for 10 min. longer with very small consumption of hydrogen. After addition of 35 mmoles of sodium acetate, the catalyst was filtered and extracted with methanol. The combined methanolic solutions were vacuum-concentrated to about 20 ml. After addition of 200 ml. of water, the mixture was extracted with ether and the combined ethereal solutions were washed with sodium bicarbonate solution and water. After vacuum evaporation of the ether and water, 4.61 g. (96% yield) of crude product was obtained which analyzed (infrared) for 83% cycloöctanoneoxime and 17% cycloöctanone. The vapor phase chromatogram of this crude product showed that the two major compounds were nearly uncontaminated with other by-products. An aliquot of the mixture was separated by microdistillation to give 78% oxime II and 16% ketone VII. The infrared spectrum of cycloöctanone VII, which was isolated by preparative vapor phase chromatography also, was identical with that of authentic material ($\epsilon_{5.88\mu}/\epsilon_{3.40\ \mu} = 1.44$). The infrared spectrum of the oxime II was identical with that of authentic cycloöctanoneoxime obtained by a 16-hr. reaction of equimolar amounts of cycloöctanone, hydroxylamine hydrochloride, and sodium acetate in water–methanol solvent at room temperature and subsequent work-up as described above; b.p. 63° (0.08 mm.), m.p. 41.7–42.7° (reported[10] m.p. 26–28°), $\epsilon_{2.74\ \mu} = 1.19 \times 10^2$ l. cm.$^{-1}$ mole^{-1}, $\epsilon_{2.74\ \mu}/\epsilon_{3.40\ \mu} = 0.52$.

Anal. Calcd. for $C_8H_{15}NO$: C, 67.99; H, 10.71; N, 9.92. Found: C, 67.66; H, 10.42; N, 9.69.

In another run, 4.05 g. of a crude hydrogenation product containing 70% of oxime II, 23% of cycloöctanone VII, and 7% of impurity was converted to cycloöctanoneoxime by treatment with a mixture of 2.8 g. (40 mmoles) of hydroxylamine hydrochloride, 10.8 g. (80 mmoles) of sodium acetate trihydrate, 40 ml. of methanol, and 15 ml. of water for 40 min. at 50°. After work-up as described above and drying of the product for 24 hr. at 5 mm., 3.76 g. (91%) of material was obtained, which analyzed for 93% oxime II and 0% ketone VII.

Cycloöctanoneoxime was also prepared by hydrogenating 5.5 wt. % 1-nitrocycloöctene in pyridine (run 3) with 1.3% palladium for 16 hr. The product was worked up as described above with the difference that the pyridine was removed by azeotropic distillation with heptane after the catalyst had been filtered and extracted with ether.

Stearaldoxime (V) (Run 2).—A solution of 594 mg. (2 mmoles) of 1-nitro-1-octadecene[1] in 10 ml. of methanol containing 1 mmole of dry hydrochloric acid was hydrogenated with 183 mg. of catalyst (1.3% palladium). During 20 min., 1.8 moles of hydrogen was consumed per mole of nitroölefin and the rate of hydrogenation decreased sharply. After addition of 2 mmoles of sodium acetate, the mixture was worked up as described for cycloöctanoneoxime. The isolated crude product (528 mg., 94% yield) analyzed for 73% stearaldoxime content. If the carbonyl absorption, present at 5.75 μ in the crude product, is assigned to stearaldehyde, the amount of the latter is estimated at 13%. Pure stearaldoxime, m.p. 88.0–89.8° (reported[11] m.p. 89°), $\epsilon_{2.74\mu} = 1.30 \times 10^2$ l. cm.$^{-1}$ mole^{-1}, was obtained by recrystallization from methanol and hexane.

Hydrogenation of 3.7 wt. % 1-nitro-1-octadecene in pyridine (run 4) for 9 hr. using 4% palladium and subsequent work-up as described for II gave a crude product (96% crude yield) which contained 60% stearaldoxime.

