ether (with charcoal) yielded 9.5 g. (48%) of the **hydrochloride salt of XV** as colorless crystals, m.p. 157–158°.

B. **2-Phenethyl-5α-(3,4,5-trimethoxybenzoxy)-6β-methoxy-*cis*-octahydroisoindole (XVIII).**—A similar treatment of XVII with trimethoxybenzoyl chloride afforded **XVIII hydrochloride**, m.p. 174° after recrystallization from acetone–ether. The melting point of a mixture of the hydrochloride salts of XV and XVIII was depressed to 135–143°.

C. **2-(3-Indolylethyl)-5β-(3,4,5-trimethoxybenzoxy)-6α-methoxy-*cis*-octahydroisoindole (XXIV).**—A solution of 40.0 g. (0.13 mole) of XXIII in 300 ml. of dry pyridine, cooled in an ice-bath, was treated with 90 g. (0.4 mole) of 3,4,5-trimethoxybenzoyl chloride. The solution was allowed to warm to room temperature and then stored in the dark for 5 days. The solution was poured on a slurry of cracked ice and 10% hydrochloric acid solution and the resultant mixture thoroughly washed with ethyl acetate to remove trimethoxybenzoic anhydride. The remaining aqueous acid layer was cooled in ice, made alkaline with solid potassium carbonate and extracted with ether. Drying and removal of the ether left a red resin that was dissolved in ethyl acetate and shaken with a 3% hydrochloric acid solution to precipitate the crude hydrochloride salt of the product as a red oil, not soluble in either layer. The red oil was washed with fresh solvent and crystallized (with charcoal) from isopropyl alcohol–ether to yield 32.1 g. of crystalline material, m.p. 119–125° (with gas evolution). Recrystallization from isopropyl alcohol–ether and then from acetone–ether afforded 17.5 g. of the anhydrous **hydrochloride salt of XXIV** as colorless crystals, m.p. 198–199.5° (gas evolution).

Dilution of the isopropyl alcohol mother liquors with more ether precipitated 12.6 g. of crystals which analyzed as the **hemi-isopropyl alcoholate of XXIV hydrochloride**, m.p. (gas evolution) 125–126°, followed by resolidification and remelting at 198–200°. The alcoholate could be converted to the anhydrous salt by treatment with hot isopropyl alcohol or hot acetone. The combined yield of analytically pure material was 42%.

D. **2-Phenethyl-5β-(N-ethylcarbamyloxy)-6α-methoxy-*cis*-octahydroisoindole (XVI).**—A mixture of 7.0 g. (0.025 mole) of XIV and 3 ml. of ethyl isocyanate was heated on a steam-bath for 45 minutes. The reaction mixture was taken up in benzene and the solution was evaporated under reduced pressure to a thick oil. Crystallization of this from petroleum ether (b.p. 60–70°) afforded 6.9 g. (80%) of XVI, m.p. 64–67°.

Acknowledgment.—The authors are grateful to Mr. R. Garver for skillful technical assistance and to Mr. D. F. Cortright and Miss M. Unroe for the ionic halogen and basic nitrogen determinations.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY, AMES, IOWA]

Synthesis of Olivacine[1]

BY ERNEST WENKERT AND K. G. DAVE

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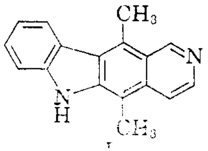
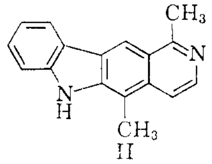
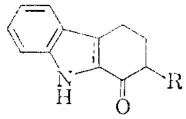
A synthesis of the indole alkaloid olivacine is described.

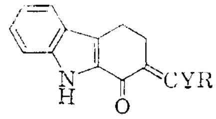
The year 1959 witnessed the completion of the structure elucidation of an array of indole alkaloids one of whose common features was their lack of structural correspondence with the well-known natural bases of the yohimbine–ajmalicine–corynantheine and strychnos types. It was of interest to synthesize some of these compounds in order to corroborate their structures as well as study their chemistry. The first alkaloid chosen was olivacine, a $C_{17}H_{14}N_2$ base, which had been isolated recently from four sources, *Aspidosperma olivaceum* Müll. Arg.,[2a] *Aspidosperma longepetiolatum* Kuhlm.,[2b] *Aspidosperma australe* Müll. Arg.[2c] and *Tabernaemontana psychotrifolia*,[2d] and a comparison of whose basicity, spectral properties and possible biosynthesis with those of ellipticine, an isomeric alkaloid of structure I,[3] had led Marini-Bettolo and Schmutz to suggest II as its structure.[4,5]


