with lithium aluminum hydride produced the corresponding amine, 5-benzyloxytryptamine, which was isolated as the hydrochloride, m.p. 265° (*Anal.* Calcd. for $C_{17}H_{18}N_2O\cdot HCl$: C, 67.43; H, 6.33; N, 9.26. Found: C, 67.39; H, 6.22; N, 9.32). Catalytic debenzylation of this amine hydrochloride afforded the desired 5-hydroxytryptamine hydrochloride, a light-sensitive hygroscopic salt, m.p. 167–168° (*Anal.* Calcd. for $C_{10}H_{20}N_2O\cdot HCl$: C, 56.47; H, 6.16; N, 13.18. Found: C, 56.07; H, 6.20; N, 12.94). The picrate, formed in water from the hydrochloride, melted (Fischer–Johns apparatus) from 103–111°, resolidified at 124–134° and remelted from 185–189° (*Anal.* Calcd. for $C_{10}H_{12}N_2O\cdot C_6H_3N_3O_7\cdot H_2O$: C, 45.40; H, 4.05; N, 16.55. Found: C, 45.20; H, 3.94; N, 16.62). The absorption spectrum of 5-hydroxytryptamine in aqueous solution at *p*H 5.4 has a maximum at 2750 Å., a shoulder with a point of inflection at 2990 Å., and a minimum at 2500 Å. At *p*H 11.6, the position of the maximum at 2750 Å. is essentially unchanged while the second peak shifts from 2990 to 3220 Å. The data on the picrate and the absorption data on the hydrochloride are in excellent agreement with that published by Rapport[2] for the vasoconstrictor principle, serotonin.

Preliminary pharmacological investigation has shown 5-hydroxytryptamine to have vasoconstrictive properties.

ABBOTT LABORATORIES K. E. HAMLIN
NORTH CHICAGO, ILLINOIS F. E. FISCHER

RECEIVED AUGUST 16, 1951

NINE OR MORE LIQUID PHASES

Sir:

The discovery of an ever-increasing number of incompletely miscible liquid phases has furnished an interesting challenge to physical chemists, not without value in that it has served to direct attention to the variety of factors which can contribute to immiscibility. In 1934 I exhibited a system of five stable liquid phases; in 1940 a sixth was added, and in 1949 a seventh.[1] In 1950 Kittsley and Goeden[2] added to the former set an eighth, a silicone oil; this owes its low solubility in the other liquids to its large cross-linked molecules. I wish now to point out that the "incompatibility" of different high polymers may be invoked to split a liquid in which they are soluble into two or even more liquid layers. Dobry and Boyer-Kawenoki[3] have made an experimental study of a number of such systems and Stockmayer[4] and Scott[5] have given their theoretical interpretation.

For example, the water layer of the previous set can be split into two by using two incompatibles reported by Dobry and Boyer-Kawenoki, methyl cellulose and polyvinyl alcohol, yielding nine layers and there seems no reason to doubt that the same principle could be applied to yield almost unlimited further splitting of any layer for which sufficiently soluble high polymers of different molecular weights and configurations can be found.

(1) J. H. Hildebrand, *J. Phys. Colloid Chem.*, **53**, 944 (1949).
(2) S. L. Kittsley and H. A. Goeden, THIS JOURNAL, **72**, 4841 (1950).
(3) A. Dobry and F. Boyer-Kawenoki, *J. Polymer Sci.*, **2**, 90 (1947).
(4) W. H. Stockmayer, ACS Meeting, Atlantic City, N. J., April, 1949.
(5) R. L. Scott, *J. Chem. Phys.*, **17**, 279 (1949); see also J. H. Hildebrand and R. L. Scott, "Solubility of Nonelectrolytes," 3rd Edition, Reinhold Publishing Corp., New York, N. Y., 1950; H. Tompa, *Trans. Faraday Soc.*, **45**, 1142 (1949).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA J. H. HILDEBRAND
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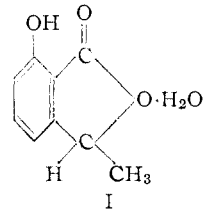
RECEIVED AUGUST 30, 1951

A DEGRADATION PRODUCT OF TERRAMYCIN

Sir:

The hydrolysis of the antibiotic terramycin, $C_{22}H_{24-26}N_2O_9$, in hot 20% sodium hydroxide in the presence of zinc has been previously reported[1] to yield terracinoic acid ($C_{13}H_{12}O_6$), ammonia, dimethylamine, acetic acid, carbon dioxide, and a phenolic lactone, $C_9H_8O_3\cdot H_2O$, m.p. 110–112°. *Anal.* Calcd. for $C_9H_8O_3\cdot H_2O$: C, 59.33; H, 5.54; H_2O, 9.89. Found: C, 59.32; H, 5.79; H_2O (K.F.) 9.30. The structure of the phenolic lactone has been shown by degradation and by synthesis to be 7-hydroxy-3-methylphthalide (I).



