solid, m.p. 106–107° (lit.[16] m.p. for picolinamide 106.5°). A melting point with 2-pyridinealdoxime was depressed.

Anal. Calcd. for $C_6H_6N_2O$: C, 59.01; H, 4.91; N, 22.95. Found: C, 59.35; H, 5.34; N, 23.07.

Following the same procedure, 4-pyridineazidoxime gave isonicotinic acid, m.p. above 300°, but starting to sublime around 270° (lit.[17] sublimes at 315°; in a sealed tube, 325–326°).

Anal. Calcd. for $C_6H_5O_2N$: C, 58.53; H, 4.06; N, 11.38. Found: C, 58.32; H, 4.04; N, 11.69.

Acknowledgment.—The authors wish to thank P. Wheeler and A. Richardson of the Analytical Branch for the microanalysis.

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[16] I. Heilbron, ref. 14, p. 203.

[17] I. Heilbron, ref. 14, Vol. III, p. 97.

Nitration of Indoles. II. The Mononitration of Methylindoles[1]

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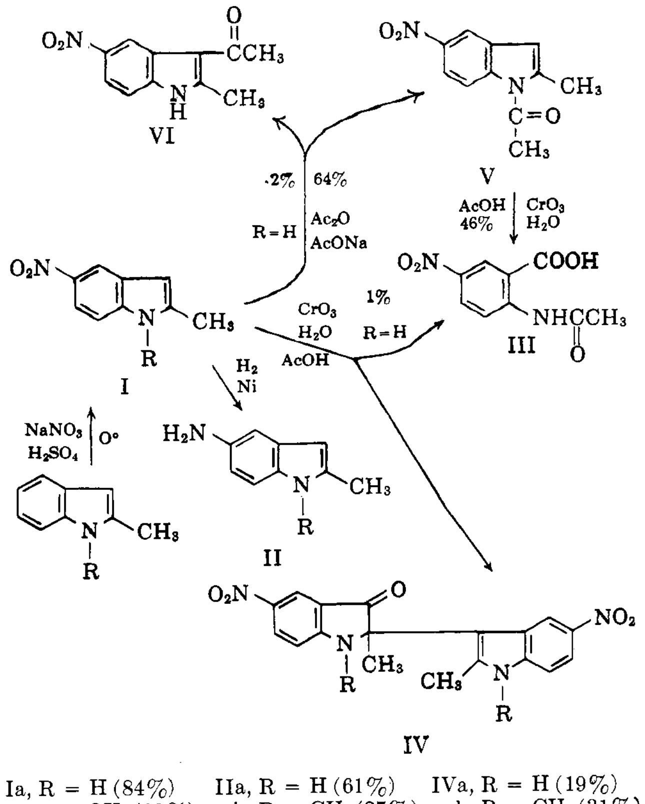
Nitration of 2-methylindole and 1,2-dimethylindole in concentrated sulfuric acid gives the corresponding 2-methyl-5-nitroindoles (Ia, 84%, and Ib, 82%). Methylation of Ia with sodamide and dimethyl sulfate in liquid ammonia gave Ib (47%). Acetylation of Ia with sodium acetate and acetic anhydride gave the 1-acetyl (V, 64%) and 3-acetyl (VI, 2%) derivatives. Chromic acid oxidation of the 1-acetyl derivative gave N-acetyl-5-nitroanthranilic acid (III, 46%), thus proving the 5-position as the position of mononitration in Ia and Ib, analogous to the corresponding nitration of 2,3-dimethylindole. Chromic acid oxidation of Ia and Ib gave the oxidative dimers IVa (19%) and IVb (31%). Catalytic hydrogenation of Ia and Ib gave the corresponding 5-amino-2-methylindoles (IIa, 61%, and IIb, 37%). Condensation of Ia with formaldehyde and benzaldehyde gave the corresponding 3,3′-methylenediindoles (XIIa, 100%, and XIIb, 58%), while the Mannich reaction of Ia with formaldehyde and dimethylamine gave 2-methyl-5-nitrogramine (XIII, 18%, and XIIa, 51%). The mechanism of formation of the various products is discussed.

In this paper, nitration of 2-methylindole and 1,2-dimethylindole in concentrated sulfuric acid clearly is shown to occur in the 5-position, and this observation is reconciled with previously known facts concerning nitration of indoles. In addition, several derivatives of the nitration products are described.

