowledge the generous financial support of the National Institutes of Health (GM12755 and FR00354).

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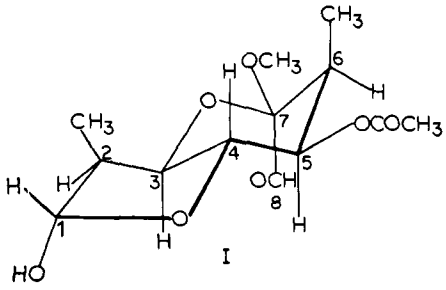
Chemistry of the Streptovaricins. IV. Structure of Varicinal A[1]

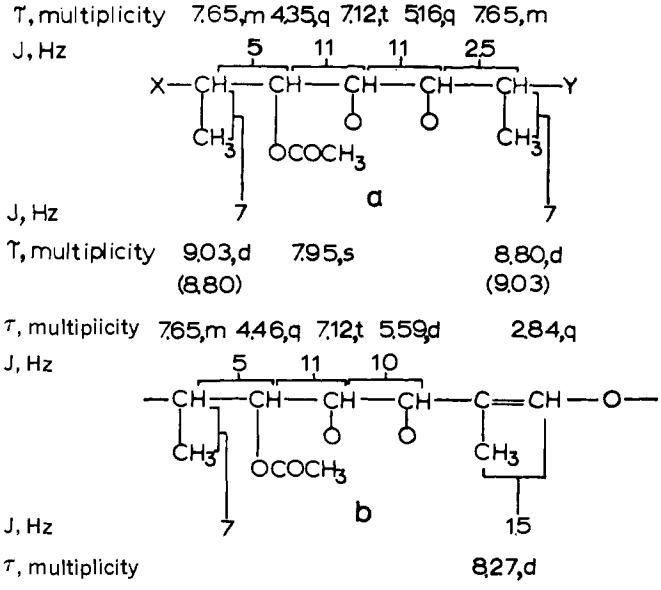
Sir:

We recently reported[2] that streptovaricin A ($C_{42}H_{53}NO_{16}$), a crystalline component of the antituberculosis streptovaricin antibiotic complex, on periodate oxidation gives prestreptovarone ($C_{29}H_{29}NO_9$), containing the chromophore of the antibiotic. We have now isolated the other, nonchromophoric product of this oxidation and assign structure I to the compound, which we have named varicinal A.



I

Although the electron impact produced mass spectrum of varicinal A ($C_{13}H_{20}O_7$. *Anal.* Found: C, 53.95; H, 7.17) does not contain a molecular ion, characteristic ions are found at *m/e* 271 (M − OH), 270 (M − H_2O), 257 (M − CH_3O), and 228 (M − HOAc), and the field ionization produced high-resolution mass spectrum[3,4] contains a molecular ion at the expected *m/e* 288.1201. Decoupling of the nuclear magnetic resonance spectrum (100 MHz, $CDCl_3$) of varicinal A indicates the structural unit a shown. Other protons are found at τ 0.39 (–CH=O, singlet), 4.96 (–CH(O)-O–, broad singlet), and 6.29 (–C(O)OCH_3).



The presence of two aldehyde groups (one masked as a hemiacetal) allows only two carbon skeletons, X = O=HCC(O)(OCH_3)–, Y = –CHO, in a, and the reverse. A decision is provided by the acetylation of varicinal A, which gives a dimeric acetate (mass spectral peak at *m/e* 660) containing the new structural unit b.

The formula (I) shown for varicinal A indicates the relative stereochemistry assigned from the coupling constants listed for partial formula a. The three all-*trans*-axial carbinyl protons of the pyranose ring are readily assigned (J = 11 Hz),[5] as is the adjacent *cis*-equatorial proton (J = 2.5 Hz). The hemiacetal and adjacent methine proton of the furanose ring must be *trans* to one another (J < 1 Hz),[6] but coupling constants do not allow assignment of the relative stereochemistry of the furanose methine proton (on C-2) and the adjacent bridgehead proton (H-3). Similarly, the stereochemistry of the methoxyl and formyl groups at C-7 remains unassigned.

Acknowledgment. This investigation was supported by Public Health Service Research Grants No. AI 01278 and AI 04769 from the National Institute of Allergy and Infectious Diseases. We also thank the Upjohn Co. for generous samples of streptovaricin.

(3) Determined at the Purdue Mass Spectrometry Center.

(4) E. M. Chait, T. W. Shannon, J. W. Amy, and F. W. McLafferty, *Anal. Chem.*, **40**, 835 (1968).

(5) R. U. Lemieux, R. K. Kullnig, and R. Y. Moir, *J. Am. Chem. Soc.*, 80, 2237 (1958); *cf.* also J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 397.

(6) K. L. Rinehart, Jr., W. S. Chilton, M. Hichens, and W. von Phillipsborn, *J. Am. Chem. Soc.*, **84**, 3216 (1962); I. J. McGilveray and K. L. Rinehart, Jr., *ibid.*, **87**, 4003 (1965).

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Chemistry of the Streptovaricins. V.[1] Structures of Streptovaricins A and C

Sir:

Structures I and II have recently been assigned to varicinal A[1] and prestreptovarone,[2,3] respectively, the products of periodate oxidation of the antibiotic streptovaricin A (III).[4]

The structural unit which leads to I can be located in the 100-MHz nmr spectrum of streptovaricin A in unit a_{III} [where the terminal carbons of prestreptovarone (II) are in the shaded area], identified in part by spin

(1) Paper III: R. J. Schacht and K. L. Rinehart, Jr., *J. Am. Chem. Soc.*, **89**, 2239 (1967).

(2) K. L. Rinehart, Jr., C. E. Coverdale, and P. K. Martin, *ibid.*, **88**, 3150 (1966).

(1) K. L. Rinehart, Jr., and H. H. Mathur, *J. Am. Chem. Soc.*, **90**, 6240 (1968).

(2) K. L. Rinehart, Jr., C. E. Coverdale, and P. K. Martin, *ibid.*, **88**, 3150 (1966).

(3) Structure II has the *cis* linkage about the γ,δ-double bond of the dienamide group (rather than the *trans* linkage shown earlier),[2] in keeping with the H_γ,H_δ coupling constant, 11.5 Hz. The same coupling constant is found in the 100-MHz spectrum of the intact antibiotic (III).

(4) K. L. Rinehart, Jr., P. K. Martin, and C. E. Coverdale, *J. Am. Chem. Soc.*, **88**, 3149 (1966).