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).

(13) To whom inquiries should be addressed at the Department of Chemistry, Cornell University, Ithaca, N. Y. 14850.

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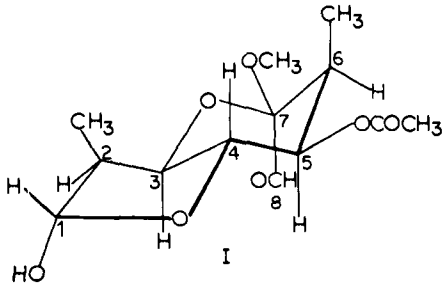
Chemistry of the Streptovaricins. IV. Structure of Varicinal A[1]

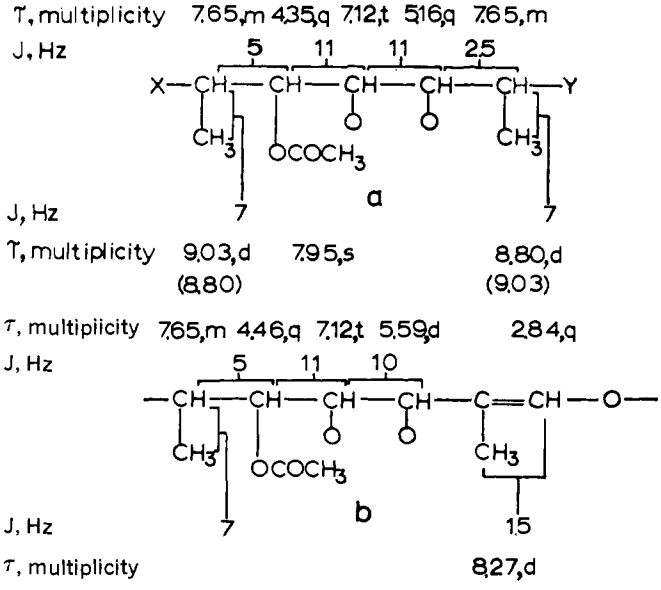
Sir:

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).

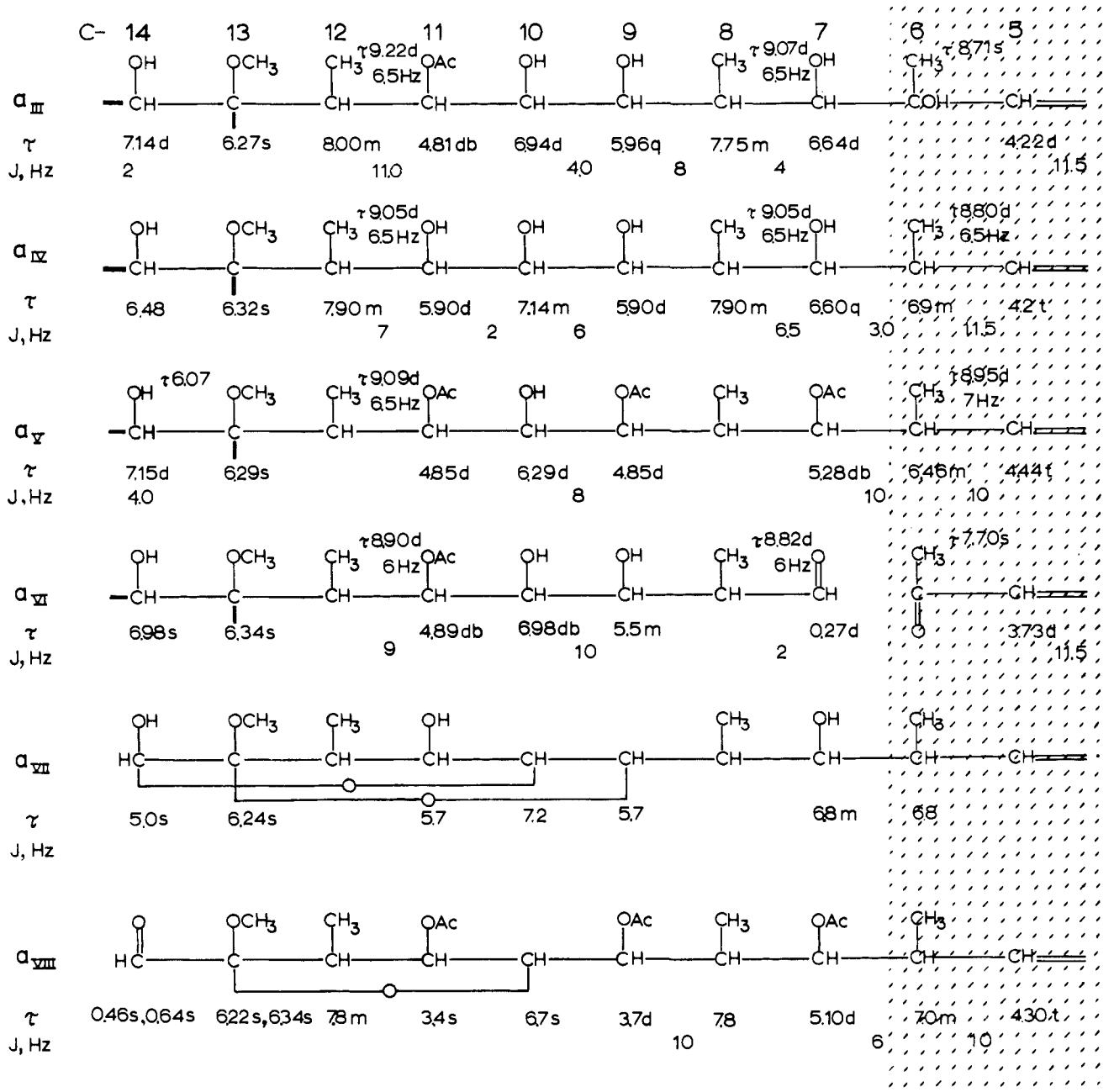
(2) K. L. Rinehart, Jr., C. E. Coverdale, and P. K. Martin, *ibid.*, **88**, 3150 (1966).