Nitrocycloöctane (III) (Run 5).—A solution of 2.15 g. (13.8 mmoles) of 1-nitrocycloöctene in 100 ml. of methanol and 1 g. of pyridine was hydrogenated with 0.94 g. of catalyst (2.2% palladium). The rate of hydrogenation dropped when slightly less than 1 mole of hydrogen had been consumed (10 min.) per mole of nitroölefin. After filtration, methanolic extraction of the catalyst, and vacuum evaporation of the solvents with added heptane, 2.05 g. (96% crude yield) of crude product was obtained which analyzed for 83% nitrocycloöctane and10% cycloöctanone. Pure nitrocycloöctane, n^{20}D 1.4819 (reported[12] n^{20}D 1.4812), $\epsilon_{6.45\mu}/\epsilon_{3.40\mu} = 3.29$, was obtained by preparative vapor phase chromatography (6 ft. × 3/4 in. o.d. column packed with 25% GE-30 silicone gum rubber on Chromosorb W; helium flow rate, 200 ml./min.; temperature, 165°; retention time, 12 min. for VII, 37 min. for III). The isolated cycloöctanone was spectrally identified (100% pure).

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(11) H. Stephen, *J. Chem. Soc.*, 1876 (1925).

(12) Badische Anilin-u.-Soda-Fabrik, British Patent 720,646 (December 22, 1954).

1-Nitroöctadecane (VI) (Run 6).—A solution of 672 mg. (2.26 mmoles) of 1-nitro-1-octadecene in 10 ml. of methanol and 0.17 g. of pyridine was hydrogenated with 1.3% palladium. Since there was no break in the hydrogen uptake/time curve, the reaction was terminated after 1.1 moles of hydrogen had been consumed per mole of nitroölefin (11 min.). After work-up, as described for III, 612 mg. of crude product (90% crude yield) was isolated. When 489 mg. of this material was chromatographed on silicic acid, using *n*-hexane containing 10% benzene as eluent, 255 mg. (yield about 50%) of pure 1-nitroöctadecane VI, m.p. 39.5–41°, $\epsilon_{6.44\ \mu}/\epsilon_{3.40\mu} = 0.91$, was isolated.

Anal. Calcd. for $C_{18}H_{37}NO_2$: C, 72.18; H, 12.45; N, 4.67; mol. wt. (in benzene), 299.5. Found: C, 72.16; H, 12.41; N, 4.56; mol. wt. (in benzene), 308.

N-Methyl-1,2,3,4,4a,9a-hexahydrocarbazoles by Catalytic Hydrogenation

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For forty years N-methyl-1,2,3,4,4a,9a-hexahydrocarbazole,[3] prepared by tin–hydrochloric acid reduction of N-methyl-1,2,3,4-tetrahydrocarbazole,[4] has been the only known N-methylated 1,2,3,4,4a,9a-hexahydrocarbazole, although a respectable number of 1,2,3,4-tetrahydrocarbazoles, with or without methyl groups in 9-position, have been obtained by Fischer indole synthesis and its improved versions.[5] When metal–acid, including sodium and ethanol, was applied to N-methyl-1,2,3,4-tetrahydrocarbazoles, the benzene ring of which had been substituted by one or more methyl groups, the corresponding hexahydrocarbazoles were actually found, but the yields failed to exceed 13%. An estimation of the equilibria involved in the catalytic hydrogenation of tetrahydrocarbazoles suggested the application of low hydrogen pressure together with an acidic solvent, which would both favor the formation of hexahydrocarbazoles and inhibit their overreduction to 1,2,3,4,5,6,7-8-octahydrocarbazoles.

With Adams' platinum oxide,[6] 9-methyl- and the (5–8),9-dimethyl-1,2,3,4-tetrahydrocarbazoles gave the corresponding 1,2,3,4,4a,9a-hexahydrocarbazoles in yields of 85% and better. Glacial acetic acid served as the solvent; occasionally a small amount of hydrochloric acid had to be added. Prolonged hydrogenation under these conditions led to other acid-soluble oils, presumably dodecahydrocarbazoles, which were not investigated. The formation of acid-insoluble by-products was negligible. The hydrogenation rates were nearly identical for all reactions.