I


II

The ketotetrahydrocarbazole IIIa appeared to be the most likely candidate as starting material for the synthesis of the pyridocarbazole system. It could be converted to its hydroxymethylene (IVa) and ethoxalyl (IVb) derivatives by sodium ethoxide-induced acylation with ethyl formate and ethyl oxalate, respectively. Transformations of the two compounds to further useful intermediates were carried out in parallel investigations.


IIIa, R = H
b, R = CH_2CO_2Et
c, R = CH_2CO_2H


IVa, R = H, Y = OH
b, R = CO_2Et, Y = OH
c, R = CO_2Et, Y = OAc
d, R = CO_2Et, Y = H
e, R = H, Y = OAc
f, R = H, Y = O*i*-Pro

Acetylation of the ethoxalyl derivative IVb led to the diester IVc, which afforded the ketoester IVd on partial hydrogenation over palladium–charcoal. Zinc–acetic acid reduction of either ester IVc or IVd led to the saturated ketoester IIIb. Methyllithium addition to the latter or to its acid IIIc yielded two products both of which seemed to have suffered dehydration, presumably

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[1] This work was presented for the first time at the International Symposium on the Chemistry of Natural Products, under the auspices of the Section of Organic Chemistry of the International Union of Pure and Applied Chemistry, Melbourne, Canberra and Sydney, Australia, August 15–25, 1960. It was supported by U. S. Army Chemical Corps contract DA18-108-405-CML-269.

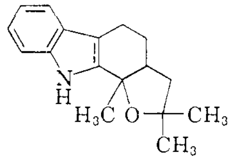
[2] (a) J. Schmutz and F. Hunziker, *Pharm. Acta Helv.*, **33**, 341 (1958); (b) G. B. Marini-Bettolo, *Ann. Chim.*, **49**, 869 (1959); (c) M. A. Ondetti and V. Deulofeu, *Tetrahedron Letters*, No. **7**, 1 (1959); (d) M. Gorman, N. Neuss, N. J. Cone and J. A. Deyrup, *J. Am. Chem. Soc.*, **82**, 1142 (1960).

[3] R. B. Woodward, G. A. Iacobucci and F. A. Hochstein, *ibid.*, **81**, 4434 (1959).

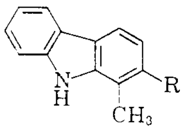
[4] G. B. Marini-Bettolo and J. Schmutz, *Helv. Chim. Acta*, **42**, 2146 (1959).

[5] Just prior to completion of our work there appeared a synthesis of olivacine (II) by J. Schmutz and H. Wittwer [*ibid.*, **43**, 793 (1960)]. While this constituted a rigorous proof of the structure of the alkaloid, our work was continued, since it involved a route of synthesis quite dissimilar from that of the Swiss workers.

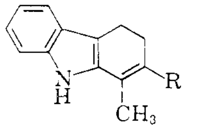
on work-up. One product, whose elemental analysis indicated it to be the product of an uptake of three methyl groups, was assumed tentatively to possess structure V on the basis of an ultraviolet spectrum characteristic of tetrahydrocarbazoles and the absence of hydroxyl and carbonyl absorption peaks from its infrared spectrum. The other product, one resulting from the uptake of two methyl groups, could be assigned structure VIa in view of the presence of characteristic saturated ketone absorption in its infrared spectrum and in view of its dihydrocarbazole ultraviolet spectrum. Palladium-induced dehydrogenation of V and VIa in p-cymene solution led to the carbazoles VIIa and b, respectively. Ozonolysis of the olefin VIIa gave the aldehyde VIIc, which, in the end, proved to be a vital intermediate of the total synthesis.



