## Experimental

**Materials.**—Dry silver propionate was prepared from the acid by standard procedures.

Resublimed reagent grade iodine was used without further purification. Solutions could be labeled with carrier-free $I^{131}$ obtained from the Oak Ridge National Laboratory.

The saturated hydrocarbon solvent was mostly hexane. It was prepared from Skellysolve B by treatment with fuming sulfuric acid. Tests with $I^{131}$ indicated that different preparations contained impurities capable of reacting with no more than $6 \times 10^{-6}$ mole/l. of iodine.

**Procedure.**—Because of the extreme sensitivity to moisture of iodine(III) tripropionate, solutions were dried over phosphorus pentoxide and all experiments were conducted in an atmosphere of dry carbon dioxide. Samples of solid silver propionate were treated with hexane solutions of iodine, and the resulting silver iodide was removed by filtration during transfer of the solution to a thermostated flask that was kept in the dark under dry carbon dioxide. Aliquots could be withdrawn at appropriate times for analysis.

**Analytical Procedures.**—Concentrations of $I^{131}$ were determined with thin-walled Geiger tubes. Empirical corrections were applied because of different efficiencies for counting iodine in water and in hexane solution. Counting procedures could be used to determine number of moles of iodine in a particular phase regardless of its chemical form.

Elementary iodine in hexane was determined with a Beckman DU spectrophotometer.

Ethyl iodide was also determined spectrophotometrically. The molar extinction coefficient of $451 \pm 5$ at 259 m$\mu$ agreed well with the value reported by Scheibe.[8] The presence of this compound in a reacted mixture was also confirmed by forming the ethyl 3,5-dinitrobenzoate and taking a mixed melting point with the derivative prepared from commercial ethyl iodide.

As has been indicated above, positive iodine esters were determined by shaking the hexane solution with water, adding an excess of acid and iodide to the aqueous layer, and titrating with thiosulfate. In some experiments in which the hexane layer contained only iodine(III) ester, the hexane layer was also reduced with aqueous sulfite and titrated with silver nitrate. The combined argentometric and iodometric procedures demonstrated that iodate was the only iodine containing species present in the aqueous extract.

**Acknowledgment.**—This work was supported in part by the U.S. Atomic Energy Commission under Contract AT(45-1)-1310.

(8) G. Scheibe, *Ber.*, **58**, 592 (1925).

# Alkaloids of *Geissospermum vellosii*. Isolation and Structure Determinations of Vellosimine, Vellosiminol, and Geissolosimine

HENRY RAPOPORT AND RICHARD E. MOORE[1]

*Department of Chemistry, University of California, Berkeley, California*

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By systematic fractionation of the alkaloid-rich pH 7 fraction[2] from *G. vellosii* three new alkaloids, *viz.*, vellosimine, vellosiminol, and geissolosimine, have been isolated. Vellosomine and vellosiminol are indoles, and by n.m.r. studies and comparison with known alkaloids, have been shown to have structures I and III, respectively. Geissolosimine (formerly called $D_2$[2]) is a dimeric alkaloid and is cleaved by acid to the indole, vellosimine, and the indoline, geissoschizoline. From this cleavage reaction, its reconstitution from vellosimine and geissoschizoline, and its n.m.r. spectrum, geissolosimine has been assigned structure VII.

A detailed procedure has been described[2] for the separation of the *Geissospermum vellosii* alkaloids into various fractions by systematic liquid-liquid extraction at a series of different pH's. From the alkaloid-rich pH 7 fraction, geissospermine was isolated, usually by crystallization, and large-scale chromatography on alumina then was applied to the residual material. In this way, a number of other alkaloids were isolated, the chief one being alkaloid $D_2$. By further refinement of the pH 7 fraction, we have isolated two additional crystalline alkaloids. These new alkaloids, vellosimine and vellosiminol, and geissolosimine (alkaloid $D_2$) are the subject of the present report.