The N-methyl-1,2,3,4,4a,9a-hexahydrocarbazoles are basic liquids,[7] virtually insoluble in water or aqueous

(1) A portion of this work was submitted to Tuskegee Institute as a M.S. thesis.

(2) Presented at the Southeastern Regional Meeting of the American Chemical Society in Birmingham, Ala., November 4, 1960.

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(6) R. Adams, V. Vorhees, and R. L. Shriner, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 463.

(7) Exception: 6,8,9-trimethyl-1,2,3,4,4a,9a-hexahydrocarbazole, m.p. 59–60°, glassy prisms; J. C. Kelley, in progress.

alkali, but reversibly soluble in 2 *N* mineral acids. In the absence of rough surfaces they may be distilled in an aspirator vacuum without decomposition. Their odor resembles that of N,N-dimethylaniline. Despite their reducing nature they are quite stable on the shelf, although they gradually darken. They undercool easily and, as a rule, congeal glassy rather than crystallize.

As tertiary anilines the N-methyl-1,2,3,4,4a,9a-hexahydrocarbazoles add methyl iodide with great ease to give the water-soluble, benzene-insoluble N,N-dimethyl-1,2,3,4,4a,9a-hexahydrocarbazolium iodides. These salts crystallize slowly from water, alcohol, or acetone as white needles or glass-clear prisms of remarkable mechanical strength, which tend to stick tightly to glass. When forced out of solution rapidly, the salts may appear as milky emulsions, settle soon as oils, but within an hour they are usually crystallized. They are completely stable on the shelf. At-random tests on gradient agar plates[8] revealed some activity against *Escherichia coli* and *Staphylococcus aureus*.

The hydrogenation of tetrahydrocarboline derivatives to hexahydrocarbolines by the same technique has been accomplished,[9] which fact may be of interest in the Rauwolfia alkaloid chemistry.

Experimental

6,9-Dimethyl-1,2,3,4-tetrahydrocarbazole.—To a mixture of 50 ml. of acetic acid and 23.6 g. of cyclohexanone 18.3 g. of α-methyl-α-(*p*-tolyl)hydrazine was added during 0.5 hr. while stirring and refluxing. After another hour's refluxing and stirring the cooled solution deposited 17 g. of pink needles, m.p. 87°. A second crop of 3 g. was obtained by diluting the mother liquor with its volume of water. Distillation and recrystallization from methanol gave 16.2 g. of pure 6,9-dimethyl-1,2,3,4-tetrahydrocarbazole, m.p. 89–90°, b.p. 213–214°; (25 mm.); yield 59%. No peroxide formation was observed.[10]

6,9-Dimethyl-1,2,3,4,4a,9a-hexahydrocarbazole.—A 3.0-g. sample of 6,9-dimethyltetrahydrocarbazole in 35 ml. of glacial acetic acid containing 2 ml. of hydrogen chloride-saturated glacial acetic acid was hydrogenated on 100 mg. of platinum oxide (Adams')[6] with 400 ml. of hydrogen at room temperature and atmospheric pressure (2.5 hr.) in a modified Parr apparatus.[11] The solution was suction-filtered and rendered alkaline with 30% sodium hydroxide; the oily base and three subsequent ether extracts, 50 ml. each, were combined and extracted three times with 30 ml. of 2 *N* hydrochloric acid. The ether extract of the alkalinified aqueous extract was dried with potassium carbonate, evaporated, and the residue (1.4 g.) distilled at 122° (0.8 mm.) to give 1.2 g. of an almost colorless oil, which began to darken when exposed to air for several days.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.53; H, 9.51: N, 6.96. Found: C, 83.50; H, 9.56; N, 7.14.