Nitration of 2-methylindole in concentrated sulfuric acid previously has been reported to give a mononitro derivative.[4] The structure has now been proved to be 2-methyl-5-nitroindole[5] (Ia, 84%) by oxidative degradation. Chromic acid oxidation gave N-acetyl-5-nitroanthranilic acid (III, 1%), a more important, insoluble product (IVa, 19%) being the result of oxidative dimerization. Acetylation of 2-methyl-5-nitroindole, however, to its 1-acetyl derivative V, 64% (formed along with 2% of the isomeric 3-acetyl derivative, VI), in the presence of sodium acetate,[6] and subsequent chromic acid oxidation, gave N-acetyl-5-nitroanthranilic acid (III) in greatly improved yield (46%). Nitration of 1,2-dimethylindole under the conditions used with 2-methylindole gave 1,2-dimethyl-5-nitroindole (Ib, 82%), the structure of which was proved by its identity with a sample prepared by methylation of 2-methyl-5-nitroindole. Chromic acid oxidation of Ib proceeded similarly to that of Ia, giving the insoluble product of oxidative dimerization IVb, 31%.



Ia, R = H (84%) IIa, R = H (61%) IVa, R = H (19%)
b, R = CH_3 (82%) b, R = CH_3 (37%) b, R = CH_3 (31%)

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[1] For Paper I of this series, see W. E. Noland and R. D. Rieke, *J. Org. Chem.*, **27**, 2250 (1962).

[2] It is a pleasure to acknowledge support of the first portion of this work from the General Research Fund of the Graduate School of the University of Minnesota, used to employ Donald C. Johnson and Lowell R. Smith as research assistants during the summer of 1958. The subsequent portion of this work, not supported by the Graduate School, is contained in the Ph.D. thesis of Lowell R. Smith.[3]

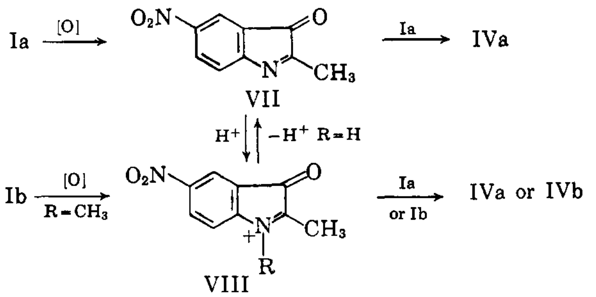
[3] Taken in part from the Ph.D. thesis of Lowell R. Smith, University of Minnesota, May 1960; *Dissertation Abstr.*, **21**, 1766 (1961). It is a pleasure to acknowledge support of this portion of the work through a Frederick Gardner Cottrell grant from the Research Corporation.

[4] R. von Walther and J. Clemen, *J. prakt. Chem.*, [2] **61**, 249 (1900).

[5] Chloranil dehydrogenation of 2-methyl-5-nitroindoline also is reported to give 2-methyl-5-nitroindole, m.p. 171.5–172.5°, which was assumed to be the same as the mononitration product of 2-methylindole, m.p. 170° (ref. 4); A. P. Terent'ev, M. N. Preobrazhenskaya, A. S. Bobkov, and G. M. Sorokina, *J. Gen. Chem. USSR* (Eng. Transl.), **29**, 2504 (1959).

[6] N-Alkylation generally occurs in preference to 3-alkylation of indoles having both 1- and 3-positions open only under conditions when the anion of the indole is the reactive species (normally only under basic conditions). For a listing of several examples see, J. Szmuszkovicz, *J. Am. Chem. Soc.*, **79**, 2819 (1957). Since acylation resembles alkylation in that it too is an electrophilic reaction, it seems likely that N-acylation also occurs preferentially only under conditions when the anion of the indole (in this case, of Ia) is the reactive species. In the present case (with sodium acetate), the acidity of the indole, and hence the ease of formation of its anion, is enhanced by the fact that the indole nitrogen is also part of a *p*-nitroaniline system.

The oxidative dimerization products, IVa and IVb, resemble in some aspects of their ultraviolet and infrared spectra and in their probable mode of formation, the oxidative dimer IVa ($NO_2 = H$)[7] formed by autoxidation or peroxide oxidation of 2-methylindole. The oxidative dimerization is assumed to proceed through a highly reactive intermediate[7]: 2-methyl-5-nitro-3*H*-indol-3-one (VII) or its conjugate acid (VIIIa) in the case of Ia; and VIIIb in the case of Ib. The intermediate (VII or VIII) then undergoes rapid nucleophilic attack at its reactive 2-position by an unoxidized indole molecule, giving the oxidative dimer IVa or IVb.

