from trimethylsilyl radicals have been proposed for the pyrolysis of trimethylsilane[6] and tetramethylsilane.[7] Roark and Peddle did detect a 3% yield of trimethylsilane in their low temperature extrusion reactions, and a similar quantity is found in our experiments at 700 °C.

However, we detect no trimethylsilane at 600 °C, and the yields of dimethyldisilacyclobutanes are much higher at both temperatures than that of the trimethyl compound. Therefore whatever secondary reaction is the source of the small amount of trimethyldisilacyclobutane, it seems certain that the dimethyldisilacyclobutanes, formed in competition with silylene addition reactions, are the result of reactions second order in silylene. We favor the dimerization of silylene followed by rearrangements as the operative reaction mechanism.

While the possibility of silylene dimerization has entered previous mechanistic discussions,[8] the facile dimerization even in the presence of a tenfold excess of propyne found in this work suggests that dimerization may compete successfully with other silylene reactions under a variety of reaction conditions.

Acknowledgments. The influence of Professor Maitland Jones is very strong on this work, and we thank him for his insight and encouragement. This work was supported by the United States Energy Research and Development Administration. This is technical report COO-1713-61.

References and Notes

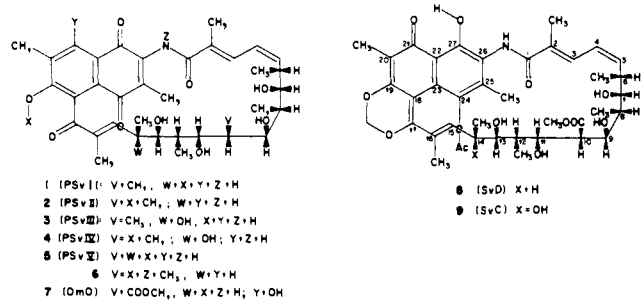
(1) (a) W. H. Atwell and D. R. Weyenberg, *Angew. Chem., Int. Ed. Engl.*, **8**, 469 (1969); (b) P. P. Gaspar and B. J. Herold, "Carbene Chemistry", 2nd ed, W. Kirmse, Ed., Academic Press, New York, N.Y., 1971, p 504.
(2) (a) W. H. Atwell and D. R. Weyenberg, *J. Am. Chem. Soc.*, **90**, 3438 (1968); (b) W. H. Atwell, L. G. Mahone, S. F. Hayes, and J. G. Uhlmann, *J. Organomet. Chem.*, **18**, 69 (1969).
(3) D. N. Roark and G. J. D. Peddle, *J. Am. Chem. Soc.*, **94**, 5837 (1972).
(4) The formation of monomeric products from addition of a silylene to an acetylene has only recently been observed by Ring and co-workers. See C. H. Haas and M. A. Ring, *Inorg. Chem.*, **14**, 2253 (1975). Normally only dimeric products, 1,4-disila-2,5-cyclohexadienes are obtained from addition of silylenes to acetylenes. See ref 1 and T. J. Barton and J. A. Kilgour, *J. Am. Chem. Soc.*, **96**, 7150 (1974).
(5) Ring (see ref 4) has obtained $SiH_3C{\equiv}CH$ from SiH_2 + $HC{\equiv}CH$. The mechanism of this reaction is under active investigation. We believe that ethynylsilane derivatives result from rearrangement of silacyclopropene initial adducts as suggested by Ring.
(6) I. M. T. Davidson and C. A. Lambert, *J. Chem. Soc. A*, 882 (1971).
(7) R. P. Clifford, B. G. Gowenlock, C. A. F. Johnson, and J. Stevenson, *J. Organomet. Chem.*, **34**, 53 (1972).
(8) See the discussion by Barton and Kilgour, ref 4.