**Isolation.**—The large amounts of material accumulated after removing geissospermine from the pH 7 fraction made detailed alumina chromatography quite unappealing as a fractionation procedure. Instead, a pass through a short alumina column first was applied and this clearly removed about one fourth of the material as crystalline geissoschizoline.[2] The remaining three fourths was subjected to systematic, continuous liquid-liquid extraction at pH 6, 6.6, and 10. From the pH 10 fraction, more geissoschizoline was isolated, and the pH 6.6 fraction yielded additional geissospermine. The pH 6 fraction, originally obtained by extraction with ether, now was separated into two portions by extraction with benzene at pH 4.9, fraction 1, and ether at pH 7, fraction 2.

Further purification of fraction 2 by chromatography on alumina was fruitful and resulted in the isolation of two crystalline minor alkaloids, vellosimine and vellosiminol. Geissolosimine was not isolated anew; it was the material (alkaloid $D_2$) obtained by the previous procedure.[2]

**Structure Determinations.**—Vellosimine has the molecular formula $C_{19}H_{20}N_2O$ and an ultraviolet

(1) National Institutes of Health Predoctoral Fellow.

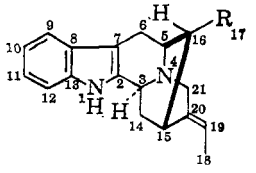
(2) H. Rapoport, T. P. Onak, N. A. Hughes, and M. G. Reinecke, *J. Am. Chem. Soc.*, **80**, 1601 (1958).

absorption typical of an indole ($\lambda_{max}$ 280, 289). From its infrared spectrum the presence of an indolic NH (3473 cm.$^{-1}$) and an unconjugated aldehyde (1720, 2720, 2820 cm.$^{-1}$) are demonstrated.

Many significant structural features are revealed by the n.m.r. spectrum of vellosimine in liquid sulfur dioxide. The multiplet at $\delta$ 7.1–7.7 is attributed to four aromatic protons, and the absence of absorption at $\delta$ 6.2–6.9 shows that the alkaloid is a 2,3-disubstituted indole.[3] The sharp singlet at $\delta$ 9.58 is characteristic of an aliphatic aldehydic proton and the broad band centered at $\delta$ 8.66 is assigned to the indole NH. The 1:3:3:1 quartet centered at $\delta$ 5.57 and the doublet centered at $\delta$ 1.72 ($J$ = 7.0 c.p.s.) are attributed to olefinic and methyl protons, respectively, of an ethylidene group. Since each of the bands of the doublet at $\delta$ 1.72 is further split into 1:2:1 triplets with $J$ = 1.7 c.p.s., the methyl protons must be coupled with the protons of a methylene group attached to the double bond. The olefinic proton is also coupled to this methylene group since each of the bands of the quartet are broad. The quartet centered at $\delta$ 4.45 is assigned to a methine proton which is coupled to two protons of a neighboring methylene group and situated between the $\alpha$-carbon of the indole ring and the basic nitrogen, $N_4$.

Wolff-Kishner reduction of vellosimine gives deoxydihydrovellosimine, $C_{19}H_{22}N_2$, whose n.m.r. spectrum in liquid sulfur dioxide shows a doublet centered at $\delta$ 1.03 ($J$ = 7.5 c.p.s.) for the new methyl protons. The doublet indicates the presence of one proton on the adjacent carbon and the $\delta$-value of 1.03 suggests that the methyl group is directed away from the aromatic ring, since a much lower $\delta$-value would be expected for a methyl group influenced by the aromatic $\pi$-system. The bands of the doublet for the methyl protons of the ethylidene group are still split into 1:2:1 triplets.

On the basis of the n.m.r. spectra and analogy with other indole alkaloids, structures I and II were proposed for vellosimine and desoxydihydrovellosimine, respectively.



I. R = CHO III. R = $CH_2OH$
II. R = $CH_3$ IV. R = $CH_2OAc$

Vellosimine (I) was readily reduced with sodium borohydride, or catalytically, to vellosiminol, identical with the naturally occurring alkaloid. Vellosiminol, therefore, was assigned structure III. In Table I, the physical properties of vellosiminol (III) are compared with those of normacusine-B,[4] desformoakuammidinol,[5] and tombozine,[6] all of which have structure III. Acetylation of III gave O-acetylvellosiminol (IV), and the comparison with O-acetyldesformoakuammidinol[5] and O-acetyltombozine[6] is also given in Table I.