V



VIIa, R = $CH{=}C(CH_3)_2$
b, R = CH_2Ac
c, R = CHO
d, R = CO_2Me
e, R = CH_3
f, R = CH_2OH
g, R = $CH{=}CHAc$
h, R = CH_2CH_2Ac
i, R = n-Bu



VIa, R = CH_2Ac
b, R = CHO
c, R = $CH{=}CHAc$

In an attempt to degrade the acetone side-chain in VIIb to an acetic acid residue, the behavior of the ketone in a haloform reaction was studied. While exposure of an alkyl methyl ketone to hypohalite solution leads to demethylation, this being the basis of the well-known qualitative test for methyl ketones,[6] ketones with α-substituents which enhance enolization toward the alkyl side of the ketones may decompose by dealkylation rather than by demethylation. Indeed, phenylacetone, a simple model for VIIb, was converted to benzoic acid, instead of phenylacetic acid, on treatment with sodium hypoiodite solution. This fragmentation is best represented as

$$C_6H_5CH_2COCH_3 \xrightarrow{I_2,\ OH^\ominus} C_7H_6CI_2COCH_3 \xrightarrow{OH^\ominus}$$

$$CH_3CO_2^\ominus + C_6H_5CHI_2 \xrightarrow{OH^\ominus}$$

$$C_6H_5CHO \xrightarrow{I_2,\ OH^\ominus} C_6H_5CO_2^\ominus$$

It was hoped that steric hindrance by the o-methyl group lowering the rate of iodination of the benzyl carbon atom of ketone VIIb would be sufficient to permit the latter's fragmentation to a carbazoleacetic acid and iodoform. Unfortunately, VIIb behaved the same way as phenylacetone; hypoiodite oxidation gave a carbazolecarboxylic acid which was characterized as its methyl ester VIId. Its structure was verified by its identity with the ester obtained from the permanganate oxidation of the aldehyde VIIc and diazomethane treatment of the resulting acid. In view of the consequent availability of carbazoles with only single-carbon side-chains useful for further elaboration into a pyridine ring, the experiments based on compound IVa, paralleling the above work, assumed greater significance.

Ready acylation and alkylation of the hydroxymethylene ketone IVa led to derivatives IVe and f, respectively. Methyllithium addition to the latter yielded the aldehyde VIb, which on palladium-induced dehydrogenation in p-cymene surprisingly gave the dimethylcarbazole VIIe. Equally surprising was the discovery of the extreme ease of palladium dehydrogenation of the aldehyde VIb to the desired aromatic aldehyde VIIc. This transformation was accomplished by merely refluxing a benzene solution for one-half hour. Even in this case a small amount of undesired dimethyl compound VIIe accompanied the product. It is quite likely that the facility of the reaction is due to a rapid, palladium-catalyzed disproportionation of the dihydroaromatic aldehyde VIb to an aromatic alcohol VIIf prior to a reduction to VIIe or oxidation to VIIc. Such disproportionation is reminiscent of the recently reported uncatalyzed oxidation of tetrahydrocarbazole by ketones or imines.[7] When, in fact, a benzene solution of the starting aldehyde VIb was heated in the absence of palladium under previously described conditions,[7] the same products, VIIc and e, could be isolated.

Base-catalyzed condensation of the carbazole aldehyde VIIc with acetone gave the chalcone VIIg. Hydrogenation of the latter yielded the dihydro product VIIh. The chalcone could be prepared also by the base-induced condensation of the dihydroaromatic aldehyde VIb with acetone and palladium-catalyzed dehydrogenation of the condensation product VIc.[8] Phosphorus pentoxide treatment of the oxime of ketone VIIh and palladium-induced dehydrogenation of the cyclization product yielded olivacine (II), identical in all physical properties with an authentic sample.[9] This completed a nine-step total synthesis of the alkaloid.

Experimental[10]

1-Keto-2-ethoxalyl-1,2,3,4-tetrahydrocarbazole (IVb) and Its Acetate IVc.—Ethyl acetate, 3.0 g., was added to a solution of 3.7 g. of 1-keto-1,2,3,4-tetrahydrocarbazole (IIIa) and 0.6 g. of sodium in 10 ml. of ethanol and the mixture stirred at room temperature under nitrogen. After 1 hr. it was poured into ice-water, made alkaline by the addition of 10 ml. of 10% sodium hydroxide, and filtered. The filtrate was neutralized with dilute hydrochloric acid and the resulting precipitate filtered. The solid exhibited a strong $FeCl_3$ test. Its crystallization from dilute methanol led to 3.5 g. of yellow-orange needles of IVb, m.p. 156–

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[6] *Cf.* R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Fourth Edition, John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 156–158.