Robert T. Conlin, Peter P. Gaspar*
Department of Chemistry, Washington University
St. Louis, Missouri 63130
Received October 6, 1975

Protostreptovaricins I-V[1]

Sir:

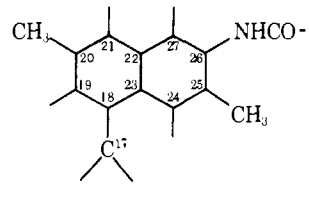
Biosynthetic studies of the ansamycins,[2] antibiotics of interest both for their remarkable structures and their biological properties, have recently demonstrated that the rifamycins,[3] the streptovaricins,[4] and geldanamycin[5] arise from propionate (methylmalonate), acetate (malonate), methionine, and a C_7 unit apparently derived from shikimate or a related compound. In our continuing investigation of the accompanying minor components of the streptovaricin complex,[1b,6,7] we describe here the isolation and properties of protostreptovaricins I-V, apparent precursors of streptovaricins containing the complete carbon skeleton of the antibiotics but lacking much of their oxygenation, and assign them structures **1-5**, respectively. The protostreptovaricins, which are active inhibitors of reverse transcriptase, appear to be still earlier precursors of the naphthoquinone ansamycin antibiotics than damavaricin D(DmD, **7**)[1b] or the very recently reported rifamycin W.[8-10]



Protostreptovaricins I-V were isolated in small amounts by repeated chromatography of fractions from the streptovaricin complex.[11] The most abundant, protostreptovaricin I (PSvI), mp 270-271 °C, $[\alpha]^{25}D$ +703° (*c* 0.202, $CHCl_3$), has a molecular formula, $C_{36}H_{47}NO_9$,[12] which lacks four carbons and four oxygens of streptovaricin D (SvD, **8**, $C_{40}H_{51}NO_{13}$).[11] The infrared spectrum of PSvI contains carbonyl absorption at 1665 and 1640 cm^{-1} but lacks the enol acetate and carbomethoxyl absorption of SvD. In agreement with this conclusion, the ^1H NMR spectrum ($CDCl_3$) of PSvI lacks methoxyl protons (near 3.8 ppm) and one deshielded methyl singlet (acetate, near 2.2 ppm), as well as the methylenedioxy protons (AB quartet near 5.7 ppm) of SvD. However, one more methyl doublet is observed in the ^1H NMR spectrum of PSvI than in that of SvD. Since the carboxyl carbon of SvD is known to be derived from the methyl carbon (C-3) of propionate,[4] the extra methyl can be located at C-10 of PSvI, which is in any event the only available position; this is confirmed in the ^{13}C NMR spectrum ($CDCl_3$) discussed below. These changes (-OH for -OAc, -OH HO- for $-OCH_2O-$, $-CH_3$ for $-COOCH_3$) account for the four carbons of SvD lacking in PSvI, as well as for three of the four missing oxygens.

The remainder of the ansa bridge protons are found at nearly identical positions for PSvI and SvD:[13] 2-methyldienamide group (8.37 ppm, broad, NH; 7.69 ppm, d, J = 12 Hz, H-3; 6.50, t, J = 12 Hz, H-4; 5.70, t, J = 12 Hz, H-5); a total of five $-CHCH_3$ methyl doublets at 0.69, 0.76, 0.94, 1.00, and 1.23 ppm; four -CHOH methine protons at 3.47, 3.52, 3.65, and 4.08 ppm; an olefinic doublet at 5.66 ppm, d, J = 10 Hz; four $=C-CH_3$ singlets at 1.97, 2.02, 2.21, and 2.36 ppm. Confirming these conclusions are the ^{13}C NMR absorptions (Figure 1) for the aliphatic region, which are generally very close to those for streptovaricin D.[14] Thus, the ansa bridge is like that in SvD except for the substitution of a methyl for a carbomethoxyl group. The structural similarity of the ansa chain of PSvI to that of SvD can be extended to C-16 by the observation of an olefinic doublet at 5.66 ppm (t, J = 10 Hz, H-15) and the olefinic methyl group cited above.