TABLE I

COMPARISON OF VELLOSIMINOL, NORMACUSINE-B, DESFORMOAKUAMMIDINOL, AND TOMBOZINE

| Compound | M.p., °C. Prisms | M.p., °C. Needles | $[\alpha]_D$ (methanol) |
|---|---|---|---|
| Vellosiminol (III) | 233–235 | 273–275 | +36 |
| Normacusine-B[a] | 245 | 275 | ... |
| Desformoakuammidinol[b] | 232–238 | 275 | +35 |
| Tombozine[c] | ... | 270–272 | +37[d] |
| O-Acetylvellosiminol (IV) | 220–222 | | +11 |
| O-Acetyldesformoakuammidinol[b] | 223 | | + 9 |
| O-Acetyltombozine[c] | 220–222 | | + 1[d]; + 11[e] |

[a] Ref. 4. [b] Ref. 5. [c] Ref. 6. [d] In ethanol. [e] In chloroform.

On the basis of the coincidence of properties shown in Table I and the spectral data cited above, structure III is considered established for vellosiminol. From this, it follows that deoxydihydrovellosimine has the structure II with the stereochemistry as shown at C-16 since the n.m.r. spectrum indicates the methyl group is directed away from the benzene ring. Vellosimine then must have structure I. The stereochemistry at C-16 is assigned on the basis of (1) catalytic reduction in neutral solution to vellosiminol (III) and (2) stability to epimerizing conditions, drawing the analogy with aldehydes in the ajmaline series.[7]

In our hands the catalytic hydrogenation of vellosiminol was not as selective as was reported[4] for normacusine-B, from which, on hydrogenation over platinum in acetic acid, dihydronormacusine-B (V), m.p. 189–190°, was obtained. Hydrogenation of vellosimine (I) or vellosiminol (III) over platinum in glacial acetic acid gave material with a melting range of 150–165° and a specific rotation of +60 to +64°. Hydrogenation of vellosimine over platinum in ethanol containing a small amount of acetic acid gave an alcohol (non-olefinic) melting sharply as prisms at 162–163°, then resolidifying to needles and melting sharply at 230–231°, and having a specific rotation of +48°. This material can not have structure VI since it then would be identical with deoxydihydrosarpagine,[8] m.p. 250–251°, $[\alpha]_D$ +4°. The sterically very unlikely possibility of isomerism at C-3 is eliminated, since vellosimine and all the compounds derived from it show n.m.r. absorption in the region $\delta$ 3.65–4.45, characteristic

(3) L. A. Cohen, J. W. Daly, H. Kny, and B. Witkop, *J. Am. Chem. Soc.*, **82**, 2184 (1960).

(4) A. R. Battersby and D. A. Yeowell, *Proc. Chem. Soc.*, 17 (1961).

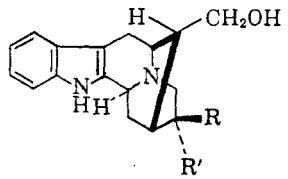
(5) J. Levy, J. LeMen, and M.-M. Janot, *Compt. rend.*, **253**, 131 (1961).

(6) D. Stauffacher, *Helv. Chim. Acta*, **44**, 2006 (1961).

(7) M. F. Bartlett, R. Sklar, W. I. Taylor, E. Schlittler, R. L. S. Amai, P. Beak, N. V. Bringi, and E. Wenkert, *J. Am. Chem. Soc.*, **84**, 622 (1962).

(8) We are indebted to Dr. W. I. Taylor, Ciba Pharmaceutical Products, Inc., Summit, N. J., for a sample of deoxydihydrosarpagine.