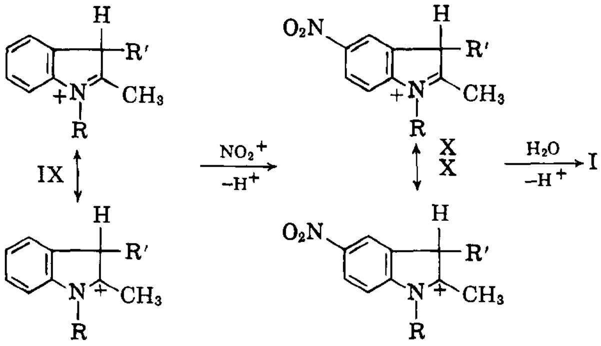


VIIIa, R = H
b, R = CH_3

Nitration of 2,3-dimethylindole in concentrated sulfuric acid also gives a 5-nitro derivative (Ic),[8-10] but in our hands nitration of indole, 1-methylindole, and skatole[11] in concentrated sulfuric acid gave only amorphous dark brown solids. Nitration of 2,3-dimethylindole with nitric acid alone at 0° gave a golden yellow amorphous solid, melting above 300°. Nitration in acetic acid gives rapid, exothermic reactions[12] with 2,3-dimethylindole, skatole, and indole-3-butyric acid, leading only to yellow,[13] amorphous polymers.[12] Analogous results were obtained with 1,3-dimethylindole.[14a] Under similar conditions, however, tryptophan gives the 6-nitro derivative,[15] while gramine and 1-methylgramine give largely the 6-nitro derivative with some of the 4-nitro derivative.[12] Since in these cases the side chain amino substituent would be protonated by nitric acid during nitration, it seems likely that the electrostatic repulsion of the positively charged nitrogen prevents oxidative attack at the 2-position or 2,3-double bond, which are vulnerable points for electrophilic attack in the simpler derivatives, skatole[16] and 2,3-dimethylindole.[17]

The 3-position is the normal site, under acidic or neutral conditions, of electrophilic attack in indoles having an open 3-position. It has been shown by ultraviolet[18,19] and n.m.r.[19,20] studies that 2-methylindoles are protonated at the 3-position in sulfuric acid solutions. The ultraviolet spectrum of 2-methylindole is reported to be shifted completely to the protonated form even in 4 *M* sulfuric acid.[19] The total absence of 3-nitration with 2-methylindole and 1,2-dimethylindole in concentrated sulfuric acid indicates that, prior to nitration, the 3-position has become fully protonated, and that this protonation has been reversed only by hydrolysis during the work-up procedure.

Thus, nitration at the 5-position of 2-methyl-3-protonated indoles (IX) occurs *para* to the 1,2-double bond and to the center of electron density at the 1-position (X, resonance form with a plus charge in the 2-position). In contrast, nitration in acetic acid of the unprotonated nucleus of 1-acetyl-2,3-dimethylindole (which gives primarily products of oxidation at the 2,3-double bond[17]) occurs *para* (6-position)[9,10,21,22] and also *ortho* (4-position)[10] to the 2,3-double bond and to the center of high electron density at the 3-position.



IXa, Xa, R = H; R′ = H
IXb, Xb, R = CH_3; R′ = H
IXc, Xc, R = H; R′ = CH_3

Catalytic hydrogenation of 2-methyl-5-nitroindole (Ia) and of its 1-methyl derivative (Ib) gave the corresponding 5-amino-2-methylindoles (IIa, 61%, and IIb, 37%). 5-Amino-2-methylindole (IIa)[23,24] and its acetyl derivative[24] had melting points in agreement with those reported. Reduction of crude 2-methyl-5-nitroindole (Ia) with tin and hydrochloric acid, however, has been reported[4] to give a mixture of products, including a 34% yield of an amino-2-methylindole having correct elemental analyses but a melting point (137°) quite different from that of authentic 5-amino-2-methylindole (157–159°). Likewise, the acetyl derivative was reported to have a melting point (188°) quite different from 5-acetamido-2-methylindole (160–161°). We found chemical reduction with tin and hydrochloric acid to be quite unsatisfactory as a method for reducing 2-methyl-5-nitroindole, and we were unable to confirm the previous report.[4] By acetylation of the reduction products, however, it was possible to isolate a chloro 5-acetamido-2-methylindole (XI) of melting point 234–235°. It is assumed that the chloride ion entered a position *ortho* (6- or 4-) to the nitroso group assumed to be formed at an intermediate stage of the reduction, and probably at the less hindered 6-position.

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[7] (a) B. Witkop and J. B. Patrick, *J. Am. Chem. Soc.*, **73**, 713 (1951); (b) B. Witkop, *Ann.*, **558**, 98 (1947).

[8] H. Bauer and E. Strauss, *Ber.*, **65**, 308 (1932).

[9] S. G. P. Plant and M. L. Tomlinson, *J. Chem. Soc.*, 955 (1933).

[10] C. M. Atkinson, J. C. E. Simpson, and A. Taylor, *ibid.*, 165 (1954).

[11] It also has been reported previously that an attempted nitration of skatole gave no definite nitro derivative (ref. 8).

[12] G. Berti and A. Da Settimo, *Gazz. chim. ital.*, **90**, 525 (1960).

[13] R. de Fazi, G. Berti, and A. Da Settimo, *Ric. Sci.*, **28**, 1013 (1958).