[7] E. Wenkert and B. F. Barnett, *J. Am. Chem. Soc.*, **82**, 4671 (1960).

[8] The observation that an uncatalyzed pyrolytic disproportionation[7] of VIc led to chalcone VIIg and dialkylcarbazole VIIi served as an interesting side light.

[9] The authors are grateful to Dr. N. Neuss for a gift of the alkaloid sample.

[10] All ultraviolet spectra were run on 95% ethanolic solutions.

157°; ultraviolet spectrum: $\lambda_{\max}$ 273 mμ (log ε 3.74), 360 mμ (log ε 4.31); $\lambda_{\min}$ 264 mμ (log ε 3.71), 285 mμ (log 3.72).

Anal. Calcd. for $C_{16}H_{15}O_4N$: C, 67.36; H, 5.26; N, 4.91. Found: C, 67.29; H, 5.45; N, 4.89.

A mixture of 3.5 g. of IVb and 1.7 g. of freshly fused sodium acetate in 30 ml. of acetic anhydride was heated with stirring at 120° for 2 hr. After the excess anhydride was removed under vacuum, the residue was treated with water and filtered. Crystallization of the crude solid, 3.4 g., from benzene–hexane yielded the acetate IVc, m.p. 206–208°; ultraviolet spectrum: $\lambda_{\max}$ 246 mμ (log ε 3.88), 328 mμ (log ε 4.33); $\lambda_{\min}$ 232 mμ (log ε 3.78), 282 mμ (log ε 3.16).

Anal. Calcd. for $C_{18}H_{17}O_5N$: C, 66.05; H, 5.24; N, 4.28. Found: C, 65.97; H, 5.37; N, 4.19.

1-Keto-2-hydroxymethylene-1,2,3,4-tetrahydrocarbazole (IVa) and Its Acetate IVe and Isopropyl Ether IVf.—A slurry of 2.13 g. of ketone IIIa and 2.5 ml. of ethyl formate was added to a warm stirring sodium ethoxide solution, prepared from 0.3 g. of sodium in 5 ml. of ethanol. The dark brown mixture was stirred under nitrogen at room temperature for 2 hr. and then heated on a steam-bath for 2 hr. Work-up in a manner identical with that of the ethoxalation reaction led to a solid whose crystallization from dilute ethanol gave 1.7 g. of IVa, m.p. 132–134°; ultraviolet spectrum: $\lambda_{\max}$ 242 mμ (log ε 4.01), 340 mμ (log ε 4.32); $\lambda_{\min}$ 228 mμ (log ε 3.88), 275 mμ (log ε 3.54).

Anal. Calcd. for $C_{13}H_{11}O_2N$: C, 73.24; H, 5.16. Found: C, 73.20; H, 5.34.

Acetylation of 50 mg. of IVa was carried out in the same way as the above procedure for IVb. Crystallization of the solid product from benzene–hexane gave yellow needles of IVe, m.p. 232–235°; ultraviolet spectrum: $\lambda_{\max}$ 253 mμ (log ε 4.05), 330 mμ (log ε 4.39); $\lambda_{\min}$ 219 mμ (log ε 3.74), 282 mμ (log ε 3.54).

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.54; H, 5.09. Found: C, 70.36; H, 5.08.

A suspension of 300 mg. of IVa, 2 g. of freshly fused potassium carbonate and 1.2 ml. of isopropyl iodide in 25 ml. of anhydrous acetone was refluxed with stirring for 18 hr. The mixture was filtered, the filtrate evaporated and the resulting residue treated with water. The insoluble solid was filtered, its benzene solution passed through a short alumina column and the eluate evaporated. Crystallization of the residue from benzene–hexane gave 190 mg. of pale yellow needles of IVf, m.p. 172–173°; ultraviolet spectrum: $\lambda_{\max}$ 243 mμ (log ε 4.00), 335 mμ (log ε 4.47); $\lambda_{\text{shoulder}}$ 255 mμ (log ε 3.93), 265 mμ (log ε 3.83), 365 mμ (log ε 4.25); $\lambda_{\min}$ 228 mμ (log ε 3.83), 274 mμ (log ε 3.54).

Anal. Calcd. for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.32; H, 6.97; N, 5.74.