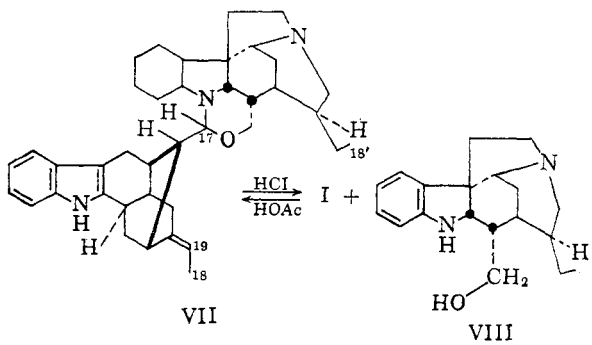
of the C-3 equatorial proton.[9] Therefore, it must be concluded that our hydrogenation products are mixtures of the $C_{20}$ epimers, V and VI. Since vellosiminol (III) is not hydrogenated over palladium or platinum in ethanol in the absence of acetic acid, vellosimine (I) can be reduced cleanly to vellosiminol under these conditions.



V. R = H, R′ = $C_2H_5$
VI. R = $C_2H_5$, R′ = H

Geissolosimine, previously called alkaloid $D_2$[2], has the revised molecular formula $C_{38}H_{44}N_4O$. Its ultraviolet spectrum (Fig. 1) is very similar to that of geissospermine,[10] showing an indole and indoline moiety. Protonation of the molecule in 1.0 *N* ethanolic hydrochloric acid completely eliminates the indoline chromophore and reduces the spectrum essentially to that of an indole and an alkylbenzene. The infrared spectrum in chloroform exhibits a sharp band of medium intensity at 3474 cm.$^{-1}$ for an indolic NH and a strong band at 758 cm.$^{-1}$ (in potassium bromide) for four adjacent aromatic protons. No carbonyl absorption is present.

By the action of concentrated hydrochloric acid at room temperature, geissolosimine is cleaved to the indole, vellosimine (I), and the indoline, geissoschizoline (VIII).[11] Conversely, geissolosimine is formed when a solution of vellosimine and geissoschizoline in 1.5 *N* acetic acid is allowed to stand at room temperature for several days. This facile cleavage and recombination is reminiscent of geissospermine and indicates a linking of the two portions through acetal formation with the aldehydo group of vellosimine. From a consideration of stereochemistry of vellosimine, this linkage must involve the indoline—NH and —$CH_2OH$ of geissoschizoline and leads to VII as the structure of geissolosimine.



VII VIII

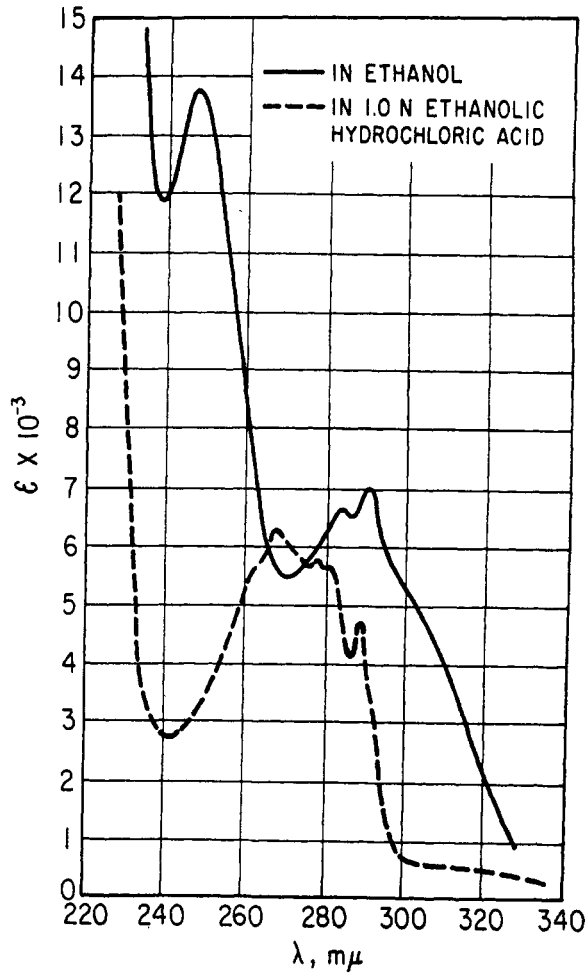



Fig. 1.—Ultraviolet absorption spectra of geissolosimine (VII).