[14] Kent R. Rush, unpublished work, University of Minnesota: (a) 1961; (b) 1963.

[15] R. de Fazi, G. Berti, and A. Da Settimo, *Gazz. chim. ital.*, **89**, 2238 (1959).

[16] W. E. Noland and D. N. Robinson, *Tetrahedron*, **3**, 68 (1958);

[17] C. M. Atkinson, J. W. Kershaw, and A. Taylor, *J. Chem. Soc.*, 4426 (1962).

[18] G. Berti, A. Da Settimo, and D. Segnini, *Ric. Sci.*, **30**, 1057 (1960); *Gazz. chim. ital.*, **91**, 571 (1961).

[19] R. L. Hinman and J. Lang, *Tetrahedron Letters*, No. **21**, 12 (1960).

[20] R. L. Hinman and E. B. Whipple, *J. Am. Chem. Soc.*, **84**, 2534 (1962).

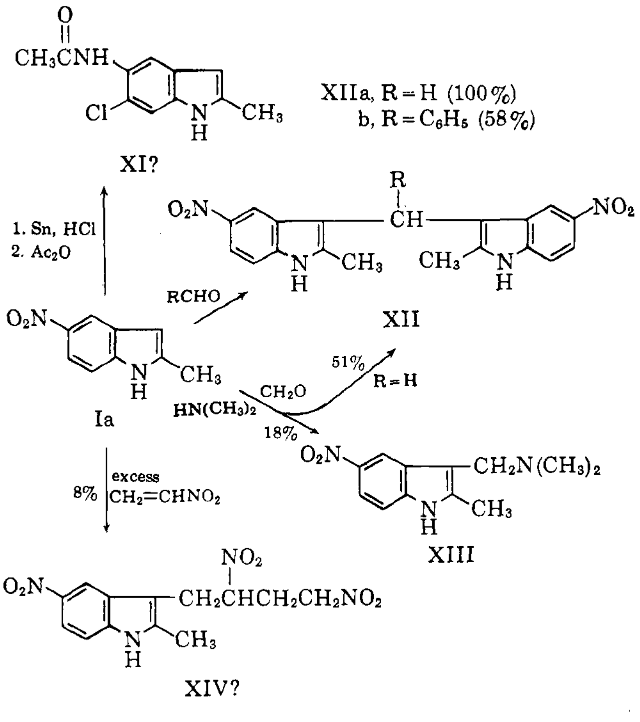
[21] K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 796 (1949).

[22] S. G. P. Plant and W. D. Whitaker, *ibid.*, 283 (1940).

[23] See reference in footnote 5.

[24] R. Adams and W. P. Samuels, Jr., *J. Am. Chem. Soc.*, **77**, 5375 (1955).

The uncatalyzed reaction of 2-methyl-5-nitroindole (Ia) with benzaldehyde gave in 58% yield the 3,3′-benzylidenediindole (XIIb) previously described[4] in unstated yield. The corresponding uncatalyzed reaction with formalin, however, gave in 3% yield 5,5′-dinitro-3,3′-methylenediindole (XIIa) having a melting point (348–354°, with decomposition), 220° higher than that reported (131°).[4] The yield of XIIa became quantitative when the reaction was carried out with paraformaldehyde, catalyzed by a small amount of hydrochloric acid. A Mannich reaction with 2-methyl-5-nitroindole (Ia) also gave Xa (51%), as well as 2-methyl-5-nitrogramine (XIII, 18%). Because of extensive hydrogen bonding with the basic side-chain nitrogen, the infrared spectrum of the latter contains no well defined NH band, but the presence of ND bands (which do not overlap the CH bands) was established by deuteration studies. The ultraviolet spectra of the 2-methyl-5-nitroindoles (Ia and Ib) and of their derivatives XIIa, XIIb, XIII, and XIV are in very good agreement with the spectra of 5-nitroindole derivatives reported previously.[25]



Attempted nitroethylation[26] of 2-methyl-5-nitroindole (Ia) with a sixfold molar excess of nitroethylene gave a tarry, polymeric mixture containing an 8% yield of a *1:2 adduct*. It is probable that one nitroethyl group has become substituted at the 3-position of the indole nucleus. Presence of an NH band in the infrared spectrum of the product indicates that the second nitroethyl group is not attached at the 1- or 3-positions, and the similarity of the ultraviolet spectrum to that of the other 2-methyl-5-nitroindole derivatives suggests that no nitroethyl group is substituted on the benzene ring. The second nitroethyl group is, therefore, probably attached at the α-nitro position of the 3-(2-nitroethyl) substituent (structure XII) or, less likely, to the 2-methyl group. The substituted nitroolefin, β-nitrostyrene, was unreactive towards 2-methyl-5-nitroindole at steam bath temperature, the latter being recovered in 79% yield.