1-Keto-2-carboxymethyl-1,2,3,4-tetrahydrocarbazole (IIIc) and Its Ester IIIb.—A mixture of 32 mg. of the enol acetate IVc, 12 mg. of sodium carbonate and 10 mg. of 5% palladium–charcoal in 5 ml. of dioxane was hydrogenated at atmospheric pressure. After the cessation of hydrogen uptake the mixture was filtered and the filtrate evaporated. A benzene solution of the residual brownish-yellow oil was filtered through a short alumina column. Crystallization of the residue, m.p. 118–126°, from benzene–hexane gave yellow needles of IVd, m.p. 176–177°; ultraviolet spectrum: $\lambda_{\max}$ 235 mμ (log ε 3.92), 308 mμ (log ε 4.00); $\lambda_{\text{shoulder}}$ 335 mμ (log ε 3.79); $\lambda_{\min}$ 272 mμ (log ε 3.13).

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.37; H, 5.57. Found: C, 71.42; H, 5.79.

A mixture of 45 mg. of the ketoester IVd and 45 mg. of zinc dust in 2 ml. of acetic acid was stirred at room temperature for 2 hr. It was diluted with benzene and filtered, and the filtrate taken to dryness. Crystallization of the residue from benzene–hexane and recrystallization from ether yielded colorless crystals of IIIb, m.p. 136–137°; ultraviolet spectrum: $\lambda_{\max}$ 236 mμ (log ε 4.19), 307 mμ (log ε 4.33); $\lambda_{\min}$ 217 mμ (log ε 3.93), 263 mμ (log ε 3.04).

A mixture of 3.00 g. of IVc and 3.0 g. of zinc dust in 30 ml. of acetic acid was stirred at room temperature for 4 hr. Upon work-up as above 1.50 g. of crystalline IIIb, m.p. and m.m.p. 136–137°, was obtained.

A solution of 1.50 g. of the ketoester IIIb in 50 ml. of 5% ethanolic potassium hydroxide was stirred at room temperature under nitrogen for 2 hr. The solution was neutralized with dilute hydrochloric acid and the resulting precipitate filtered, washed with water and dried. Crystallization of the solid from ethyl acetate gave 1.20 g. of crystalline ketoacid IIIc, m.p. 180–182°; ultraviolet spectrum the same as that of its ester IIIb.

Anal. Calcd. for $C_{14}H_{13}O_3N$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.23; H, 5.60; N, 5.85.

Methyllithium Reactions.—A solution of 0.5 ml. of methyl iodide in 5 ml. of ether was added dropwise with stirring to a suspension of 70 mg. of lithium in ether under nitrogen. After dissolution of all lithium a solution of 120 mg. of the ketoacid IIIc in 5 ml. of tetrahydrofuran was added dropwise and the mixture kept at 65–70° for 12 hr. After the addition of 20 ml. of saturated ammonium chloride solution to the cooled reaction mixture, the latter was extracted with ether. The extract was washed with dilute hydrochloric acid, with sodium bicarbonate and with 10% potassium hydroxide solutions, was dried over anhydrous potassium carbonate and evaporated. A benzene solution of the oily residue was chromatographed on alumina. Benzene elution led to a solid which on crystallization from hexane gave 18.5 mg. of V, m.p. 194–195°; ultraviolet spectrum: $\lambda_{\max}$ 226 mμ (log ε 4.54), 282 mμ (log ε 3.89), 289 mμ (log ε 3.79); $\lambda_{\text{shoulder}}$ 274 mμ (log ε 3.81); $\lambda_{\min}$ 247 mμ (log ε 3.32), 287 mμ (log ε 3.78).

Anal. Calcd. for $C_{17}H_{21}ON$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.54; H, 8.41; N, 5.49.

Elution with 3:1 benzene–ether gave 52 mg. of an oily solid which on crystallization from benzene–hexane afforded ketone VIa, m.p. 153–157°; ultraviolet spectrum: $\lambda_{\max}$ 215 mμ (log ε 4.62), 238 mμ (log ε 4.81), 258 mμ (log ε 4.50), 295 mμ (log ε 4.42), 324 mμ (log ε 3.82), 337 mμ (log ε 3.74); $\lambda_{\text{shoulder}}$ 312 mμ (log ε 3.79); $\lambda_{\min}$ 222 mμ (log ε 4.59), 256 mμ (log ε 4.49), 273 mμ (log ε 3.93), 317 mμ (log ε 3.75), 332 mμ (log ε 3.68).

