(1) conversion of mezcaline to 3,4,5-trimethoxyphenylethyl chloride; (2) reaction of the chloride with dimethylamine.

Mezcaline hydrochloride (1.3 g.) was dissolved in 5 ml. of 10% hydrochloric acid, and 0.71 g. of sodium nitrite dissolved in 1.1 ml. of water added. A vigorous reaction followed, which was completed by heating in the water-bath.

The reaction mixture was extracted with ether, and the crude chloride was obtained by evaporation of the dried extract.

The crude chloride was heated in a sealed tube with 5 ml. of a 14% solution of dimethylamine in alcohol, during 6 hours at 100°. The reaction mixture was evaporated, dissolved in diluted hydrochloric acid, filtered, alkalinized with K_2CO_3 and extracted with ether. The residue of this ether extract was neutralized with hydrochloric acid, and recrystallized from alcohol. White crystals were obtained, m.p. 204–205°. No m.p. depression was observed when mixed with natural trichocereine chloride.

Anal. Calcd. for $C_{13}H_{22}O_3NCl$: C, 56.61; H, 8.04. Found: C, 56.77; H, 8.13.

The picrate, picrolonate and methiodide obtained from the synthetic chlorhydrate did not depress the melting points of the derivatives of the natural base.

Mezcaline Hydrochloride.—The chloroform solution B was extracted twice with 40 ml. of 5% hydrochloric acid and once with 20 ml. of water. The aqueous extract was then washed with 20 ml. of chloroform and 20 ml. of ether. After alkalinization with K_2CO_3, the solution was extracted with chloroform and the extract evaporated to dryness. It weighed 4 g. After neutralization with alcoholic hydrochloric acid, the crude hydrochloride was dissolved in 30 ml. of abs. alcohol and the filtered solution overlayed with 30 ml. of ether. The hydrochloride crystallized. Recrystallized from alcohol, the pure salt melted at 181–182°.

Anal. Calcd. for $C_{11}H_{18}O_3NCl$: C, 53.32; H, 7.32; N, 5.65; Cl, 14.32. Found: C, 52.84; H, 7.24; N, 5.64; Cl, 13.91.

Several derivatives of this substance were prepared and the m.p. compared with those of the corresponding compounds obtained starting from synthetic mezcaline. In all cases a perfect concordance was observed between both series, alone or after admixture.

A summary of the results are given in Table I.

TABLE I

Substance	Synth. mezcaline, m.p., °C.	Mezcaline from *T. lerscheckii*, m.p., °C.	Mixture, m.p., °C.
Hydrochloride	181–182	181–182	181
Picrate	216–218	219	218–219
Chloroplatinate	187–188	188	188
Methiodide	226–228	226–228	227
Picrate of the quaternary cmpd.	165	165	165

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The Papilionaceous Alkaloids. X. Identity of Hexalupine with *d*-Thermopsine[1,2]

BY LÉO MARION, WILLIAM F. COCKBURN[3] AND JAMES F. COUCH[4]

Hexalupine has been shown to be identical with *d*-thermopsine by means of their infrared spectra, and the melting points of several of their derivatives.

The alkaloid hexalupine occurs in *Lupinus corymbosus*, Heller.[5] As the physical constants of this compound differ very little from those of *d*-thermopsine,[6] a comparison of the two bases and several of their derivatives was made.

Hexalupine was found to be separable by careful vacuum distillation, into a colorless crystalline solid and a small amount of oily impurity whose nature has not yet been established. Reanalysis of the purified alkaloid showed the formula to be $C_{15}H_{20}ON_2$, without the third of a molecule of water of crystallization reported previously,[5] while measurement of the optical rotation gave $[\alpha]^{28}D$ + 152.4° (*c*, 4.62 in ethanol), as compared with +154.4° (*c* 0.8 in ethanol) for *d*-thermopsine.[6] The melting points of the free base, picrate, perchlorate and chloroplatinate were almost identical with those of the corresponding derivatives of *d*-thermopsine, and admixture caused no depression.