Experimental

Melting points were determined on a calibrated Kofler micro hot stage. Ultraviolet spectra were determined on a Cary Model 11 recording spectrophotometer, and infrared spectra were determined on a Perkin-Elmer Model 21 spectrophotometer.

2-Methyl-5-nitroindole (Ia).[2,3]—The procedure of von Walther and Clemen for the nitration and subsequent work-up, which gave a 20% yield,[4] has been greatly improved by keeping the reaction at 0°, adding the nitrating solution very slowly, and subsequently quenching the reaction by pouring it on crushed ice.

A solution of 2-methylindole[27] (8.40 g., 0.0640 mole) in concentrated sulfuric acid (50 cc.) was cooled to 0° in a salt–ice bath. A solution of sodium nitrate (5.40 g., 0.0635 mole) in concentrated sulfuric acid (50 cc.) was then added dropwise, with stirring, over a period of 1.5 hr. while cooling was continued in the salt–ice bath. The mixture was stirred for an additional 5 min. and then was poured onto crushed ice (400 g.). The bright yellow precipitate was filtered and washed with cold water. One recrystallization, with charcoal, from methanol–water (or better from methylene chloride[14a]) yielded yellow crystals (9.37 g., 84%); m.p. 176–176.5°, reported m.p. 170°,[4] 171.5–172.5°[5]; λ_{max} mμ (log ε) in 95% ethanol: 266 (4.32), 330 (3.94); ν_{NH} 3500 m in chloroform, 3360 m in Nujol, ν_{NO_2} 1330 ms in chloroform 1511 m, 1333 s cm.$^{-1}$ in Nujol.

The compound was recovered unchanged in 79% yield, m.p. 175–176°, from attempted reaction with β-nitrostyrene by fusion of equimolar portions on a steam bath for 4 hr.

Oxidative Degradation of 2-Methyl-5-nitroindole.[3]—A solution of chromium(VI) oxide (0.7 g., 0.007 mole) in water (2 cc.) and acetic acid (5 cc.) was added gradually, with shaking, at 0° to a solution of 2-methyl-5-nitroindole (0.65 g., 0.00369 mole) in acetic acid (20 cc.). The solution was kept overnight and then acetic anhydride (5 cc.) was added. The solution was kept for 0.5 hr. and water (100 cc.) was added. The aqueous solution was extracted with chloroform and the chloroform extract was washed with water and extracted with aqueous saturated sodium bicarbonate solution until carbon dioxide was no longer evolved. The bicarbonate extract was acidified to pH 2 with sulfuric acid and the acidified solution was extracted with chloroform. The chloroform extracts from the acidified solution were dried over anhydrous magnesium sulfate and concentrated to a small volume. Addition of petroleum ether (b.p. 40–75°) caused precipitation of impure **N-acetyl-5-nitroanthranilic acid (III)** (0.01 g., 1%), m.p. 210–213°. The mixture melting point with a sample of m.p. 213–214° prepared[28] from 4′-nitro-*o*-acetotoluidide[29] was undepressed, 210–214°, and the infrared spectra of the two samples in Nujol were somewhat similar.

2-Methyl-3-(2-methyl-5-nitro-3-oxo-2-indolinyl)-5-nitroindole (IVa).[2]—A solution of chromium(VI) oxide (4.5 g., 0.045 mole) in water (5 cc.) was added dropwise, with stirring and cooling in an ice bath, which kept the temperature below 35°, to a solution of 2-methyl-5-nitroindole (4.0 g., 0.0227 mole) in acetic acid (60 cc.). The resulting mixture was stirred overnight. The mixture, containing a solid residue, was diluted with water (100 cc.) and filtered, giving a tan solid (0.8 g., 19%), m.p. 250–253° dec. One recrystallization with charcoal from ethanol–water and three recrystallizations from methanol–water yielded bright yellow crystals, m.p. 271–272° dec.; λ_{max} mμ (log ε) in 95% ethanol: 227 (4.36), 245 (4.36), 267 (4.28), 271 (4.29), 351 (4.31); ν_{NH} 3380 ms, $\nu_{C=O}$ 1705 s, $\nu_{C=C}$ 1620 vs, ν_{NO_2} 1521 s, 1329 vs cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{18}H_{14}N_4O_5$ (366.32): C, 59.01; H, 3.85; N, 15.30. Found: C, 58.99; H, 4.13; N, 15.51.

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(25) For a good summary of ultraviolet spectra of 4-, 5-, 6-, and 7-nitroindoles, see G. Berti, A. Da Settimo, and D. Segnini, *Gazz. chim. ital.*, **90**, 539 (1960).

(26) (a) W. E. Noland and P. J. Hartman, *J. Am. Chem. Soc.*, **76**, 3227 (1954); (b) W. E. Noland, G. M. Christensen, G. L. Sauer, and G. G. S. Dutton, *ibid.*, **77**, 456 (1955); (c) W. E. Noland and R. F. Lange, *ibid.*, **81**, 1203 (1959).