The remainder of the structure (a) of PSvI ($C_{13}H_8O_4$)



a

includes C-17 through C-27 of SvD, with C-26 attached to the amide nitrogen and C-20 and C-25 to methyl groups. The remaining two hydrogens are found at 7.89 (aromatic)

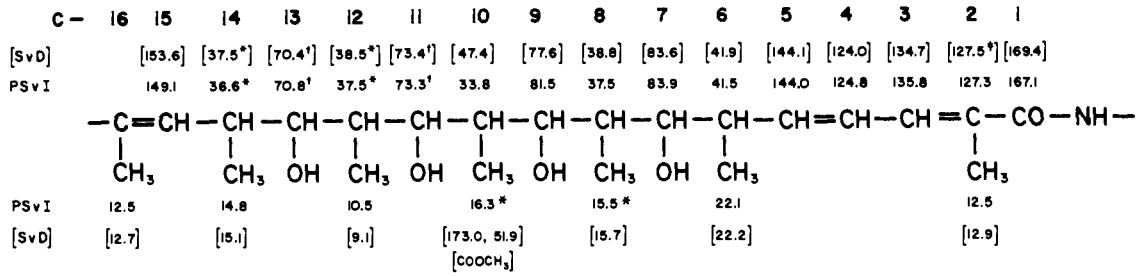
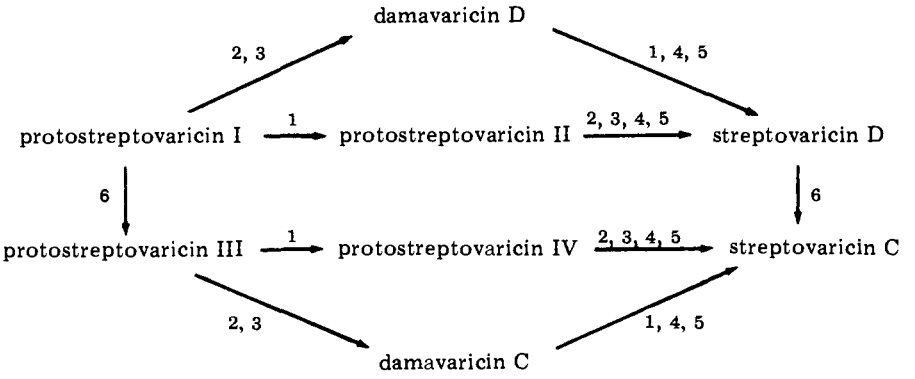


Figure 1. Carbon absorption in the aliphatic regions of protostreptovaricin I (PSvI) and streptovaricin D (SvD). Signals marked * or † may be interchanged.

Scheme I. Proposed Routes from Protostreptovaricins to Streptovaricins[a]



[a] Numbered steps are: (1) methylation of 19-hydroxyl; (2) conversion of 10-methyl to 10-carbomethoxyl group; (3) hydroxylation at C-21; (4) enolization at C-17, oxidation of 17-hydroxyl and 19-methoxyl to methylenedioxy group; (5) reduction at C-24 and C-27 to hydroquinone, acetylation of 24-hydroxyl; (6) hydroxylation at C-14.

and 9.47 ppm (hydrogen-bonded hydroxyl) in the ^{1}H NMR spectrum. Carbon-17, C-19, C-21, C-24, and C-27 all bear oxygen atoms in SvD, but one of the five must be unsubstituted in PSvI. Quinone absorption in the infrared, at 1665 cm^{-1},[15] and quinone carbons in the ^{13}C NMR spectrum, at 180.8 and 184.7 ppm,[16] indicate C-22 through C-27 constitute a naphthoquinone ring; thus, the aromatic ring contains C-18 through C-23. A ketone carbon, at 201.7 ppm in the ^{13}C NMR spectrum, is assigned to C-17. Thus, either C-19 or C-21 of the aromatic ring is hydroxyl substituted. Two lines of evidence show C-19 to be hydroxyl bearing. First, the C-17 carbonyl group's infrared absorption (1640 cm^{-1}) and ^{13}C NMR absorption (201.7 ppm) are like those of *o*-hydroxyacetophenone (1640 cm^{-1},[17] 204.4 ppm).[16] Second, the ^{1}H NMR absorption of the hydroxyl proton is at too high field for a *peri*-hydroxynaphthoquinone, the latter's absorption occurring near 12 ppm or lower.[1b,18] Thus, the chromophore is assigned as that shown for PSvI (**1**). In the light of our assignment of the hydroxyl to C-19, we must dispute the location of a hydroxyl with identical ^{1}H NMR properties at C-21 in the structure recently assigned to naphthomycin;[19] we locate it at C-19 instead.