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This phthalide is insoluble in bicarbonate and slowly soluble in cold aqueous sodium hydroxide. It gives a purple color with ferric chloride and a positive aminoantipyrine test. Titration of anhydrous I at room temperature shows it to be a monobasic acid with *pK* 8.5 and equivalent weight 162 (calcd. 164). A drop in *p*H occurs when the titrated solution is heated to 100° for one hour indicating the presence of a lactone. In hot sodium ethoxide, I yields an alcohol insoluble crystalline disodium salt of the free acid. *Anal.* Calcd. for $C_9H_8O_4Na_2\cdot H_2O$: C, 44.30; H, 4.12; Na, 18.79. Found: C, 44.00; H, 4.34; Na, 18.45.

Methylation with diazomethane yields a monomethyl ether, m.p. 73–74°, which is very slowly soluble in cold alkali. *Anal.* Calcd. for $C_{10}H_{10}O_3$: C, 67.46; H, 5.76; methoxyl, 17.41. Found: C, 67.45; H, 5.65; methoxyl, 18.0. This methyl ether forms a crystalline alcohol soluble monosodium salt.

Oxidation of the methyl ether of I by potassium permanganate in strongly alkaline solution yields a small amount of 3-methoxyphthalic acid, which has been identified as its anhydride. Fusion of 7-hydroxy-3-methylphthalide (I) with alkali yields salicylic acid, m.p. 159–60°, and acetic acid, identified through its *p*-nitrobenzyl ester, m.p. 77–78°. Cleavage of the aromatic ring-to-carbon bond to yield benzoic acids and aliphatic acids is characteristic of 3-monoalkylated phthalides. This cleavage suggests that the phenolic hydroxyl of I is in the 7 position. This assignment was also favored

(1) R. Pasternack, P. P. Regna, R. L. Wagner, A. Bavley, F. A. Hochstein, P. N. Gordon and K. J. Brunings, THIS JOURNAL, **73**, 2400 (1951).

by the color of the ferric chloride test, and by the abnormally low frequency of the carbonyl absorption in the infrared absorption spectrum (1740 cm.$^{-1}$ in chloroform) as contrasted to the characteristic γ-lactone carbonyl absorption (1765 cm.$^{-1}$ in chloroform) observed for the methyl ether.[2]

Synthesis was effected through the pyridine–piperidine catalysed condensation of 3-methoxyphthalic anhydride with malonic acid, hydrolysis of the resulting 3-methylene-7-methoxyphthalide to 2-acetyl-6-methoxybenzoic acid, and reduction of this intermediate to 7-methoxy-3-methylphthalide by sodium amalgam. This product, which was obtained in low yield, is identical with that derived from terramycin as indicated by melting points, mixed melting point, and the identity of their infrared absorption spectra. Several alternative synthetic routes yielded 4-hydroxy-3-methylphthalide rather than the desired product.

(2) R. S. Rasmussen and R. R. Brattain, THIS JOURNAL, **71**, 1073 (1949).

RESEARCH LABORATORIES
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RECEIVED SEPTEMBER 7, 1951

DEGRADATION OF SOLASODINE

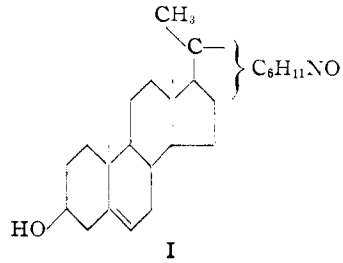
Sir:

In view of the present acute interest in new sources for steroids we wish to report the degradation of solasodine to a pregnane derivative.

To solasodine, the aglycone of the alkaloidal glycoside solasonine obtainable from a number of *Solanum* species[1] has been assigned a steroidal structural formula mainly, because it yielded Diels' hydrocarbon[2,3] in the selenium dehydrogenation.