(27) C. F. H. Allen and J. Van Allan, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 597; *Org. Syn.*, **22**, 94 (1942).

(28) S. Hillers, A. Lokenbachs, and L. Majs, *Latvijas PSR Zinatnu Akad. Vestis*, No. **3** (Whole No. 32), 7 (1950); *Chem. Abstr.*, **48**, 9965 (1954).

(29) H. Franzel and E. Engel, *J. prakt. Chem.*, [2] **102**, 173 (1921).

1-Acetyl-2-methyl-5-nitroindole (V) and **3-Acetyl-2-methyl-5-nitroindole** (VI).[3]—A solution of 2-methyl-5-nitroindole (2.50 g., 0.0142 mole) and sodium acetate trihydrate (8.00 g., 0.059 mole) in acetic anhydride (60 cc., 0.64 mole) was refluxed for 48 hr. The reaction mixture was cooled, ice–water (150 cc.) was added, and the mixture was stirred until the excess acetic anhydride was hydrolyzed (1 hr.). The mixture was cooled and filtered. One recrystallization of the filtered solid from methanol–water with charcoal yielded first **3-acetyl-2-methyl-5-nitroindole** (VI) as a light yellow solid (0.05 g., 2%), m.p. 305–307°; $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 239 infl. (4.18), 261 (4.43), 320 (4.01); ν_{NH} 3180 m, $\nu_{C=O}$ 1613 s, ν_{NO_2} 1541 m or 1510 m, 1322 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{11}H_{10}N_2O_3$ (218.21): C, 60.54; H, 4.62; N, 12.84. Found: C, 60.79; H, 4.77; N, 13.06.

Concentration and cooling of the methanol–water mother liquor caused precipitation of **1-acetyl-2-methyl-5-nitroindole** (V) as a metallic yellow solid (1.97 g., 64%), m.p. 130.5–132°; $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 262 (4.35), 310 (3.86); ν_{NH} none, $\nu_{C=O}$ 1706 s, ν_{NO_2} 1520 s, 1377 s or 1345 m or 1291 s cm.$^{-1}$ in Nujol. The compound gave a red Ehrlich test.

Anal. Calcd. for $C_{11}H_{10}N_2O_3$ (218.21): C, 60.54; H, 4.62; N, 12.84. Found: C, 60.83; H, 4.58; N, 12.89.

Oxidative Degradation of 1-Acetyl-2-methyl-5-nitroindole.[3]—A solution of chromium(VI) oxide (0.80 g., 0.0080 mole) in water (1 cc.) and acetic acid (15 cc.) was added gradually, with shaking, to a solution of 1-acetyl-2-methyl-5-nitroindole (0.70 g., 0.0032 mole) in acetic acid (35 cc.). The solution was kept at room temperature for 24 hr. and then water (100 cc.) was added. The solution was extracted with chloroform and the chloroform extract was washed with water and extracted with aqueous saturated sodium bicarbonate solution until carbon dioxide was no longer evolved. The bicarbonate extract was acidified to pH 2 with sulfuric acid and the acidified solution was extracted with chloroform and ether. The combined extracts were washed with water and treated with anhydrous sodium sulfate and charcoal. Evaporation of the dried solution to a small volume and addition of petroleum ether (b.p. 40–75°) caused precipitation of **N-acetyl-5-nitroanthranilic acid** (III) (0.33 g., 46%), m.p. 213–214°. There was no depression in mixture melting point with a sample prepared[28] from 4'-nitro-*o*-acetotoluidide,[29] and the infrared spectra of the two samples in Nujol were identical.

1,2-Dimethyl-5-nitroindole (Ib).[2] A. **By Nitration of 1,2-Dimethylindole.**—A solution of 1,2-dimethylindole[30] (8.0 g., 0.055 mole) in concentrated sulfuric acid (50 cc.) was cooled to 2°. A solution of sodium nitrate (4.7 g., 0.055 mole) in concentrated sulfuric acid (50 cc.) was then added dropwise, with stirring, over a period of 20 min. The temperature rose to a peak of 15° midway during the addition. The solution was stirred for an additional 10 min. until the temperature returned to 2° and then was poured onto crushed ice (400 g.). The bright yellow precipitate was filtered, washed with water, and recrystallized once from 5:1 (by volume) methanol–ethyl acetate, yielding hygroscopic yellow crystals (8.6 g., 82%), m.p. 129–130°; $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 260 infl. (4.24), 274 (4.33), 333 (3.94); ν_{NO_2} 1333 s in chloroform, 1523 ms, 1340 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$ (190.20): C, 63.14; H, 5.30; N, 14.73. Found: C, 62.72; H, 5.29; N, 14.66.