6,9,9-Trimethyl-1,2,3,4,4a,9a,-hexahydrocarbazolium Iodide.—A solution of 0.5 g. of 6,9-dimethylhexahydrocarbazole and 0.5 ml. of methyl iodide in 5 ml. of benzene was allowed to stand at room temperature. After 2 days the hard yellowish crystals were collected and repeatedly recrystallized from alcohol to give white crystals, m.p. 168–70° dec.

Anal. Calcd. for $C_{15}H_{22}IN$: C, 52.48; H, 6.46; I, 36.98; N, 4.08. Found: C, 52.69; H, 6.63; I, 37.09; N, 3.98.

8,9-Dimethyl-1,2,3,4-tetrahydrocarbazole.—This compound was first obtained by a method analogous to the 6,9-dimethyltetrahydrocarbazole synthesis from α-methyl-α-(*o*-tolyl)hydrazine. Since the reaction of methyl-*o*-tolylnitrosamine by Fischer–Arbuzov[12] method gave only low yields, *o*-tolylhydrazine [m.p. 53–56°, b.p. 145–150° (15 mm.)] was prepared in 66.5% yield by sulfite reduction of *o*-toluenediazonium chloride at −10 to −5° with subsequent heating to 60°, and 8-methyl-1,2,3,4-tetrahydrocarbazole[10] was obtained in 51% yield by Borsche[13] condensation in glacial acetic acid; m.p. 91–95° after distillation at 206° (14 mm.). To avoid the formation of peroxide,[10] the substance was not recrystallized.

Dimethyl sulfate (30 ml.) was added during 1 hr. to a stirred, refluxing mixture of 150 g. of sodium hydroxide, 46.5 g. of 8-methyltetrahydrocarbazole, 100 ml. of water, and 40 ml. of acetone. After stirring for 15 additional minutes and refluxing, the mixture was diluted with an equal volume of water and acidified with a mixture of 100 ml. of concentrated sulfuric acid and 100 ml. of water. The 8,9-dimethyltetrahydrocarbazole was washed with water, air-dried, stirred with a little cold methanol to remove unchanged 8-methyltetrahydrocarbazole, recrystallized from ethyl acetate and from acetone or ligroin (b.p. 100–105°) to give colorless needles, m.p. 151–152°. The substance did not form peroxides.[10]

8,9-Dimethyl-1,2,3,4,4a,9a-hexahydrocarbazole.—The procedure was analogous to the preparation of the 6,9-isomer; however, the low solubility of the 8,9-dimethyltetrahydrocarbazole in glacial acetic acid (0.4%) at room temperature required a different solvent. A mixture of 75 ml. of benzene, 75 ml. of glacial acetic acid, and 2 ml. of hydrogen chloride-saturated glacial acetic acid was used for 3 g. of 8,9-dimethyltetrahydrocarbazole, from which were obtained 1.55 g. of crude 8,9-dimethyl-1,2,3,4,4a,9a-hexahydrocarbazole and 1.3 g. of starting material. The 8,9-dimethyl-1,2,3,4,4a,9a-hexahydrocarbazole, distilled at 172° (15 mm.), turned green after short standing in the air and deposited a dark amorphous material in the course of 2 weeks. The remaining yellow liquid was distilled to give an almost colorless oil which became brown after 3 months.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.22; H, 9.88; N, 7.14.

Although the freshly prepared compound did not crystallize under any circumstances and stayed liquid for months at −27°, repeated cooling of the 1-year-old sample with liquid nitrogen and allowing it to reach −5° caused crystallization. The 1-year-old material liquefied at −4 to −2°.

8,9,9-Trimethyl-1,2,3,4,4a,9a-hexahydrocarbazolium Iodide.—The preparation was analogous to that of the 6,9,9-isomer; m.p. 188–189° dec.

Anal. Calcd. for $C_{15}H_{22}IN$: C, 52.48; H, 6.46; I, 36.98; N, 4.08. Found: C, 52.43; H, 6.74; I, 36.72; N, 3.79.