Anal. Calcd. for $C_{16}H_{17}ON$: C, 80.3; H, 7.11. Found: C, 79.9; H, 6.61.

A similar reaction of methyllithium, from 70 mg. of lithium and 0.5 ml. of methyl iodide, and ketoester IIIb, 170 mg., and similar workup led to 65 mg. of V and 12 mg. of VIa. The compounds were identified by m.p., m.m.p. and infrared spectral comparison.

A reaction of methyllithium, from 0.5 ml. of methyl iodide and 45 mg. of lithium, and the ketoether IVf, 70 mg., for 22 hr. and its work-up were carried out as before. Elution of the alumina chromatogram with 3:1 benzene–ether yielded 42 mg. of a solid which on crystallization from benzene–hexane gave yellow needles of the unsaturated aldehyde VIb, m.p. 218°; ultraviolet spectrum: $\lambda_{\max}$ 213 mμ (log ε 5.38), 267 mμ (log ε 4.97), 405 mμ (log ε 5.34); $\lambda_{\text{shoulder}}$ 240 mμ (log ε 4.93); $\lambda_{\min}$ 253 mμ (log ε 4.16), 294 mμ (log ε 3.44).

Anal. Calcd. for $C_{14}H_{13}ON$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.22; H, 6.1; N, 6.58.

Aromatization of V and VIa.—A suspension 30 mg. of 10% palladium–charcoal and 104 mg. of ether V in 10 ml. of *p*-cymene was refluxed with stirring under nitrogen for 48 hr. After filtration of the catalyst and steam distillation of the solvent the product was extracted with benzene. The solution was dried, partly concentrated and filtered through a small alumina column. Evaporation of the solution and crystallization of the solid residue gave 80 mg. of the olefin VIIa, m.p. 102°; ultraviolet spectrum: $\lambda_{\max}$ 218 mμ (log ε 4.33), 248 mμ (log ε 4.67), 298 mμ (log ε 4.30); $\lambda_{\text{shoulder}}$ 325 mμ (log ε 3.72), 340 mμ (log ε 3.54); $\lambda_{\min}$ 220 mμ (log ε 4.33), 272 mμ (log ε 3.57).

Anal. Calcd. for $C_{17}H_{17}N$: C, 86.81; H, 7.23. Found: C, 87.19; H, 7.25.

A suspension of 50 mg. of 10% palladium–charcoal and 50 mg. of ketone VIa in 5 ml. of *p*-cymene was refluxed for 40 hr. and the reaction worked up as above. Crystallization of the product from benzene–hexane yielded the ketone VIIb, m.p. 146°; ultraviolet spectrum: $\lambda_{\max}$ 215 mμ (log ε 4.46), 239 mμ (log ε 4.65), 248 mμ (log ε 4.55), 258 mμ (log ε 4.34), 295 mμ (log ε 4.24), 325 mμ (log ε 3.65), 338 mμ (log ε 3.57); $\lambda_{\text{shoulder}}$ 283 mμ (log ε 3.88); $\lambda_{\min}$ 223 mμ (log ε 4.44), 246 mμ (log ε 4.54), 256 mμ (log ε 4.33), 274 mμ (log ε 3.78), 317 mμ (log ε 3.58), 332 mμ (log ε 3.51).

1-Methyl-2-carbazolecarboxaldehyde (VIIc).—A suspension of 50 mg. of 10% palladium–charcoal and 100 mg. of the aldehyde VIb in 5 ml. of *p*-cymene was refluxed for 4 hr. under above conditions and the reaction worked up as above. Crystallization of the product from hexane yielded 66 mg. of 1,2-dimethylcarbazole (VIIe), m.p. 112–114°; ultraviolet spectrum similar to that of ketone VIIb.

Anal. Calcd. for $C_{14}H_{13}N$: C, 86.15; H, 6.66. Found: C, 86.56; H, 6.31.

Dehydrogenation of 70 mg. of the aldehyde VIb with 30 mg. of 10% palladium–charcoal in 5 ml. of refluxing benzene for 30 min. yielded a mixture. Its chromatography on alumina and benzene elution gave 7 mg. of 1,2-dimethylcarbazole (VIIe), m.p. and m.m.p. 112–114°. Elution with 3:1 benzene–ether yielded a pale yellow solid which on crystallization from carbon tetrachloride afforded 55 mg. of the aldehyde VIIc, m.p. 156–158°; infrared spectrum ($CHCl_3$), NH 2.90(m) μ, aldehydic CH 3.70(m)μ, C=O 5.93(s) μ, C=C 6.19(m) μ.