This structural assignment for geissolosimine (VII) is confirmed by its n.m.r. spectrum in deuterochloroform (Fig. 2). There is a doublet at δ 5.21 ($J$ = 10 c.p.s.) characteristic for a methine proton (C–17) situated between an oxygen and a nitrogen and coupled with a proton on the adjacent carbon. The 1:3:3:1 quartet at δ 5.55 and the doublet at 1.71 ($J$ = 7 c.p.s.) reflects the olefinic proton (C–19) and methyl protons (C–18), respectively, of an ethylidene group. The absorption of the indole-$N_1$ proton is found as a broad band at δ 9.42.

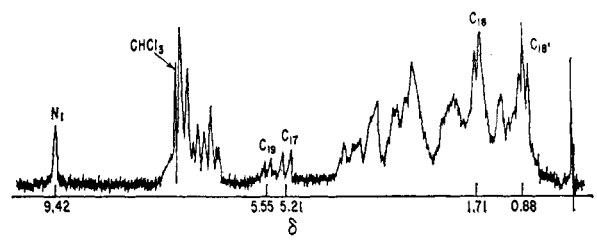



Fig. 2.—N.m.r. spectrum of geissolosimine (VII) in deuterochloroform.

(9) W. E. Rosen and J. N. Shoolery, *J. Am. Chem. Soc.*, **83**, 4816 (1961).
(10) H. Rapoport, R. J. Windgassen, Jr., N. A. Hughes, and T. P. Onak, *ibid.*, **82**, 4404 (1960).
(11) M.-M. Janot, *Tetrahedron*, **14**, 113 (1961).

To test the possibility that geissolosimine is an artifact formed during the extraction procedure, a solution of vellosimine (I) and geissoschizoline (VIII) was allowed to stand at pH 4, the acidity encountered during the extraction, and room temperature for ten days. No geissolosimine was formed and the vellosimine and geissoschizoline were recovered. From this we conclude that geissolosimine is a naturally occurring alkaloid.

## Experimental[12]

**Separation of the pH 7 Fraction into Subfractions.**—After removal of crude geissospermine by filtration of the pH 7 ether extract as previously described,[2] the gummy residue (192 g.) obtained by evaporation of the filtrate was dissolved in the minimum amount of hot chloroform and chromatographed on alumina (Merck, basic; 10 g. per g. of residue). Material was eluted with chloroform until the ultraviolet spectrum of the eluent was no longer that of geissoschizoline, and the column was then washed thoroughly with methanol. The chloroform eluent was concentrated, cooled, and filtered to give geissoschizoline chloroformate (77 g.).

The mother liquors and methanol wash were combined and evaporated, and the residue was dissolved in 5 l. of 0.5 *M* sodium dihydrogenphosphate solution. The pH was adjusted by the addition of sodium hydroxide solution, and the mixture was extracted continuously with ether at pH's 6.0, 6.6, and 10. Solution of the material extracted at pH 6.0 in two 1. of 0.5 *M* sodium dihydrogenphosphate solution (pH 4.9) was followed by continuous extraction with benzene to give fraction 1 (27 g.). The pH of the aqueous solution was raised to 7, and continuous extraction with ether gave fraction 2 (24 g.).

The pH 6.6 ether extract was filtered to remove fraction 3 (13 g.), and the filtrate on evaporation gave fraction 4 (21 g.). Crystallization of fraction 3 from methanol–water (4:1) produced geissospermine (6 g.).

Evaporation of the pH 10 ether extract gave fraction 5 (26 g.) which was dissolved in benzene and chromatographed on alumina (Woelm, neutral; 800 g.). The column was developed with 2 l. of benzene, and eluted with 3 l. of 50% chloroform–benzene and 3 l. of chloroform. From the combined 50% benzene–chloroform and chloroform eluents was obtained geissoschizoline (6 g.) by crystallization from acetone.

