tion was accomplished most conveniently by oxidizing the crude product with chromium trioxide to 22-isoallospirostan-3,11-dione (m.p. 236–237°, $[\alpha]^{20}\mathrm{D}$ −17°; found: C, 75.16; H, 9.22), followed by Raney nickel hydrogenation (room temperature) to 22-isoallospirostan-3β-ol-11-one (V)[13] (m.p. 223–226°, $[\alpha]^{20}\mathrm{D}$ −29°; found: C, 75.28; H, 9.93. The acetate[14] showed m.p. 222–224°, $[\alpha]^{20}\mathrm{D}$ −31°; found: C, 73.92; H, 9.60). Alternately, the mixture of III and IVa was converted with ethanedithiol in the presence of zinc chloride to 22-isoallospirostan-3β-ol-11,12-dione 12-cycloethylenemercaptol (m.p. 289–291°; found: S, 11.98), which upon Raney nickel desulfurization led directly to the 11-ketone V. This substance (V) has already been transformed[14] into allopregnan-3β-ol-11,20-dione *and thence*[3] *to cortisone.*

[13] The 3,11-dione as well as V proved to be identical with specimens prepared from diosgenin by the performic acid method (*cf.* G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3546 (1951)).

[14] E. M. Chamberlin, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita, and M. Tishler, *ibid.*, **73**, 2396 (1951), reported m.p. 224–229°, $[\alpha]^{21}\mathrm{D}$ −39.4° for a sample prepared from diosgenin.

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RECEIVED OCTOBER 1, 1951

THE TEMPERATURE OF THE HYDROGEN-FLUORINE FLAME

Sir:

The reaction $H_2(g) + F_2(g) \rightarrow 2HF(g)$ is highly exothermic and in addition gives rise to a reaction product possessed of exceptional thermal stability. These factors combine to produce a very high flame temperature which heretofore has not been measured.

Theoretical calculations based on the method described in Wenner[1] have produced the following flame temperature–composition relationships:

Feed composition Mole % F_2	% H_2	Theoretical flame temperature at 1 atm. total pressure, °K.
10.0	90.0	1920
33.3	66.7	3550
50.0	50.0	4300
66.7	33.3	3800

In these calculations the latest thermodynamic data were employed.[2,3,4,5]

The construction and operation of the hydrogen–fluorine torch has already been described by Priest and Grosse.[6] This torch produces a diffusion-type flame due to the present inability to premix hydrogen and fluorine.

The flame temperature was measured by means of the line-reversal technique.[7] The tungsten ribbon-filament lamp, ordinarily used as the comparison radiator for measurements of this type, could not be employed due to the fact that the flame temperature is above the melting point of tungsten (3640° K.); the same is true of the ordinary carbon arc (sublimation point of carbon 3810°K. at atm. pressure). Since no simple man-made radiator seemed to be available which had the desired characteristics the optical train was modified to use the *sun* as the comparison source. A two-mirror heliostat was used in keeping the sun's image focused on the spectroscope slit. A neutral, variable absorbing agent of good optical quality was used in adjusting the brightness of the sun so that line-reversal could be readily obtained and easily reproduced. An optical pyrometer reading of the sun *through the same filter then gave the flame temperature.* The maximum flame temperature was measured at 4300°K. using stoichiometric quantities of hydrogen and fluorine. The agreement between this value and the theoretical temperature is admittedly fortuitous, the accuracy of our measurements being approximately ±150°.

In this particular line-reversal application it is not possible to employ the sodium lines for reversal due to the occurrence of sodium in the solar spectrum. Lithium was used in the present work since, for all practical purposes, it does not appear in the solar spectrum.

Complete details of our theoretical calculation and experimental work will be published elsewhere.

[1] R. R. Wenner, "Thermochemical Calculations," McGraw-Hill Book Co., New York, N. Y., 1941.

[2] G. M. Murphy and J. E. Vance, *J. Chem. Phys.*, **7**, 806 (1939).

[3] M. G. Evans, E. Warhurst, and E. Whittle, *J. Chem. Soc.*, 1524 (1950).

[4] W. M. Latimer, MDDC-1462, United States Atomic Energy Commission, Declassified Document, November 13, 1947.

