configuration,[3] its configuration would be all-*trans* also (III).

(3) Wolfrom and Olin, THIS JOURNAL, **72**, 1724 (1950).

RESEARCH LABORATORIES
MERCK & CO., INC.
RAHWAY, N. J.

FREDERICK A. KUEHL, JR.
MARY NEALE BISHOP
KARL FOLKERS

RECEIVED JANUARY 4, 1951

A NEW REACTION IN ORGANOSILICON CHEMISTRY

Sir:

We wish to report a new reaction which proceeds readily with certain organosilicon structures in the presence of concentrated sulfuric acid and involves cleavage of *one* methyl group from trimethylsilyl, Me_3Si, in a variety of compounds containing functional groups linked to carbon. This reaction makes possible the synthesis of a large number of hitherto unavailable new-type organosiloxanes.[1]

β-Trimethylsilylpropionic acid[2] (294 g.) was added dropwise with stirring to 400 cc. of cold (10°) concentrated sulfuric acid during one and one-half hours. A vigorous evolution of methane (identified by infrared absorption spectrum) occurred during the addition. Reaction was completed by warming on the steam-bath for one hour until gas evolution ceased. The reaction mixture was cooled and poured onto cracked ice, giving immediate formation of a white solid. Recrystallization from *n*-hexane gave 265 g., 95% yield, of 4,4,6,6-tetramethyl-4,6-disila-5-oxanonanedioic acid, m.p. 53–54°. *Anal.* $C_{10}H_{22}Si_2O_5$: Si, 20.16; neut. equiv., 139. Found: Si, 20.02; neut. equiv., 140.

$$2\ Me_3SiCH_2CH_2CO_2H \xrightarrow{H_2SO_4} \xrightarrow{H_2O} (H_2OCCH_2CH_2SiMe_2)_2O + 2\ CH_4$$

Reaction of β-trimethylsilylethylamine,[3] $Me_3SiCH_2CH_2NH_2$, with concentrated sulfuric acid by the procedure described above, followed by treatment with base, gave a 76% yield of 1,7-diamino-3,3,5,5-tetramethyl-3,5-disila-4-oxa-heptane, $(NH_2CH_2CH_2SiMe_2)_2O$, b.p. 115° (13 mm.), $n^{20}D$ 1.4473. *Anal.* $C_8H_{24}Si_2N_2O$: Si, 25.51. Found: Si, 25.46.

Similarly, reaction of 4-trimethylsilyl-2-butanone,[4] $Me_3SiCH_2CH_2COCH_3$, with concentrated sulfuric acid, followed by treatment with water, gave 42% yield of 5,5,7,7-tetramethyl-5,7-disila-6-oxa-2,10-undecanedione, $(CH_3COCH_2CH_2SiMe_2)_2O$, b.p. 142° (6 mm.), $n^{20}D$ 1.4390. *Anal.* $C_{12}H_{26}Si_2O_3$: Si, 20.46; mol. wt., 274. Found: Si, 20.60; mol. wt., 283.

The general scope, definitive constitutional factors, and the mechanism of the above reaction, are under investigation.

(1) It is, of course, important to recognize that organosilicon structures capable of yielding a β-carbonium ion (Me_3-Si-C-C$^+$) with concentrated sulfuric acid will give cleavage of the organic group containing the functional group, and hence cannot undergo the above reaction: *cf.* F. C. Whitmore, L. H. Sommer, J. Gold and R. E. Van Strien, THIS JOURNAL, **69**, 1551 (1947); L. H. Sommer, L. J. Tyler and F. C. Whitmore, *ibid.*, **70**, 2872 (1948); J. Gold, L. H. Sommer and F. C. Whitmore, *ibid.*, **70**, 2874 (1948).

(2) L. H. Sommer, J. Gold, G. M. Goldberg and N. S. Marans, *ibid.*, **71**, 1509 (1949).

(3) β-Trimethylsilylethylamine, b.p. 121° (734 mm.), $n^{20}D$ 1.4241, Si, 24.06% (calcd. 23.93), was prepared by the Hofmann reaction from β-trimethylsilylpropionamide, m.p. 95–96°, Si, 19.43% (calcd. 19.31); which was in turn prepared from β-trimethylsilylpropionyl chloride, b.p. 92° (65 mm.), Si, 16.84% (calcd. 17.03). The latter resulted from treatment of β-trimethylsilylpropionic acid[2] with thionyl chloride.

(4) L. H. Sommer and N. S. Marans, *ibid.*, **72**, 1935 (1950).

THE WHITMORE LABORATORY
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PA.