**Isolation of Vellosimine and Vellosiminol.**—Twenty grams of fraction 2 was dissolved in 100 ml. of benzene and applied to an alumina (Woelm, neutral; 600 g.) column. Elution with benzene (500 ml.) was followed by benzene–chloroform (10:1), and evaporation of the latter produced crystalline material on trituration with ether. Recrystallization from chloroform gave 1.6 g. of vellosimine. The remaining material (2.5 g.) was dissolved in benzene and rechromatographed on alumina (200 g.), developing the chromatogram with 1 l. of benzene, 500 ml. of 2% chloroform–benzene, 400 ml. of 5% chloroform–benzene, and 300-ml. portions of 7.5, 10, and 15% chloroform–benzene. Elution was continued with 15% chloroform–benzene and 125-ml. fractions were collected. Fractions 1–7 (1.6 g.) were combined and dissolved in chloroform, and the solution was extracted with dilute phosphoric acid. The acid solution was washed with chloroform and then made alkaline with ammonium hydroxide. Extraction with chloroform and evaporation of the chloroform gave crystalline material from which 300 mg. of vellosimine was obtained after recrystallization from chloroform.

(12) All melting points were taken on a Kofler hot stage; microanalyses were performed by V. Tashinian, Microchemical Laboratory, University of California, Berkeley. Rotations were taken on 0.8–1% solutions in methanol.

Fractions 8–13 (600 mg.) were combined and treated with methanol from which 200 mg. of crude vellosiminol crystallized.

The crude **vellosimine** (I) was recrystallized twice from methanol, sublimed at 180–200° (0.01 mm.), and dried at 110° (1 mm.; 12 hr.); m.p. 305–306°; $[\alpha]^{26}D$ +48°; ultraviolet absorption $\lambda_{max}^{ethanol}$ 280 mμ (ε 8000), 289 (6430).

*Anal.* Calcd. for $C_{19}H_{20}N_2O$: C, 78.1; H, 6.9; N, 9.6; C—$CH_3$, 5.1. Found: C, 77.9; H, 6.6; N, 9.3; C—$CH_3$, 4.7.

An ethanolic solution of the crude **vellosiminol** (III) was evaporated and the residual gum was dissolved in chloroform. Upon standing, small prisms were formed which were removed by filtration and dried at 105° (0.1 mm.; 18 hr.); m.p. 273–275°, with a change of crystalline form to needles at 233–235°; $[\alpha]^{23}D$ +36°.

*Anal.* Calcd. for $C_{19}H_{22}N_2O$: C, 77.5; H, 7.5; N, 9.5. Found: C, 77.4; H, 7.5; N, 9.7.

**Deoxydihydrovellosimine** (II).—A solution of 130 mg. (0.4 mmole) of vellosimine and 0.7 ml. of anhydrous hydrazine in 10 ml. of ethanol was boiled for 1 hr. Ten milliliters of purified diethylene glycol was added, the mixture was distilled until the internal temperature reached 170°, 100 mg. of potassium hydroxide was added, and the mixture was heated under reflux for 3 hr. in a nitrogen atmosphere. The cooled solution was diluted with 50 ml. of water and extracted with three 25-ml. portions of chloroform. Evaporation of the dried chloroform extract gave a white crystalline solid which was crystallized from ethanol and sublimed at 150–160° (0.01 mm.), m.p. 307–308°.

*Anal.* Calcd. for $C_{19}H_{22}N_2$: C, 82.0; H, 8.0. Found: C, 82.2; H, 8.2.

**Vellosiminol (III) from Reduction of Vellosimine (I).**—A solution of 80 mg. of vellosimine in 25 ml. of methanol was treated with 100 mg. of sodium borohydride in small portions over 15 min. Dilute sodium hydroxide solution was added, the mixture was concentrated *in vacuo*, and the precipitate was dissolved in ethanol. Evaporation of the solution left a gum which was dissolved in chloroform and then ether was added to the warm solution. On standing, crystals, m.p. 273–275°, appeared which were recrystallized from chloroform and dried at 100° (0.1 mm.; 15 hr.) to give 50 mg. of vellosiminol, m.p. 242–243°; $[\alpha]^{24}D$ +37.7°.

The same product was obtained when vellosimine was hydrogenated in ethanol at atmospheric pressure using a platinum oxide catalyst. After 2.5 hr., hydrogen absorption ceased at 98 mole %. The vellosiminol thus obtained, the vellosiminol from borohydride reduction, and the naturally occurring vellosiminol had identical infrared spectra.