The structure of PSvII ($C_{37}H_{49}NO_9$,[12a] mp 159–161 °C, $[\alpha]^{25}D$ +241° (*c* 0.315, $CHCl_3$)) follows directly from that of PSvI. The ^{1}H NMR and ^{13}C NMR spectra show an extra methoxyl group (3.89 ppm, 3 H, s; 62.7 ppm, quartet in off-resonance spectrum). The hydrogen-bonded hydroxyl (at 9.47 ppm in the ^{1}H NMR spectrum of PSvI) is lacking and the keto carbonyl appears at 1670 cm^{-1} (non-hydrogen bonded) and 195.8 ppm (shifted upfield from PSvI). These data argue for a 19-*O*-methyl substituent, and this was confirmed by treatment of PSvI with silver oxide–methyl iodide to give PSvII (**2**) together with *N*-methylprotostreptovaricin II (**6**, $C_{38}H_{51}NO_9$,[12a] yellow powder). Protostreptovaricin I inhibits Rauscher leukemia virus RNA-dependent DNA polymerase to the extent of 69% under the previously described conditions,[11] while PSvII inhibits the same enzyme to the extent of 66%.

Protostreptovaricin III (PSvIII, $C_{36}H_{47}NO_{10}$,[12a] mp 135–137 °C, $[\alpha]^{24}D$ +286° (*c* 0.206, $CHCl_3$)) is also closely related to PSvI, differing from PSvI by its hydroxyl group at C-14, as evidenced by a methyl singlet at 1.02 ppm and an olefinic singlet at 5.79 ppm in its ^{1}H NMR spectrum, rather than the corresponding doublets in the ^{1}H NMR spectrum of PSvI; its ketone absorption is at 1630 cm^{-1}. Other protons are like those of PSvI. Thus, PSvIII (**3**) is to PSvI as SvC (**9**) is to SvD (**8**).

Protostreptovaricin IV ($C_{37}H_{49}NO_{10}$,[12a] mp 140–142 °C, $[\alpha]^{24}D$ +302° (*c* 0.281, $CHCl_3$)) is the 19-*O*-methyl derivative (**4**) of PSvIII, as evidenced by methoxyl absorption (3.77 ppm), a methyl singlet (1.24 ppm) and an olefinic singlet (5.94 ppm) in the ^{1}H NMR spectrum, and ketonic absorption at 1660 cm^{-1}.

Protostreptovaricin V ($C_{35}H_{45}NO_9$,[12a] mp 160–162 °C, $[\alpha]^{25}D$ +490° (*c* 0.145, $CHCl_3$)) is tentatively assigned the structure **5**. This is based on its ketonic absorption at 1625 cm^{-1}, its lack of one methyl doublet (four remaining) found in the ^{1}H NMR spectrum of PSvI, and the presence of methylene absorption at 1.57 ppm. The methyl group missing should be the C-10 methyl, since that methyl has been oxidized to a carboxyl in the streptovaricins.

Our present view of the role of the protostreptovaricins in the biosynthesis of the streptovaricins is summarized in Scheme I. Parallel pathways are required to accommodate both PSvII and DmD[1b] on the biosynthetic pathway, and to allow for the biosynthetic conversion of SvD to SvC.[1b]

The present findings are of particular interest in that they establish a point in the biosynthetic scheme at which methionine methylation[4] of the 19-oxygen of SvD occurs; they also would agree with the well-established conversion of an *O*-methyl group to a methylenedioxy group.[20]

Acknowledgment. This work was supported by Contract NIH-NCI-C-72-3208 from the Division of Cancer Treat-

ment, National Cancer Institute. High resolution and field desorption mass spectra were obtained on a mass spectrometer provided by grants from the National Cancer Institute (CA 11,388) and National Institute of General Medical Sciences (GM 16864). Carbon magnetic resonance spectra were obtained on a spectrometer purchased with an instrumentation grant from the National Science Foundation.