[5] A.P.I. Research Project 44, National Bureau of Standards.

[6] H. F. Priest and A. V. Grosse, *Ind. Eng. Chem.*, **39**, 431 (1947).

[7] See B. Lewis and G. v. Elbe's chapter in "Temperature, Its Measurement and Control in Science and Industry," Reinhold Publ. Corp., New York, N. Y., 1940; and C. W. Jones, B. Lewis, J. B. Friauf, and C. St. J. Perrott, THIS JOURNAL, **53**, 869 (1931).

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RECEIVED OCTOBER 1, 1951

THE SYNTHESIS OF THE BLOOD SERUM VASOCONSTRICTOR PRINCIPLE SEROTONIN CREATININE SULFATE

Sir:

The existence of a potent vasoconstrictor agent in the sera of mammals was reported as early as 1868 by Ludwig and Schmidt[1] and since that time has been the subject of over eighty publications.[2] Experiments with sera obtained under various conditions and allowed to stand for variable periods before use have produced a maze of conflicting biological data. This problem has been clarified only recently by Rapport[3,4] who isolated from beef serum a very active vasoconstrictor substance in crystalline form. Rapport was able to show that the crystalline material was a complex, or mixed salt, composed of equimolecular proportions of sulfuric acid, creatinine and an indole base.[5] On the basis of chemical tests as well as analytical and spectral data Rapport has proposed that the indole base is 5-hydroxy-3-beta-aminoethylindole (I) (5-hydroxytryp-

[1] C. Ludwig and A. Schmidt, *Arb. physiol. Anstalt Leipsig*, **1** (1868).

[2] For literature reviews see (a) T. C. Janeway, H. B. Richardson, and E. A. Park, *Arch. Int. Med.*, **21**, 565 (1918); (b) G. Reid and M. Bick, *Austral. J. Exp. Biol. Med. Sci.*, **20**, 33 (1942).

[3] M. M. Rapport, A. A. Green and I. H. Page, *Science*, **108**, 329 (1948).

[4] M. M. Rapport, A. A. Green and I. H. Page, *J. Biol. Chem.*, **176**, 1243 (1948).

[5] M. M. Rapport, *ibid.*, **180**, 961 (1949).

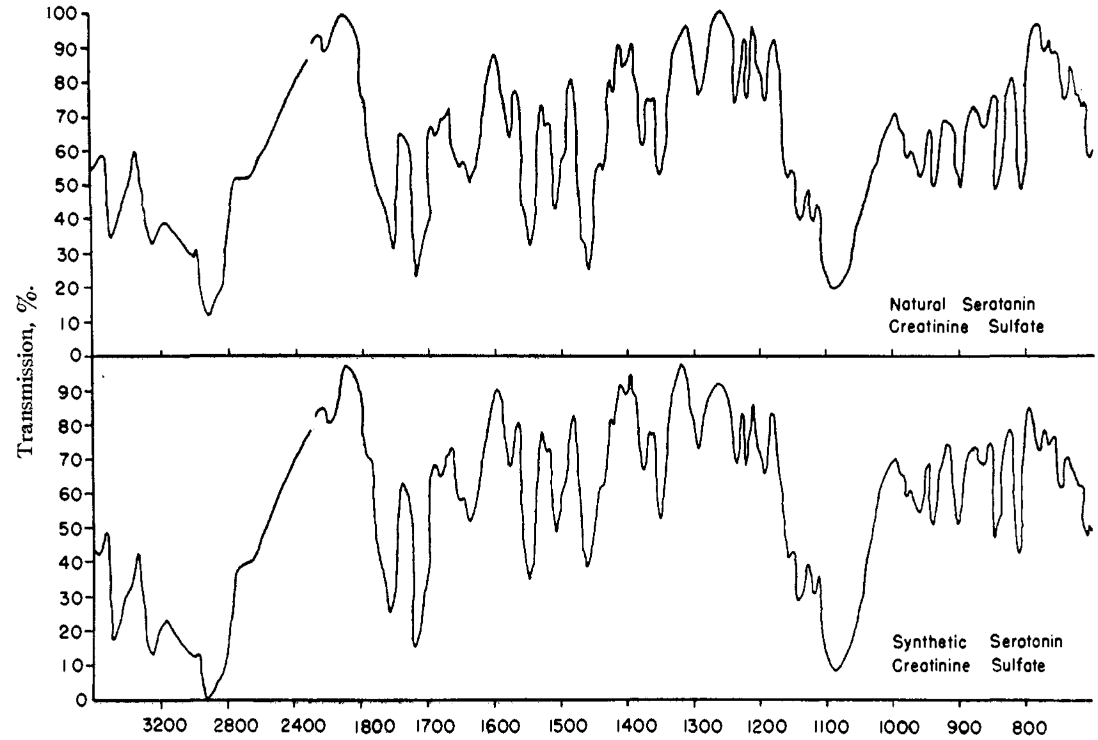
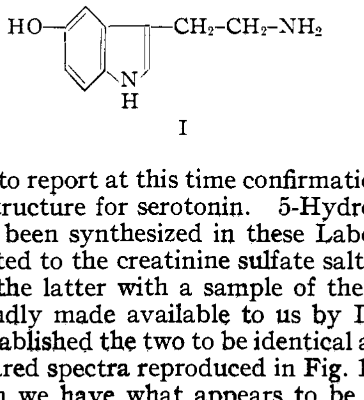


