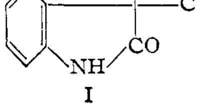
THE OXINDOLE NATURE OF GELSEMINE[1]

Sir:

It was claimed by Moore[2] that gelsemine contained a free hydroxyl group which could be acetylated with acetic anhydride. All attempts to prepare an O-acetylgelsemine have failed in our hands, and other workers[3] have been similarly unsuccessful. It can now be stated quite definitely that gelsemine does not contain a hydroxyl group. The base has been found to contain only one active hydrogen (Zerewitinow) and its infrared absorption spectrum to show a sharp absorption band at 3443 cm.$^{-1}$ indicative of an imino group. Since gelsemine is an indole alkaloid[4,5] and since the basic nitrogen is known to be tertiary, it follows that the one active hydrogen in the base must be attributed to the indole imino group.

The reaction of dihydrogelsemine with lithium aluminum hydride in dioxane gave rise to tetrahydrodesoxygelsemine, prisms, m. p. 138–139°. *Anal.* Calcd. for $C_{20}H_{26}ON_2$: C, 77.42; H, 8.39; N, 9.03; 1 act. H, 0.32. Found: C, 77.51, 77.34; H, 8.01, 8.21; N, 9.14; act. H, 0.33. This base forms a picrate, orange needles, m. p. 216–217° (dec.). *Anal.* Calcd. for $C_{20}H_{26}ON_2 \cdot C_6H_3O_7N_3$: C, 57.88; H, 5.38; N, 12.99. Found: C, 57.23, 57.40; H, 5.23, 5.19; N, 12.80. The new base contained one strongly basic nitrogen atom (pK 8.9) and one weakly basic (pK 3.4). The infrared absorption spectra[6] of both gelsemine and dihydrogelsemine showed an absorption band at 1720 cm.$^{-1}$ in the region of carbonyl absorption, while that of tetrahydrodesoxygelsemine showed no absorption in this region, but still contained an absorption band (3414 cm.$^{-1}$) indicative of a weakly associated imino group. Tetrahydrodesoxygelsemine contained one active hydrogen (Zerewitinow); it was acetylated by boiling acetic anhydride to an N-acetyl base, prisms, m. p. 131–132°. *Anal.* Calcd. for $C_{22}H_{28}O_2N_2$: C, 75.00; H, 7.95. Found: C, 75.81; H, 7.44. The acetyl derivative formed a crystalline acetate, plates, m. p. 182–186°. *Anal.* Calcd. for $C_{22}H_{28}O_2N_2 \cdot C_2H_4O_2$: C, 69.90; H, 7.77; N, 6.80. Found: C, 69.96, 69.70; H, 7.77, 7.58; N, 6.74, 6.77. The infrared absorption spectrum of the acetyl derivative showed no absorption band indicative of an imino group, but contained a carbonyl absorption band (1650 cm.$^{-1}$) obviously due to the acetyl group.

It can, therefore, be postulated that



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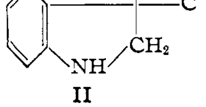

II

partial structure I is present in gelsemine and that it is the reduction of a carbonyl to a methylene group that gives rise to tetrahydrodesoxygelsemine in which partial structure II must be present. Oxindoles still containing a hydrogen atom in the 3-position are converted to indoles by the action of lithium aluminum hydride[7] and hence, the 3-position of the oxindole system in gelsemine must be assumed to be disubstituted. Indeed, the disubstituted 3,3-dimethyloxindole gave color changes with sulfuric acid and potassium dichromate very similar to those given by strychnine and gelsemine and its ultraviolet absorption curve was almost superposable on that of gelsemine. Furthermore, it has been ascertained that 3,3-dimethyloxindole is readily reduced by lithium aluminum hydride in dioxane solution to 3,3-dimethyldihydroindole (m. p. 34–34.5°). It is noteworthy that this result is contrary to the literature statement that N-unsubstituted oxindoles are virtually unaffected by lithium aluminum hydride.[7]

The partial structures I and II are further supported by the strychnidine-like properties of tetrahydrodesoxygelsemine. Like strychnine it must contain a nitrogen atom directly attached to an aromatic nucleus with a free and reactive para-position. When coupled with diazotized sulfanilic acid, it gave rise to a methyl orange which resembled in its indicator behavior that of sulfobenzoazostrychnidine.

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[1] Issued as N. R. C. Bull. No. 2082.

[2] Moore, *J. Chem. Soc.*, 1231 (1911).

[3] Forsyth, Marrian and Stevens, *ibid.*, 579 (1945).

[4] Marion, *Can. J. Research*, **21B**, 247 (1943).

[5] Witkop, This Journal, **70**, 1424 (1948).

[6] All infrared spectra were determined in chloroform solution by Dr. R. Norman Jones.

[7] Julian and Printy, This Journal, **71**, 3206 (1949).

THE SEPARATION AND IDENTIFICATION OF KETOACIDS BY FILTER PAPER CHROMATOGRAPHY

Sir:

In the course of studies on the amino acid metabolism of microörganisms carried out in this laboratory, it became desirable to isolate and identify minute quantities of ketoacids.

It was found that mixtures of ketoacids could be separated by unidimensional ascending partition chromatography on filter paper. The positions of the ketoacids on the chromatogram were made visible by spraying the paper (E. and D. 613), with an aqueous solution containing 0.1% semicarbazide hydrochloride and 0.15% sodium acetate, drying at 110°, and inspection under an ultraviolet lamp ("Mineralight").[1] The semicarbazones of the ketoacids appear as dark shadows on the faintly fluorescing paper. As little as 5 μg. of ketoacid could be demonstrated.

The approximate R_F values in a solvent system consisting of 95 parts *n*-butanol, 5 parts formic acid, saturated by shaking with water,

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[1] Chargaff, Magasanik, Doniger and Vischer, This Journal, **71**, 1513 (1949).