Final confirmation was obtained by comparison of the infrared spectra of the two bases, taken in carbon disulfide solution, with a rock-salt prism. As can be seen from the figure, the two curves are identical.

It has been shown recently that thermopsine is a stereoisomer of anagyrine giving rise to α-isosparteine when fully reduced catalytically.[7]

Acknowledgment.—The infrared spectra were taken by Dr. R. N. Jones and Mr. R. Lauzon, of these laboratories, whose courtesy is gratefully acknowledged.

Experimental

Purification of the Alkaloid.—Hexalupine dihydrochloride[5] was decomposed with sodium hydroxide, the free base extracted with ether and distilled in a Späth bulb at 150° (0.2 mm.). A small amount of impurity was obtained as two distinct oily fractions, one colorless, the other yellow, while the bulk of the material sublimed as colorless stubby prisms m.p. 207–209° (cor.). This melting point was not altered by admixture with pure *d*-thermopsine, m.p. 207–209° (cor.); $[\alpha]^{28}D$ +152.4° (*c* 4.62 in ethanol).

Anal. Calcd. for $C_{15}H_{20}ON_2$: C, 73.72; H, 8.23; N, 11.47. Found: C, 73.91, 73.74; H, 8.07, 8.22; N, 11.47.

Picrate.—Treatment of a methanolic solution of hexalupine with an equivalent amount of picric acid in methanol gave a yellow crystalline precipitate, which could be recrystallized from methanol in rectangular efflorescent plates, m.p. 248° (uncor.) with decomposition. This melting point was not depressed by admixture with *d*-thermopsine picrate m.p. 249° (uncor.).

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot C_6H_3N_3O_7$: C, 53.27; H, 4.90; N, 14.79. Found: C, 53.55, 53.65; H, 4.78, 4.90; N, 14.07.

(1) For Part IX see *Can. J. Chem.*, **29**, 22 (1951).

(2) Published as National Research Council Bull. No. 2352.

(3) National Research Council of Canada Postdoctorate Fellow.

(4) Eastern Regional Research Laboratory, Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture, Philadelphia 18, Penna.

(5) J. F. Couch, THIS JOURNAL, **56**, 155 (1934).

(6) L. Marion, F. Turcotte and J. Ouellet, *Can. J. Chem.*, **29**, 22 (1951).

(7) W. F. Cockburn and L. Marion, *ibid.*, **29**, 13 (1951).

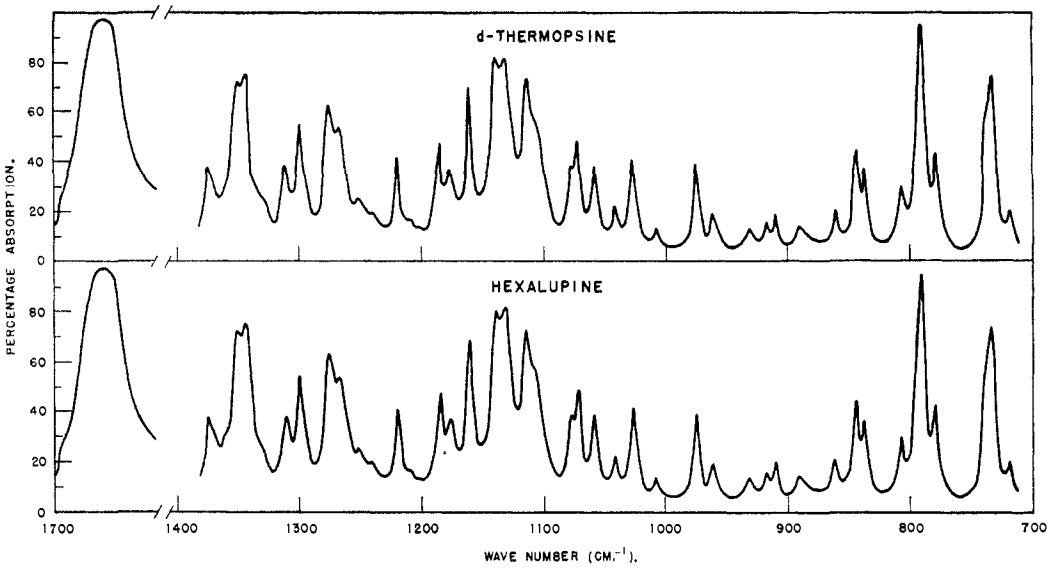

Fig. 1.