(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).



decoupling.[5] Related units are identified in streptovaricin C (IV)[4] and its triacetate V, mp 230–231° [$C_{46}H_{57}NO_{17}$. *Anal.* Found: C, 61.36; H, 6.65; N, 1.90; OAc, 18.46; mol wt (mass spectrometry), 895], as a_{IV} and a_V, respectively.

Quantitative oxidation studies and molecular formulas of the compounds concerned (streptovaricin A, $C_{42}H_{53}NO_{16}$; prestreptovarone, $C_{29}H_{29}NO_9$; varicinal A, $C_{13}H_{20}O_7$) show that I and II are the products of 2 mol of periodate oxidation of III. With limited periodate, III gives a 1-mol product, VI [$C_{42}H_{51}NO_{16}$. *Anal.* Found: mol wt (mass spectrometry), 825], which consumes a second mole on further oxidation, to give I and II. That varicinal and prestreptovarone are not formed from 1-mol uptake indicates a second linkage of the two, oxidizable with periodate.

This linkage is defined by the observation that both streptovaricin C (IV), which lacks the allylic hydroxyl of III (and thus one vicinal glycol grouping of III), and its triacetate V consume only 1 mol of periodate, to give products VII and VIII, respectively, containing the groupings a_{VII} and a_{VIII}, analogous to varicinal A (I). Since the only bonds unaccounted for in unit a_V of triacetate V are those shown (dark lines), C-13 and C-14 must be attached to the prestreptovarone unit of the streptovaricins.

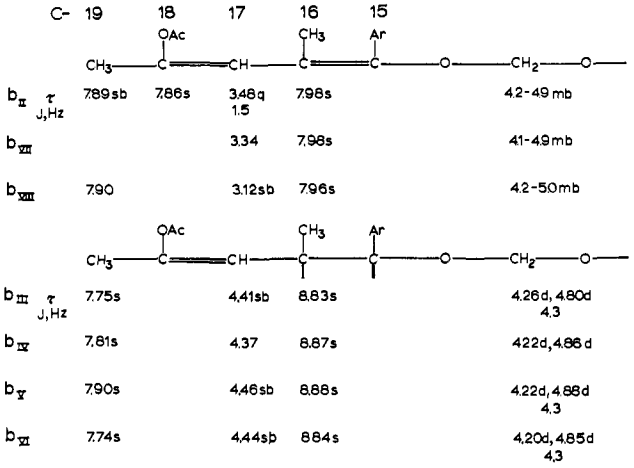
The C-16 methyl protons of prestreptovarone (II) are found in the olefinic methyl region and the methylenedioxy protons as a broad multiplet[6] (see unit b_{II}); similar observations obtain for these protons of strepto-

(5) Chemical shifts and coupling constants will be discussed more extensively in the full paper.

(6) That the methylenedioxy protons of III, IV, V, and VI appear as an AB quartet indicates a rigid six-membered ring system without rapid inversion. This situation is found also in certain degradation products of streptovarone, for example, in methyl desazavarone (IX),[7] isolated from basic methanolysis of streptovarone. In prestreptovarone and in streptovarone ring inversion is of intermediate rate and the methylene protons appear as a broad multiplet which can be sharpened to a singlet on warming or split to an AB quartet on cooling.

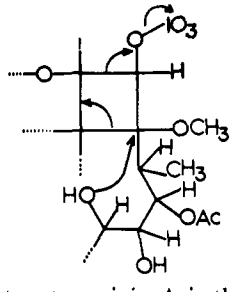
(7) P. K. Martin, Ph.D. Thesis, University of Illinois, Urbana, Ill., June 1965.

varone,[2] VII and VIII (b_{VII} and b_{VIII}). However, these same protons occur, respectively, in the aliphatic methyl region and as an AB quartet[6] in the 100-MHz spectra of streptovaricins A and C, and of V and VI as well, indicating introduction of a C-15,C-16 double bond in the periodate oxidation. Similar evidence is provided by the shift of the C-17 olefinic proton from the unconjugated to the conjugated region after oxidation.