(5,7),9-Dimethyl-1,2,3,4-tetrahydrocarbazole.—To a stirred, refluxing solution of 6 g. of cyclohexanone in 50 ml. of glacial acetic acid, 7.8 g. of α-methyl-α-(*m*-tolyl)hydrazine [b.p. 90–92° (1.9 mm.); by Fischer–Arbuzov[12] reduction] was added dropwise. After refluxing for a total of 1.25 hr. the mixture deposited 7.6 g. of the two isomers at room temperature, and an additional 0.8 g. in the refrigerator. The product was washed, air-dried, distilled at 158–160° (1.8 mm.), and recrystallized from methanol to give white needles, m.p. 66–80°. The isomers could partly be separated by fractional high-vacuum sublimation at 50° (0.03 mm.) in an Emich flask packed with Podbielniak Heli-Pak. The sublimate reached a m.p. of 85–94°, the residue 98–106°.[14] No peroxides were noticed.

(5,7),9-Dimethyl-1,2,3,4,4a,9a-hexahydrocarbazole.—The mixture of isomers, 3.0 g., was hydrogenated as described for 6,9-dimethyl-1,2,3,4-tetrahydrocarbazole to give 0.5 g. of the (5,7),9-dimethylhexahydrocarbazoles, b.p. 136° (0.4 mm.), and 2.5 g. of starting material.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.31; H, 9.91; N, 7.19.

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(11) The Parr catalytic apparatus (Parr no. 3911) was modified as follows. The pressure tank and gage was replaced by a set of three inverted graduated cylinders serving as gas burets of 1000, 500, and 100 ml. They were connected by a manifold with each other, the reaction vessel and a three-way stopcock leading to the vacuum line and to the hydrogen tank (Matheson lecture bottle with prepurified-grade hydrogen). The commercial reaction vessel was replaced by a 100- or 250-ml. round-bottom flask with a standard-taper 29/42 connected with the gas inlet by a glass tubing with a 29/42 male ground joint and a short piece of vacuum rubber tubing. A rubber stopper, size 12, with a depression accommodated the round-bottom flask in the shaker. The hydrogen uptake was read on the gas burets with leveled bulbs.

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Ring Nonplanarity and Aromaticity in Porphyrins. Nuclear Magnetic Resonance Spectra of Etioporphyrin II and Its N-Alkyl Compounds

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To account for the known existence of N-alkylporphyrins it has been proposed from considerations of steric factors and visible spectra[1,2] and, more recently, analog computations[3] that at least one pyrrole ring must be out of the over-all plane of the porphyrin ring. However, no detailed experimental investigations of the manner in which the porphyrin ring accommodates the alkyl group substituted on nitrogen at the center of the ring and of the effect such an accommodation has on the aromaticity of the macrocycle have been reported. Here we report the n.m.r. spectra of etioporphyrin II (Fig. 1, R = H),[4] N-methyletioporphyrin II (Fig. 1, R = CH_3), and N-ethyletioporphyrin II (Fig. 1, R = CH_2CH_3) in deuteriochloroform. These spectra are interpreted as indicating that the porphyrin ring in etioporphyrin II is planar, whereas in each of the N-alkyl compounds there are definite deviations from planarity. N-Alkylation results in only a small change in ring current field strength and, consequently, the aromaticity may also be considered to be altered only slightly.

With the presumably planar[5] etioporphyrin II the ring positions for each type of substituent appear equivalent (Fig. 2, I) and the assignments are clear (Table I).[4] The spectra of the N-alkyl etioporphyrins are characterized by non-equivalence in ring positions. The N-alkyl protons appear at extremely high field consistent with the findings for porphyrin nitrogen bound protons[4,6] and their being within a strong ring current field. The fact that both N—CH_3[7] and N—Et—CH_2 are at significantly higher fields than N—Et—CH_3 provides evidence for the ring current effect being stronger near the center of the macrocycle.