References and Notes

(1) (a) Paper XV in the series "Chemistry and Biochemistry of the Streptovaricins". (b) Paper XIV: K. L. Rinehart, Jr., F. J. Antosz, P. V. Deshmukh, K. Kakinuma, P. K. Martin, B. I. Milavetz, K. Sasaki, T. R. Witty, L. H. Li, and F. Reusser, *J. Antibiot.*, in press.
(2) A review: K. L. Rinehart, Jr., *Acc. Chem. Res.*, **5**, 57 (1972).
(3) (a) R. J. White, E. Martinelli, G. G. Gallo, G. Lancini, and P. Beynon, *Nature (London)*, **243**, 273 (1973); (b) A. Karlsson, G. Sartori, and R. J. White, *Eur. J. Biochem.*, **47**, 251 (1974); (c) R. J. White and E. Martinelli, *FEBS Lett.*, **49**, 233 (1974).
(4) B. Milavetz, K. Kakinuma, K. L. Rinehart, Jr., J. P. Rolls, and W. J. Haak, *J. Am. Chem. Soc.*, **95**, 5793 (1973).
(5) (a) R. D. Johnson, A. Haber, and K. L. Rinehart, Jr., *J. Am. Chem. Soc.*, **96**, 3316 (1974); (b) A. Haber, unpublished results.
(6) K. Kakinuma and K. L. Rinehart, Jr., *J. Antibiot.*, **27**, 733 (1974).
(7) K. Kakinuma, C. A. Hanson, and K. L. Rinehart, Jr., *Tetrahedron*, in press.
(8) E. Martinelli, G. G. Gallo, P. Antonini, and R. J. White, *Tetrahedron*, **30**, 3087 (1974).
(9) Rifamycin W is actually more closely related to the streptovaricins than to the previously reported rifamycins.
(10) R. J. White, E. Martinelli, and G. Lancini, *Proc. Natl. Acad. Sci. U.S.A.*, **71**, 3260 (1974).
(11) K. L. Rinehart, Jr., F. J. Antosz, K. Sasaki, P. K. Martin, M. L. Maheshwari, F. Reusser, L. H. Li, D. Moran, and P. F. Wiley, *Biochemistry*, **13**, 861 (1974).
(12) In agreement with the molecular formulas assigned are (a) high resolution mass spectral data, and (b) microanalyses.
(13) K. L. Rinehart, Jr., M. L. Maheshwari, F. J. Antosz, H. H. Mathur, K. Sasaki, and R. J. Schacht, *J. Am. Chem. Soc.*, **93**, 6273 (1971).
(14) K. Kakinuma, B. I. Milavetz, and K. L. Rinehart, Jr., *J. Org. Chem.*, in press.
(15) K. Nakanishi, "Infrared Absorption Spectroscopy–Practical", Holden-Day, San Francisco, Calif., 1969, p 42.
(16) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
(17) C. J. Pouchert, "The Aldrich Library of Infrared Spectra", Aldrich Chemical Co., Milwaukee, Wisc., 1970, p 642.
(18) K. L. Rinehart, Jr., C. E. Coverdale, and P. K. Martin, *J. Am. Chem. Soc.*, **88**, 3150 (1966).
(19) T. H. Williams, *J. Antibiot.*, **28**, 85 (1975).
(20) M. Sribney and S. Kirkwood, *Nature (London)* **171**, 931 (1953).

Prabhakar V. Deshmukh, Katsumi Kakinuma
John J. Ameel, Kenneth L. Rinehart, Jr.*
Roger Adams Laboratory, University of Illinois
Urbana, Illinois 61801

Paul F. Wiley, Li H. Li
The Upjohn Company
Kalamazoo, Michigan 49001

Received September 17, 1975

Stable Chromium(V) Compounds[1]

Sir:

Chromium(V) is known in the form of several solid compounds.[2,3] Solutions of chromium(V) compounds in nonaqueous media, like fuming sulfuric acid[4] or ethylene glycol, have also been prepared; the latter have received a great deal of attention during recent years.[5] Aqueous solutions of chromium(V) are very unstable and undergo rapid disproportionation to chromium(VI) and chromium(III). Thus, although chromium(V) is well known to be formed as an intermediate in the course of chromic acid oxidations, it normally does not accumulate in detectable concentrations. The formation and decay of a chromium(V) intermediate, however, becomes observable in the chromic acid oxidation of oxalic[6-9] and glycolic[10] acids, which seem able to combine with chromium(V) to form relatively stable complexes.