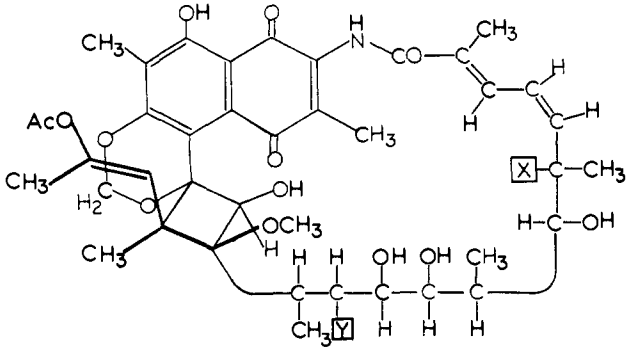


Thus, the linkage of C-13 and C-14 to streptovarone must be at C-15 and C-16, *i.e.*, in a cyclobutanol ring. Biosynthetic considerations (acetate–propionate pathway) suggest a C-14,C-15 linkage.

Oxidation of the substituted cyclobutanol unit then accounts for the uptake of the second mole of periodate in III and of the single mole in IV and V. Although periodate oxidation of an alcohol is unusual, it can be rationalized by the mechanism shown.



The structure of streptovaricin A is then assigned as III and that of streptovaricin C as IV. This represents the second identification of an *ansa* macrolide in nature, the first being rifamycin B, whose structure is related.[8]



III: X = OH, Y = OAc

IV: X = H, Y = OH

(8) W. Oppolzer, V. Prelog, and P. Sensi, *Experientia*, **20**, 336 (1964).

Acknowledgment. This investigation was supported in part by Public Health Service Research Grant AI-01278 from the National Institute of Allergy and Infectious Diseases. We also thank the Upjohn Co. for generous samples of streptovaricin and Mr. Robert Thrift for considerable assistance in the spin-decoupling experiments.

(9) Holder of Union Carbide and Standard Oil of California Fellowships, and of Koppers and U. S. Rubber Summer Fellowships.

(10) Du Pont Teaching Fellow, National Science Foundation Summer Fellow.

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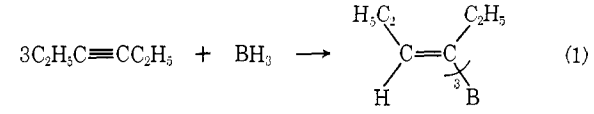
A Stereoselective Synthesis of Conjugated Dienes from Alkynes *via* the Hydroboration–Iodination Reaction[1]

Sir:

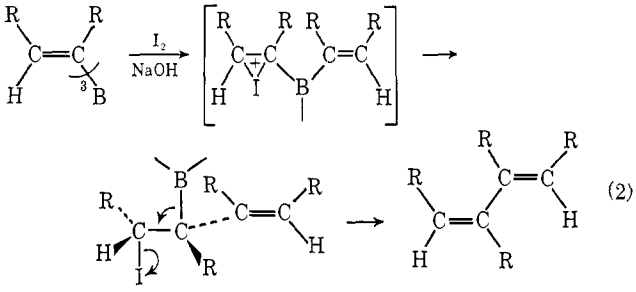
Recently we reported that the addition of iodine to vinyldialkylboranes in tetrahydrofuran solvent results in the migration of one alkyl group from boron to the adjacent carbon atom to afford isomerically pure *cis* olefins.[2] In the course of a study to establish the migratory aptitudes of various groups, and to determine whether the migrating group retains its configuration in the rearrangement step, we have now investigated the iodination of di- and trivinylboranes.

The hydroboration of disubstituted alkynes with borane in a 3:1 ratio in tetrahydrofuran solvent gives the corresponding trivinylboranes. Thus, 3-hexyne is converted by this procedure into tris(*cis*-3-hex-3-enyl)borane in excellent yield[3] (eq 1). Addition



(1)

of iodine and sodium hydroxide to the tetrahydrofuran solution of this vinylborane gives a 68% yield of *cis,trans*-4,5-diethyl-3,5-octadiene. The formation of the *cis,trans*-diene may be rationalized in terms of an initial addition of iodine to the double bond followed by the subsequent migration of a vinyl group from boron to the adjacent carbon atom to give the β-iodoorganoborane (eq 2). It has been suggested that



(2)

the migration of an alkyl group, which results from the iodination of a dialkylvinylborane, proceeds with inversion at the migration terminus, and that the

(1) This research was supported by National Science Grant No. GP-6633.

(2) G. Zweifel, H. Arzoumanian, and C. C. Whitney, *J. Amer. Chem. Soc.*, **89**, 3652, (1967).

(3) H. C. Brown and G. Zweifel, *ibid.*, **83**, 3834 (1961).