The compound was recovered unchanged in 74% yield, m.p. 129–130°, after attempted acetylation by being refluxed for 8 hr. with sodium acetate (1.5 equivalents) in excess acetic anhydride (15 equivalents).

B. **By Methylation of 2-Methyl-5-nitroindole.**—Ferric nitrate nonahydrate (one small crystal) was dissolved in liquid ammonia (75 cc.) and sodium (0.20 g., 0.0087 g.-atom) was added in small pieces. The solution was stirred for 5 min. and then a slurry of 2-methyl-5-nitroindole (1.45 g., 0.00823 mole) in benzene (25 cc.) was added, with stirring. The bright red solution was stirred for 5 min. and a solution of dimethyl sulfate (1.26 g., 0.0100 mole) in ether (10 cc.) was added dropwise, with stirring. The solution was stirred for 0.5 hr. and the ammonia allowed to evaporate overnight. Ethanol and water were added and the mixture was extracted with ether and ethyl acetate. The combined extracts were washed with water, treated with charcoal, and dried over calcium chloride. The bright yellow solution was evaporated to a small volume and methanol was added, causing separation of yellow crystals (0.73 g., 47%), m.p. 129–130°. The mixture melting point with the sample prepared by nitration of 1,2-dimethylindole was undepressed, 129–130°, and the infrared spectra of the two samples in Nujol were identical.

1,2-Dimethyl-3-(1,2-dimethyl-5-nitro-3-oxo-2-indolinyl)-5-nitroindole (IVb).[2]—A solution of chromium(VI) oxide (2.20 g., 0.0220 mole) in water (3 cc.) was added dropwise, with stirring and cooling in an ice bath, which kept the temperature below 30°, to a suspension of 1,2-dimethyl-5-nitroindole (2.0 g., 0.0105 mole) in acetic acid (50 cc.). The resulting mixture was stirred overnight and then poured into water, producing an orange precipitate. The precipitate was dissolved in chloroform and anhydrous ether was added causing separation of bright yellow microcrystals (0.65 g., 31%), m.p. 252–256° dec.; $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 231 (4.38), 247 (4.37), 275 (4.24), 362 (4.35); ν_{NH} none, $\nu_{C=O}$ 1719 s, $\nu_{C=C}$ 1620 vs, ν_{NO_2} 1525 ms, 1318 vs cm.$^{-1}$ in Nujol. A molecular weight determination in 1,2-dibromomethane gave a green solution, indicating dissociation, and the result was low, 245.

Anal. Calcd. for $C_{20}H_{18}N_4O_5$ (394.38): C, 60.91; 4.60; N, 14.21. Found: C, 61.07; H, 4.91; N, 13.89.

Recrystallization of a second crop from methylene chloride–petroleum ether (b.p. 60–68°) gave another form, presumably a dimorph, m.p. 285–286° dec., m.m.p. (with the preceding form) 250–285° dec., having an infrared spectrum in Nujol very similar to that of the preceding form; ν_{NH} none, $\nu_{C=O}$ 1714 s, $\nu_{C=C}$ 1617 vs, ν_{NO_2} 1524 ms, 1313 vs cm.$^{-1}$ in Nujol.

Anal. Found: C, 60.58; H, 4.69; N, 14.29.

5-Amino-2-methylindole (IIa).[3]—A solution of 2-methyl-5-nitroindole (1.0 g., 0.00566 mole) in absolute ethanol (100 cc.) was shaken with Raney nickel under hydrogen at 2 atm. for 10 min., during which time the theoretical amount of hydrogen was absorbed. The catalyst was filtered off and the solution vacuum evaporated to a small volume (about 10 cc.). Addition of an equal volume of water and cooling caused separation of colorless crystals (0.51 g., 61%); m.p. 157–159°, reported m.p. 156–156.5°,[23] 157–159°.[24] The analytical sample was prepared by sublimation at 140° (0.5 mm.); ν_{NH} 3430 m, 3390 s, 3250 mw cm.$^{-1}$ in Nujol. The compound gave a red Ehrlich test.

The **acetyl derivative** crystallized from benzene as white crystals, m.p. 160–161°, reported m.p. 159–160.5°[24]; ν_{NH} 3320 ms, $\nu_{C=O}$ 1630 s cm.$^{-1}$ in Nujol.

5-Amino-1,2-dimethylindole (IIb).[3]—A solution of 1,2-dimethyl-5-nitroindole (1.0 g., 0.00526 mole) in absolute ethanol (100 cc.) was shaken with Raney nickel under hydrogen at 2 atm. for 10 min. The catalyst was filtered off and the solution vacuum evaporated to a small volume (about 20 cc.). Addition of an equal volume of water and cooling caused separation of white crystals (0.31 g., 37%), m.p. 78–79°. The analytical sample was prepared by sublimation at 100° (0.5 mm.); $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 226 (4.45), 281 (3.90), 309 infl. (3.58); ν_{NH} 3420 mw, 3340 mw cm.$^{-1}$ in Nujol. The compound gave a red Ehrlich test.