We now wish to report that tertiary hydroxyacids 2-hydroxy-2-methylbutyric acid and citric acid form chromium(V) complexes of considerable stability, permitting for the first time the preparation and storage of aqueous solutions of chromium(V) compounds for extended periods of time.

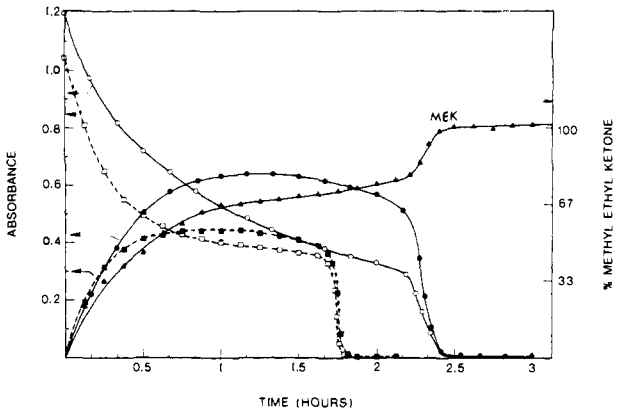


Figure 1. Time dependence of absorbance at 350 and 750 nm and of the formation of methyl ethyl ketone. Only chromium(V) absorbs at 750 nm, both chromium(VI) and chromium(V) absorb at 350 nm. Conditions: 2-hydroxy-2-methylbutyric acid = 0.5 M, $HClO_4$ = 0.5 M, chromium(VI) = 7.75×10^{-3} M, 50 °C; 350 nm, 0.1-cm cell (○); 750 nm, 5-cm cell (●); methyl ethyl ketone (▲); citric acid = 0.5 M, $HClO_4$ = 0.1 M, chromium(VI) = 7.0×10^{-3} M, 70 °C; 350 nm, 0.1-cm cell (□); 750 nm, 5-cm cell (■).

When chromic acid is allowed to react with 2-hydroxy-2-methylbutyric acid at 50 °C or with citric acid at 70 °C and the reaction is monitored spectrophotometrically, an unusual kinetic behavior is observed (Figure 1). At 350 nm (λ_{max} for chromium(VI)), the absorption first decreases almost asymptotically to about 35–40% of the original value, whereupon the reaction starts again and proceeds rapidly to completion. The absorption curve taken at 750 nm, a wavelength at which only chromium(V) absorbs,[10] shows that the concentration of chromium(V) increases until it reaches a maximum value at about the same time when the absorption curve at 350 nm has reached the plateau, and then decreases to an essentially zero value.

The chromic acid oxidation of 2-hydroxy-2-methylbutyric acid (HMBA) yields methyl ethyl ketone (MEK) and carbon dioxide according to eq 1.

$$2Cr(VI) + 3HMBA \rightarrow 2Cr(III) + 3MEK + 3CO_2 \quad (1)$$

The stoichiometry requires the formation of 1.5 mol of methyl ethyl ketone for each molecule of chromium(VI) reduced to chromium(III). Curve MEK in Figure 1 shows that about two-thirds of the expected amount of methyl ethyl ketone is formed by the time the 750-nm curve has reached its maximum.

This behavior indicates the formation of a relatively stable intermediate of chromium in almost quantitative yields at the time when two-thirds of the product has been formed. As at this point only two-thirds of the oxidizing power of chromium(VI) is utilized, chromium(VI) is reduced either to chromium(IV) (Scheme I) or to an equimolar mixture of chromium(V) and chromium(III) (Scheme II or Scheme III).

Scheme I

$$Cr(VI) + HMBA \rightarrow Cr(IV) + MEK + CO_2$$

Scheme II

$$Cr(VI) + HMBA \rightarrow Cr(IV) + MEK + CO_2$$
$$Cr(IV) + HMBA \rightarrow MEK + \cdot CO_2H + Cr(III)$$
$$Cr(VI) + \cdot CO_2H \rightarrow Cr(V) + CO_2$$