The nature of the non-equivalence of ring positions in the N-alkyl compounds proves to be consistent with a definite nonplanar conformation of the molecules. Upon examination of models, a most reasonable manner for the N-alkyl group to be accommodated involves: (1) pyrrole ring I (Fig. 1) being somewhat out of the over-all plane of the ring with its nitrogen above the plane and its β-carbons below; (2) rings II and IV being out of the plane, to a lesser extent, with their nitrogen atoms below and their β-carbons above; and (3) ring III remaining essentially in the plane. The n.m.r. spectra suggest this is indeed the case. Thus the R—CH_3 of ring I is considerably out of the over-all plane, those of rings II and IV somewhat out of the plane, and that of ring III in the plane. If it is assumed that the further the protons of a given R—CH_3 are out-of-plane the lesser will be the ring current field effect, then the R—CH_3 protons of types A, B, and C may be assigned to ring I, rings II and IV, and ring

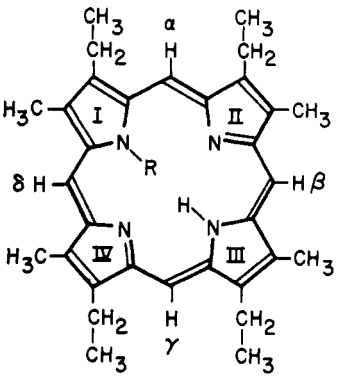

Figure 1

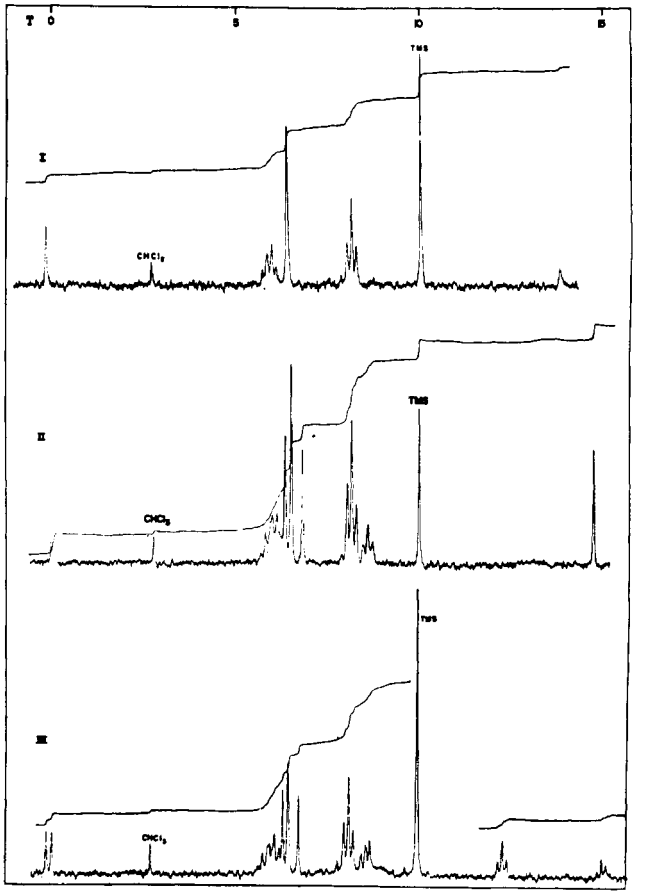

Fig. 2.—N.m.r. spectra in deuteriochloroform. I, etioporporphyrin II; II, N-methyletioporphyrin II; III, N-ethyletioporphyrin II.

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(7) For convenience the following abbreviations are used in this paper: R—CH_3 for ring methyl, R—Et—CH_3 for methyl of ring ethyl, N—CH_3 for nitrogen bound methyl, N—Et—CH_3 for methyl of nitrogen bound ethyl, R—Et—CH_2 for methylene of ring ethyl, N—Et—CH_2 for methylene of nitrogen bound ethyl.