By treatment of solasodine (m.p. 197–201°[4] $[\alpha]^{20}D$ −98.5°, *c*, 0.396, methanol; calcd. for $C_{27}H_{43}NO_2$: C, 78.40; H, 1048; N, 3.39. Found: C, 78.17; H, 10.29; N, 3.45, acetate, m.p. 191–193°) with acetic anhydride, oxidation of the reaction product with chromic acid anhydride in acetic acid, and subsequent hydrolysis with methanolic potassium hydroxide, we obtained a semi-crystalline mass which was chromatographed, acetylated and again chromatographed twice over alumina (previously washed with ethyl acetate). We eventually isolated 3β-acetoxy-$\Delta^{5,16}$-pregnadiene-20-one (of m.p. 172–174°, $[\alpha]^{20}D$ −24.5 ± 4°, *c*, 0.449, ethanol, calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.38; H, 9.39) and 3β-acetoxy-16α-methoxy-Δ^5-pregnen-20-one of m.p. 157–159°. The identity of these compounds was established by determination of the mixture-melting points, and the comparison of the infrared spectra[5] with authentic samples. A small amount of a third compound not as yet identified (m.p. 198–200.5°, $\lambda_{max.}$ 240, 280) could also be isolated. In addition, a considerable amount of acidic products was formed in the oxidation.

The isolation of the above pregnane derivatives establishes the partial structural formula I for solasodine. One point of attachment of the nitrogen-containing portion is fixed at C-20. The other point is probably at position 16.



I

(1) Henry, "The Plant Alkaloids," 4th ed., The Blakiston Company, Philadelphia, Pa., 1949, p. 666.

(2) Rochelmeyer, *Arch. Pharm.*, **274**, 543 (1936).

(3) See also Rochelmeyer, *ibid.*, **275**, 336 (1937); **277**, 329 (1939); Rochelmeyer, Stützel and Chen, *ibid.*, **282**, 92 (1944); Briggs, *et al.*, *J. Chem. Soc.*, 1, 3, 12 (1942); 3013, 3020 (1950).

(4) All melting points reported were taken on the Kofler block and are uncorrected.

(5) By Mrs. Phyllis B. Humphries, of this Laboratory.

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES YOSHIO SATO
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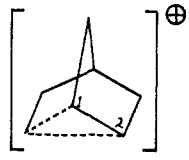
BETHESDA 14, MARYLAND ERICH MOSETTIG

RECEIVED AUGUST 27, 1951

THE NATURE OF THE INTERMEDIATE IN THE SOLVOLYSIS OF NORBORNYL DERIVATIVES[1,2]

Sir:

It has been suggested[3] on the basis of solvolysis rate and stereochemical considerations that the solvolysis of *exo*- and *endo*-norbornyl *p*-bromobenzenesulfonates in acetic acid proceeds by a bridged "non-classical" carbonium ion having a structure (I) like that proposed[4] for the cationic intermediate involved in the rearrangement of camphene hydrochloride to isobornyl chloride. The desirability of tracer experiments to confirm structure I has been pointed out earlier[5] and, as part of



I

an investigation of the mechanisms of reaction of norbornyl derivatives, solvolysis reactions of *exo*- and *endo*-norbornyl-2,3-C_2^{14} *p*-bromobenzenesulfonates are being studied in several solvents.

Solvolysis of the *exo*-isomer (II) in acetic acid via intermediate I would be expected to yield equal[6] parts of *exo*-norbornyl-2,3-C_2^{14} and *exo*-norbornyl-1,7-C_2^{14} acetates since positions 1 and 2 must become equivalent if I is to have a plane of sym-

(1) Supported by the program of research of the U. S. Atomic Energy Commission under Contract AT(30-1)-905.

(2) Presented at the Symposium on Reaction Mechanisms at the 75th Anniversary Meeting of the American Chemical Society, September 7, 1951.

(3) S. Winstein and D. S. Trifan, THIS JOURNAL, **71**, 2953 (1949); S. Winstein and D. S. Trifan, Abstracts of April, 1951, Meeting of the American Chemical Society, 53M, 54M.

(4) T. P. Nevell, E. de Salas and C. L. Wilson, *J. Chem. Soc.*, 1188 (1939).

(5) J. D. Roberts, R. E. McMahon and J. S. Hine, THIS JOURNAL, **72**, 4237 (1950).

(6) Neglecting differences in reaction rate between C^{12} and C^{14} atoms (isotope effect).