**O-Acetylvellosiminol** (IV).—A solution of 30 mg. of vellosiminol in 0.5 ml. of acetic anhydride and 0.25 ml. of pyridine was allowed to stand at room temperature for 20 hr. The solution was neutralized with cold, dilute ammonium hydroxide. The mixture was allowed to stand at 0–5° for 6 hr., and the precipitate was dissolved in ether. Evaporation of the ether under a stream of nitrogen gave crystalline material which was dried at 105° (0.1 mm.; 1 hr.), m.p. 219–221°; $[\alpha]^{22}D$ +11°.

*Anal.* Calcd. for $C_{21}H_{24}N_2O_2$: C, 75.0; H, 7.2. Found: C, 74.8; H, 6.8.

**Dihydrovellosiminol. A. From Vellosimine.**—A solution of 500 mg. of vellosimine in 50 ml. of ethanol and 1 ml. of glacial acetic acid was hydrogenated at atmospheric pressure using 125 mg. of platinum oxide catalyst. After 6 hr., hydrogen absorption ceased, the mixture was filtered, and the filtrate was made alkaline with ammonium hydroxide and concentrated *in vacuo*. The precipitate was crystallized from absolute ethanol and dried at 110° (0.1 mm.; 24 hr.) to give 470 mg. of dihydrovellosiminol as prisms, m.p. 162–163°, with resolidification into needles, m.p. 230–232°; $[\alpha]^{24}D$ +48°.

*Anal.* Calcd. for $C_{19}H_{24}N_2O$: C, 77.0; H, 8.2; N, 9.5. Found: C, 77.1; H, 7.9; N, 9.7.

When the hydrogenation was performed in glacial acetic

acid, the dihydrovellosiminol obtained melted from 150–160° and had $[\alpha]^{28}D$ +60°.

**B. From Vellosiminol.**—A solution of 25 mg. of vellosiminol in 5 ml. of glacial acetic acid was hydrogenated at atmospheric pressure using 10 mg. of platinum oxide catalyst. The product was recrystallized twice from absolute ethanol and dried at 100° (0.1 mm.; 17 hr.), m.p. 154–163°, $[\alpha]^{21}D$ +64°.

**O-Acetyldihydrovellosiminol.**—A solution of 120 mg. of dihydrovellosiminol, $[\alpha]^{24}D$ +48°, in 2 ml. of acetic anhydride and 2 ml. of pyridine, was allowed to stand at room temperature for 6 hr. The slightly brown solution was made alkaline with cold, dilute ammonium hydroxide and extracted with chloroform which gave an oil on evaporation. The oil was dissolved in a small amount of ethanol and the solution was diluted with water, giving a precipitate which was crystallized from carbon disulfide. Two recrystallizations from methanol gave prisms, m.p. 238–240°[13] after drying at 105° (0.1 mm.; 20 hr.).

*Anal.* Calcd. for $C_{21}H_{26}N_2O_2$: C, 74.5; H, 7.7. Found: C, 74.3; H, 7.4.

**Geissolosimine (VII).**—The alkaloid previously designated as $D_2$[2] was recrystallized several times from 4:1 methanol–water and dried at 125° (0.1 mm.; 24 hr.), m.p. 140°; $[\alpha]^{22}D$ +70.4°; ultraviolet absorption: $\lambda_{max}^{ethanol}$ 250 mμ (ε 13,600), 284 (6700), 292 (7000); in 1.0 *N* ethanolic hydrochloric acid, $\lambda_{max}$ 268 mμ (ε 6300), 289 (4700).

*Anal.* Calcd. for $C_{38}H_{44}N_4O \cdot {}^1/_2H_2O$: C, 78.7; H, 7.8; N, 9.7; O, 3.8. Found: C, 78.6; H, 8.1; N, 9.7; O, 3.9.

(13) O-Acetyldeoxydihydrosarpagine has been reported to melt at 253–254° [M. F. Bartlett, R. Sklar, and W. I. Taylor, *J. Am. Chem. Soc.*, **82**, 3790 (1960)] and O-acetylnormacusine-B at 192° and 219–220°.[4] Our material is undoubtedly a mixture of these $C_{20}$ epimers.