Anal. Calcd. for $C_{14}H_{11}ON$: C, 80.38; H, 5.46. Found: C, 79.98; H, 5.30.

Ozone was passed through a solution of 100 mg. of the olefin VIIa in 10 ml. of ethylene chloride for 4 min. at 0°. A mixture of the ozonide and 100 mg. of 10% palladium–charcoal was hydrogenated. After cessation of hydrogen uptake the mixture was filtered and concentrated to dryness. After seven ozonizations and hydrogenolyses of 100-mg. lots of VIIa, a benzene solution of the combined concentrates was chromatographed on alumina. Elution with benzene yielded 70 mg. of a colorless crystalline solid of unknown constitution, m.p. 136–137°; spectra: ultraviolet, characteristic of alkylcarbazoles; infrared, no carbonyl group present. Elution with 3:1 benzene–ether and crystallization of the solid from carbon tetrachloride gave 60 mg. of the aldehyde VIIc, m.p. and m.m.p. 156–158°.

Methyl 1-Methyl-2-carbazolecarboxylate (VIId).—A mixture of 2.01 g. of methyl benzyl ketone in 5 ml. of dioxane and 40 ml. of 10% aqueous sodium hypoiodite solution was stirred vigorously at 30–35° for 1 hr. After addition of sodium bisulfite the mixture was extracted with ether. When the aqueous solution was acidified with dilute hydrochloric acid, a precipitate formed, whose crystallization from water yielded 0.80 g. of benzoic acid, m.p. and m.m.p. 118–120°.

A mixture of 70 mg. of ketone VIIb in 4 ml. of dioxane and sodium hypoiodite, prepared from 2 ml. of 10% iodine in potassium iodide, and 3 ml. of 10% sodium hydroxide solution, was stirred at room temperature for 1 hr. The mixture then was diluted with water, treated with sodium bisulfite and extracted with ether. The aqueous solution was acidified and extracted with chloroform. Evaporation of the solvent gave 17 mg. of a crystalline acid, m.p. 260–265°, which was treated with an ethereal solution of diazomethane without further purification. Evaporation of the solvent and chromatography of a benzene solution of the residue on silicic acid gave a solid which on crystallization from benzene–hexane afforded the ester VIId, m.p. 132–134°; infrared spectrum ($CHCl_3$): NH 2.90(m) μ, C=O 5.85(s) μ, C=C 6.16(m) μ.

Anal. Calcd. for $C_{15}H_{13}O_2N$: C, 75.31; H, 5.44. Found: C, 75.46; H, 5.91.

A solution of 50 mg. of potassium permanganate dissolved in 5 ml. of acetone was added dropwise to a solution of 30 mg. of aldehyde VIIc in 3 ml. of acetone. The pink solution was left standing at room temperature for 2 hr. After vacuum removal of the solvent the residue was treated with 1% potassium hydroxide solution and filtered. The residue was washed with water, the combined aqueous solutions neutralized with dilute hydrochloric acid and the resulting precipitate filtered and dried. A mixture of a methanolic solution of the solid and an ethereal solution of diazomethane was left standing at 5° for 12 hr. Evaporation of the mixture and crystallization of the residue from benzene–hexane yielded the ester VIId, m.p. and m.m.p. 132–134°; identical infrared spectrum with that of sample above.

Disproportionation of 1-Methyl-3,4-dihydro-2-carbazolecarboxaldehyde (VIb).—A solution of 100 mg. of aldehyde VIb in 2 ml. of benzene was heated in a sealed tube at 235–240° for 24 hr. The tube was cooled and opened and the contents filtered. The filtrate was chromatographed on alumina. Elution with 2:1 hexane–benzene yielded 5 mg. of a non-ketonic product which on crystallization from hexane proved to be 1,2-dimethylcarbazole (VIIe), m.p. and m.m.p. 112–114°. Further elution gave traces of an oil, exhibiting 5.80 μ infrared carbonyl absorption Elution with 4:1 benzene–ether yielded 18 mg. of aldehyde VIIc, m.p. and m.m.p. 156–158°.