L. H. SOMMER
N. S. MARANS
G. M. GOLDBERG
J. ROCKETT
R. P. PIOCH

RECEIVED DECEMBER 18, 1950

LIGHT SCATTERING STUDIES ON FIBRINOGEN: PRELIMINARY REMARKS

Sir:

In view of the wide interest appertaining to the fibrinogen-fibrin system and the numerous workers currently engaged upon it, we wish to present here some pertinent results obtained by the light scattering method.[1,2,3,5] These results will also be reported in greater length and detail later.

Fibrinogen was prepared by fractionation of Armour plasma fraction I.[4] A product was obtained which displayed only a single boundary in the ultracentrifuge and with a minimum of 95% polymerizable protein.

Measurements upon three different samples at *p*H's 8.40 and 7.00 at ionic strength 0.35 gave for the native fibrinogen an average molecular weight of 540,000 and a length from the extrapolated dissymmetry coefficient of 850Å. It is apparent that the fibrinogen molecule is an asymmetric, rod-like particle.

The addition of thrombin to an activity of about 0.1 unit/ml. to a 0.14% solution of fibrinogen at *p*H 8.40 and ionic strength 0.35 brought about a rapid increase in dissymetry and turbidity. The increase in length calculated from the dissymetry was linear in time throughout the early stages of the reaction. A comparison of the average degrees of polymerization calculated from the increase in length of fibrinogen molecules as well as end to end association occurred.

Prior to gelation under these conditions the dissymmetry coefficient did not increase beyond the limiting value for a rod-like molecule. At a time immediately preceding gelation the weight average molecular weight was about 4,000,000 and the average length about 2500 Å. It was indicated that rod-like units averaging about three times the length of native fibrinogen and about eight times its molecular weight exist in solution prior to gelation under these conditions.

After gelation a slow increase in both turbidity and dissymmetry occurs. The process at *p*H 7.00 with other conditions unchanged is qualitatively quite similar except that after gelation the turbidity of the gel increased to a slightly higher value than at *p*H 8.40.

The action of papain is qualitatively similar to that of thrombin in producing a gel. The hydrolytic action of the papain slowly dissolved the gel formed, yielding eventually a product of a weight average molecular weight 200,000.

(1) J. T. Edsall, J. F. Foster and H. Scheinberg, THIS JOURNAL, **69**, 2731 (1947).

(2) J. L. Oncley, G. Scatchard and A. Brown, *J. Phys. Colloid Chem.*, **21**, 184 (1947).

(3) K. Laki, *Studies Inst. Med. Chem. Univ. Szeged*, **2**, 27 (1942).

(4) K. Laki, to be published.

(5) J. D. Ferry and P. R. Morrison, THIS JOURNAL, **69**, 388 (1947).

The gel formed by thrombin dissolved readily in 6 *M* urea at *p*H 8.40 to give products of the same molecular weight as native fibrinogen under the same conditions. It was not however possible for the present to ascertain the absolute value of the molecular weight because of uncertainties as to the contribution of selective adsorption to the scattering of such a three component system.

Further work is in progress with the aim of ascertaining the nature of the sub-units involved in the actual formation of the three dimensional network and whether they correspond in size and shape to the aggregates found immediately prior to gelation.

NAVAL MEDICAL RESEARCH INSTITUTE
NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MARYLAND ROBERT F. STEINER
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND KALOMAN LAKI

RECEIVED DECEMBER 16, 1950

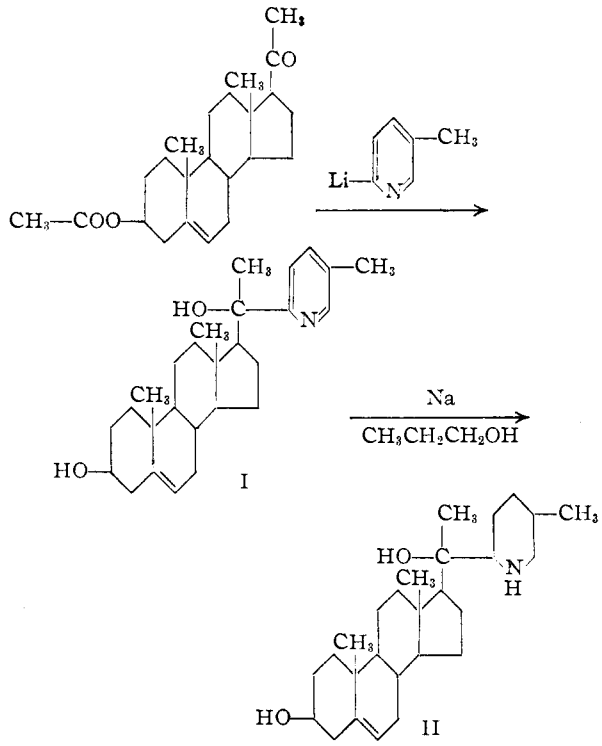
STEROID SECONDARY AMINES[1]

Sir:

The *veratrum*, and closely related *solanum*, alkaloids may be divided into two groups on the basis of the character of the nitrogen function, a separation reaffirmed in a parallel differentiation as a result of pharmacological studies. Because of the wide diversity of pharmacodynamic effects which they exhibit,[2] tertiary veratrum bases of the type of veratridine have been of interest to biologists for nearly a century, while protoveratrine and germitrine, powerful vasodepressor ester alkaloids derived from multiply oxygenated alkamines of this series, have been employed with a certain degree of success in the clinical management of hypertension.[3] The tertiary alkamines, which have been shown to be hexacyclic octahydropyrrocoline derivatives constructed from the perhydrocyclopentanophenanthrene ring system, have been obtained by partial synthesis as exemplified by the conversion of sarsasapogenin to 5-isosolanidane-3β-ol, one of the stereoisomeric dihydro derivatives of solanidine.[4]

The secondary alkamines of the class of veratramine and jervine, on the other hand, have only very recently been shown to exhibit an unprecedented type of remarkable specificity in their ability to annul the effects of accelerans stimulation, as well as to antagonize the positive chronotropic, or cardioaccelerator, properties of epinephrine and related sympathomimetic amines without disturbing the positive inotropic and vasopressor properties of these substances.[5] Steroid secondary amines characterized by the skeletal structure postulated for the naturally occurring secondary veratrum alkamines[6] and for the hydrogenation products of secondary solanum bases of the type of solasodine,[7] have now been obtained by partial synthesis.

2-Bromo-5-methylpyridine[8] has been converted to the 2-lithium derivative with *n*-butyllithium and allowed to react with Δ^5-pregnen-3β-ol-20-one 3-acetate[9] in ether solution to yield the pyridylcarbinol I, m.p. 281–282°; $[\alpha]^{25}D$ −76.8° ($CHCl_3$). *Anal.* Calcd. for $C_{27}H_{39}NO_2$: C, 79.17; H, 9.60; N, 3.42. Found: C, 79.39; H, 9.61; N, 3.42. 3-Acetate, m.p. 225–226°; $[\alpha]^{25}D$ −80.3° ($CHCl_3$); $\Delta^{Ac}_{MD} = -48°$. *Anal.* Calcd. for $C_{29}H_{41}NO_3$: C, 77.12; H, 9.15; N, 3.10. Found: C, 77.07; H, 9.11; N, 3.21. Reduction of I with sodium and *n*-propanol has afforded a fraction yielding an N-nitroso derivative and a slightly soluble picrate, m.p. 248–250°. *Anal.* Calcd. for $C_{33}H_{48}N_4O_9$: C, 61.47; H, 7.50; N, 8.69. Found: C, 61.38; H, 7.60; N, 8.82, which, on conversion to the base with dilute aqueous lithium hydroxide solution, has yielded 20-(5′-methyl-2′-piperidyl)-Δ^5-pregnen-3β,-20-diol (II) m.p. 207–208°; $[\alpha]^{25}D$ −54.8° ($CHCl_3$). *Anal.* Calcd. for $C_{27}H_{45}NO_2$: C, 78.02; H, 10.91; N, 3.37. Found: C, 78.15, H, 10.92; N, 3.64. Hydrochloride, m.p. 294–296°. *Anal.* Calcd. for $C_{27}H_{45}NO_2 \cdot HCl$: C, 71.72; H, 10.26; N, 3.10. Found: C, 71.28; H, 10.20; N, 3.04.



The synthetic alkaloid II, when examined by Dr. Otto Krayer, was found to display the antagonism to the cardioaccelerator properties of epinephrine characteristic of veratramine and jervine at a potency of the order of that exhibited by the latter naturally occurring substance.

DEPARTMENT OF PHARMACOLOGY
HARVARD MEDICAL SCHOOL
BOSTON 15, MASSACHUSETTS FREDERICK C. UHLE

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(1) This work was supported in part by a grant from the United States Public Health Service and in part by funds of the Higgins Trust of Harvard University.

(2) Krayer and Acheson, *Physiol. Rev.*, 26, 383 (1946).

(3) Meilman and Krayer, *Circulation*, 1, 204 (1950); Fried, White and Wintersteiner, THIS JOURNAL, 72, 4621 (1950).

(4) Uhle and Jacobs, *J. Biol. Chem.*, 160, 243 (1945).

(5) Krayer, *J. Pharm. Ex. Therap.*, 96, 422 (1949).

(6) Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., p. 605.

(7) Briggs, Harvey, Locke, McGillivray and Seelye, *J. Chem. Soc.*, 3013, 3020 (1950).

(8) Case, THIS JOURNAL, 68, 2574 (1946).

(9) The pregnenolone used in this work was supplied by the Schering Corporation, Bloomfield, New Jersey, and the Lederle Laboratories, Pearl River, New York.