The previous values reported[2] for alkaloid $D_2$ were m.p. 133–135°, $[\alpha]^{25}D$ +74°, and the molecular formula $C_{39}H_{46}N_4O \cdot {}^1/_2H_2O$.

**Acid Cleavage of Geissolosimine.**—A solution of 600 mg. of geissolosimine in 5 ml. of concentrated hydrochloric acid was allowed to stand at room temperature for 15 min. and then was poured into a mixture of 40 ml. of concentrated ammonium hydroxide and ice. Extraction with chloroform and evaporation of the chloroform gave 600 mg. of a gum which was dissolved in 100 ml. of 0.5 *M* sodium dihydrogenphosphate. The solution was adjusted to pH 6 with sodium hydroxide and extracted continuously with ether to give 500 mg. of a mixture of vellosimine and unchanged geissolosimine on evaporation of the ether. The pH was changed to 10, and continuous extraction with ether gave 100 mg. of crude geissoschizoline. Chromatography on 3 g. of neutral alumina and elution with 100 ml. of 1:1 chloroform–benzene gave 70 mg. of crystalline **geissoschizoline (VIII)**, identical in all respects with an authentic sample.[2]

Chromatography of the vellosimine–geissolosimine fraction on neutral alumina and elution with 100 ml. of 1:1 chloroform–benzene gave 50 mg. of crystalline **vellosimine**, identical with the vellosimine described above.

**Preparation of Geissolosimine (VII) from Vellosimine (I) and Geissoschizoline (VIII).**—A solution of 65 mg. of vellosimine and 100 mg. of geissoschizoline chloroformate in 10 ml. of 1.5 *N* acetic acid was allowed to stand at room temperature for 2 days. The solution was made alkaline with ammonium hydroxide, the resulting precipitate was dissolved in 4:1 methanol–water, and the solution was seeded with geissolosimine. After standing for 1 day, 20 mg. of crude geissolosimine crystallized and was recrystallized from 4:1 methanol–water, m.p. 140°. This material was identical with the geissolosimine described above.

# *Lythraceae* Alkaloids. I. Isolation and Structural Studies of the Alkaloids of *Decodon verticillatus* (*L.*) *Ell.*[1]

JAMES P. FERRIS

*Department of Chemistry, Florida State University, Tallahassee, Florida*

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Seven alkaloids have been isolated from *Decodon verticillatus* (*L.*) *Ell.* All are pentacyclic and contain the following structural features: a six-membered or greater lactone ring, the ether oxygen of which is derived from a secondary alcohol; a tertiary nitrogen atom; and two nonconjugated aromatic rings substituted with methoxyl and/or hydroxyl groups. Two of the alkaloids, vertine and verticillatine, have an additional olefinic bond located between one of the aromatic rings and the lactone carbonyl. This suggests that the lactone carbonyl group is gamma with respect to an aromatic ring in all *Decodon* alkaloids. The data are consistent with II as the part structure for vertine and verticillatine. The other alkaloids, with the possible exception of decaline and vertaline, may be represented by II also except that the cinnamic ester double bond is saturated.

Although some *Lythraceae* species have been investigated for alkaloidal content,[2] no structural investigation has been carried out on this plant family. We have undertaken an investigation of *Lythraceae* in hopes of finding alkaloids with unique structures and physiological activity. In this paper we wish to report structure studies on the alkaloids of *Decodon verticillatus* (*L.*) *Ell.* ("water oleander" or "swamp loosestrife"), a plant which occurs in moderate amounts in some swampy areas near Tallahassee.

The isolation of the alkaloid fraction was carried out in the usual way by extraction with methanol or chloroform followed by acid and base fractionation. Chloroform was found to be a more satisfactory extraction solvent because the alkaloids, extracted in equally good yield, were not accompanied by large quantities of nonbasic substances which tend to form very stable emulsions at later stages of the fractionation.

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(2) Technical Bulletin 1234, U.S. Department of Agriculture, Washington, D. C., p. 143.