Perchlorate.—When a methanolic solution of hexalupine was carefully neutralized with 70% perchloric acid, a crystalline precipitate was obtained in colorless plates. Melting point after two recrystallizations from methanol was 284–286° (cor.) with decomposition, when the sample was inserted at 250°. No depression was obtained on a mixture with an authentic sample of *d*-thermopsine perchlorate, m.p. 286°.

Chloroplatinate.—An ethanolic solution of hexalupine was added to an aqueous solution of chloroplatinic acid, to which had been added a few drops of concentrated hydrochloric acid. The product separated rapidly in spear-like needles, which were found to be efflorescent as reported by Orechov for *l*-thermopsine chloroplatinate.[8] After recrystallization from acidified aqueous ethanol, the salt melted at 254–256° (uncor.) with decomposition (reported for *l*-thermopsine chloroplatinate, 254–256°). This melting point was not depressed by admixture with a similar salt prepared from pure *d*-thermopsine, m.p. 256–258° (uncor.).

(8) A. Orechov, S. Norkina and H. Gurewitch, *Ber.*, **66**, 625 (1933).

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

Isolation and Some Chemical Properties of Grisein

BY FREDERICK A. KUEHL, JR., MARY NEALE BISHOP, LOUIS CHAIET AND KARL FOLKERS

Grisein has been isolated from the culture broth of *S. griseus* by a sequence of several steps including adsorption, elution, chromatography and countercurrent distribution. Grisein is a red amorphous powder; analytical data are in agreement with the composition $C_{40}H_{61}N_{10}O_{20}SFe$. The iron in the complex is in the ferric state and may be removed and added back to the complex. Degradation of grisein by acid hydrolysis yielded 3-methyluracil and at least two amino acids. One of the acids appears to be glutamic acid.

The production of the antibiotic grisein by a strain of *Streptomyces griseus*, obtained from Huleh peat, has been reported by Reynolds, Schatz and Waksman.[1] The antibiotic was purified[2] by adsorption from the broth on Norit A, elution with aqueous alcohol, and precipitation with methanol and acetone to give a concentrate having an activity of *ca.* 400 units/mg. and representing about 15% of the broth activity.

We have devised a process for the isolation of grisein in apparently pure form. Norit A was also used for adsorption of the antibiotic from the culture medium, but elution was found to be much more complete when aqueous pyridine was used instead of alcohol. An aqueous methanolic solution of material thus obtained gave, upon the addition of ether, precipitates having an activity of 300–500 units/mg. In order to facilitate further purification, the dried product was leached with methanol; this step doubled the activity, but gave only a 50% recovery.

Concentrates which were obtained by these preliminary steps were purified further by distribution between water and phenol–chloroform mixtures. The *p*H of the aqueous phase and the phenol content in the chloroform layer were altered to aid selective removal of impurities. The resulting product was dissolved in a little water and isopropyl alcohol was added to the solution. The precipitate, after removal, was found to have an activity of 50,000–100,000 units/mg., representing 35–40% recovery. The yields, as well as the potency of the product, were found to vary according to the potency of the starting material.

Further purification was accomplished by using the method of Martin and Synge.[3] Using silica gel saturated with *p*H 4.6 buffer and 17% phenol in chloroform (V/V), material having an activity of

(1) Reynolds, Schatz and Waksman, *Proc. Soc. Exp. Biol. and Med.*, **55**, 66 (1944).

(2) Reynolds and Waksman, *J. Bact.*, **55**, 739 (1948).

(3) Martin and Synge, *Biochem. J.*, **35**, 1358 (1941).