Methyl β-(1-Methyl-2-carbazolyl-)vinyl Ketone (VIIg).—A mixture of 55 mg. of aldehyde VIIc, 0.4 ml. of acetone and 0.01 ml. of 20% potassium hydroxide was left standing at room temperature under nitrogen for 3 hr. The mixture soon set to a thick yellow paste. Water was added and the precipitate filtered and crystallized from benzene. This led to 52 mg. of yellow needles of ketone VIIg, m.p. 218°; ultraviolet spectrum: λ_{max} 222 mμ (log ε 4.47), 246 mμ (log ε 4.50), 345 mμ (log ε 4.51); $\lambda_{shoulder}$ 255 mμ (log ε 4.48), 292 mμ (log ε 4.24), 314 mμ (log ε 4.38); λ_{min} 232 mμ (log ε 4.36), 272 mμ (log ε 4.01).

Anal. Calcd. for $C_{17}H_{15}ON$: C, 81.92; H, 6.02. Found C, 82.2; H, 6.1.

A similar reaction was carried out with 100 mg. of aldehyde VIb, 4 ml. of acetone and 0.2 ml. of 10% potassium hydroxide. The dark brown reaction product was chromatographed on alumina. Elution with 3:1 benzene–ether produced a solid which on crystallization from benzene yielded 60 mg. of yellow crystals of ketone VIc, m.p. 232°; infrared spectrum ($CHCl_3$): NH 2.90(m) μ, C=O 6.06(s) μ, C=C 6.15(s), 6.29(s), 6.39(s) μ.

Anal. Calcd. for $C_{17}H_{17}ON$: C, 81.24; H, 6.82. Found: C, 81.49; H, 6.96.

A mixture of 20 mg. of VIc and 10 mg. of 10% palladium–charcoal in 2 ml. of *p*-cymene was refluxed for 6 hr. The work-up corresponded to that of the dehydrogenations described above. A benzene solution of the product was filtered through a short alumina column and crystallized. The yellow product was identical in m.p. and m.m.p. 218° and spectral properties with ketone VIIg.

Methyl β-(1-Methyl-2-carbazolyl-)ethyl Ketone (VIIh).—A mixture of 52 mg. of chalcone VIIg and 40 mg. of 10% palladium–charcoal in 5 ml. of ethyl acetate was hydrogenated at slightly above atmospheric pressure. After the uptake of hydrogen ceased, the catalyst was filtered and the filtrate evaporated to dryness. Crystallization of the colorless solid from benzene–hexane yielded 48 mg. of VIIh, m.p. 164°; infrared spectrum ($CHCl_3$): NH 2.90(m) μ, C=O 5.85(s) μ, C=C 6.23(m), 6.36(w) μ. A solution of the ketone and 60 mg. of hydroxylamine hydrochloride in 2 ml. of pyridine was heated on the steam-bath for 2.5 hr. Vacuum removal of the solvent and treatment of the residue with water resulted in precipitation of a solid whose crystallization from benzene–hexane yielded 36 mg. of the oxime of VIIh, m.p. 184°.

Anal. Calcd. for $C_{17}H_{18}ON_2$: C, 76.66; H, 6.81. Found: C, 76.81; H, 7.06.

Olivacine (II).—A mixture of 0.10 g. of phosphorus pentoxide and 0.20 g. of sand was added in small portions to a solution of 30 mg. of the oxime of VIIh in 0.5 ml. of anhydrous pyridine and the entire mixture heated at 125–130° for 8 hr. with occasional stirring. The cooled mixture was treated with ice-water, acidified with dilute hydrochloric acid and filtered. The fluorescing filtrate was treated with ammonia and extracted with chloroform. The extract was washed with water, dried over anhydrous potassium carbonate and evaporated. The resulting pale yellow solid, m.p. 296–307°, was used in the next reaction without further purification. A mixture of this imine and 50 mg. of 10% palladium–charcoal in 2 ml. of *p*-cymene was refluxed for 24 hr. After usual work-up a yellow solid was obtained whose chloroform solution was filtered through a short alumina column. Crystallization from chloroform gave pale yellow crystalline olivacine (II), m.p. and m.m.p. 315–320°; infrared and ultraviolet spectra identical in all respects with the spectra[2] of an authentic sample.[9]