Fig. 1.—Infrared absorption spectra of natural and synthetic serotonin creatinine sulfate complex (Nujol mull).

tamine) to which he has given the name "serotonin."



I

We wish to report at this time confirmation of the proposed structure for serotonin. 5-Hydroxytryptamine has been synthesized in these Laboratories and converted to the creatinine sulfate salt. Comparison of the latter with a sample of the natural product kindly made available to us by Dr. Rapport has established the two to be identical as shown by the infrared spectra reproduced in Fig. 1.[6] Thus in serotonin we have what appears to be the first instance in which the 5-hydroxyindole ring system has been demonstrated to exist in the mammalian organism.

The compound was prepared from 5-benzyloxyindole.[7] This intermediate was converted to 5-benzyloxyindoleacetonitrile by the general method of Majima and Kotake.[8] Lithium aluminum hydride reduction of the nitrile gave 5-benzyloxytryptamine which was isolated as the hydrochloride salt; m.p. 248–250° (uncor.), (*Anal.* Calcd. for $C_{17}H_{19}ClN_2O$: C, 67.42; H, 6.32; Cl, 11.71; N, 9.20. Found: C, 67.26; H, 6.34; Cl, 11.78; N, 9.20.)

The 5-benzyloxytryptamine base obtained from the above salt was catalytically debenzylated using 10% palladium–charcoal catalyst. To the alcohol solution obtained on removing the catalyst was added one equivalent of sulfuric acid. Concentration of the solvent gave the sulfate as a heavy gum. The gum was dissolved in water at 60° and an equivalent of creatinine sulfate (neutral salt) and several volumes of hot acetone added. On cooling the solution the complex crystallized as microscopic plates indistinguishable from the natural product. The crystals melt somewhat higher [214–216° (Kofler)] than the value given by Rapport [212–214° (Kofler)]. Analytical data indicate that the synthetic compound crystallizes as a monohydrate as does the natural product. (*Anal.* Calcd. for $C_{14}H_{23}N_5O_7S$: C, 41.47; H, 5.72; N, 17.28. Found: C, 41.41; H, 5.52; N, 17.45.)

Synthetic serotonin creatinine sulfate has been found[9] to produce an increase in blood pressure and a contraction of intestinal smooth muscle in agreement with the findings of Rapport[3] with the natural product. These and other biological effects of serotonin and its analogs are being investigated and detailed reports will be published at a later date.

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[6] We wish to thank Dr. J. L. Johnson of our Physics Department for the infrared data and Mr. W. A. Struck and associates of our Microanalytical Laboratory for the analytical data.

[7] H. Burton and J. L. Stoves, *J. Chem. Soc.*, 1726 (1942).

[8] R. Majima and M. Kotake, *Ber.*, **58**, 2042 (1923).

[9] We wish to acknowledge the coöperation of Dr. M. J. VanderBrook and his staff of our Department of Pharmacology for these observations.