Anal. Calcd. for $C_{10}H_{12}N_2$ (160.21): C, 74.96; H, 7.55; N, 17.49. Found: C, 74.83; H, 7.44; N, 17.74.

The **acetyl derivative** was obtained by crystallization from benzene or by vacuum sublimation as white crystals, m.p. 203–204°; $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 242 (4.51), with declining absorption containing diffuse inflections at 272 (3.89), 286 (3.80), 296 (3.73), and 310 (3.35); ν_{NH} 3330 ms, $\nu_{C=O}$ 1658 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{12}H_{14}N_2O$ (202.25): C, 71.26; H, 6.98; N, 13.85. Found: C, 71.01; H, 6.91; N, 14.08.

Reduction of 2-Methyl-5-nitroindole with Tin and Hydrochloric Acid.[3]—A mixture of 2-methyl-5-nitroindole (3.0 g.), tin (3.0 g.), concentrated hydrochloric acid (25 cc.), and 95% ethanol (5 cc.) was warmed on a steam bath for 3 hr. The mixture was cooled and basified to pH 10 with aqueous 30% sodium hydroxide solution. The precipitated solid was filtered, allowed to dry briefly, boiled with benzene, and the benzene extract filtered.

A small part of the filtrate was treated with acetic anhydride and then diluted with petroleum ether (b.p. 40–75°), causing precipitation of a pink solid. Vacuum sublimation yielded a white solid, m.p. 234–235°, possibly **5-acetamido-6(?)-chloro-2-methylindole** (XI); $\lambda_{\max}$ mμ (log ϵ) in 95% ethanol: 230 (4.57), 280 (3.92); ν_{NH} 3420 m, 3280 s, $\nu_{C=O}$ 1673 s cm.$^{-1}$ in Nujol. The compound gave a red Ehrlich test.

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Anal. Calcd. for $C_{11}H_{11}N_2OCl$ (222.67): C, 59.33: H, 4.98; N, 12.58; Cl, 15.92. Found: C, 59.65; H, 5.05; N, 13.47, 13.07; Cl, 16.15.

The major portion of the benzene filtrate was evaporated to a small volume. Addition of petroleum ether (b.p. 40–75°) caused precipitation of a pink solid (1.04 g.), m.p. ~80–140°. Recrystallization from ethanol–water, with charcoal, and from benzene–petroleum ether (b.p. 40–75°) did not appreciably purify the product. Vacuum sublimation at 200° (0.5 mm.) yielded a white solid, m.p. 147–157°, which, judging from its melting point, was still a mixture.

3,3′-Benzylidene-2,2′-dimethyl-5,5′-dinitrodiindole (XIIb).[3]—2-Methyl-5-nitroindole (1.00 g., 0.00567 mole) and benzaldehyde (1.50 g., 0.014 mole) were warmed together on a steam bath for 2 hr. The resulting solid mass was then recrystallized from methanol–water, yielding a yellow solid (0.72 g., 58%), m.p. 295–298° dec., reported m.p. 291°[4]; λ_{max} mμ (log ϵ) in 95% ethanol: 276 (4.57), 335 (4.20); ν_{NH} 3460 mw, 3360 m, ν_{NO_2} 1516 m, 1331 vs cm.$^{-1}$ in Nujol.

2,2′-Dimethyl-5,5′-dinitro-3,3′-methylenediindole (XIIa).[3] **A. From Reaction with Paraformaldehyde.**—Paraformaldehyde (1.7 g., 0.057 mole CH_2O) and concentrated hydrochloric acid (2 drops) were added to a solution of 2-methyl-5-nitroindole (5.7 g., 0.0323 mole) in methanol (50 cc.). The solution was refluxed for 3 hr. and a yellow-orange solid precipitated. Water was then added, and the yellow-orange solid (6.4 g.) was recrystallized from acetone–water, yielding an orangish yellow solid (5.9 g., 100%), m.p. 348–354° dec. (darkens at 270°); λ_{max} mμ (log ϵ) in 95% ethanol: 275 (4.60), 335 (4.20); ν_{NH} 3360 s, ν_{NO_2} 1503 m, 1332 vs cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{19}H_{16}N_4O_4$ (365.36): C, 62.63; H, 4.43; N, 15.38. Found: C, 62.51; H, 4.61; N, 15.04.

B. From Reaction with Formalin.—By the procedure of von Walther and Clemen,[4] a solution of 2-methyl-5-nitroindole (1.00 g., 0.00567 mole) and formalin (0.45 g. of 37% CH_2O, 0.0055 mole) in absolute ethanol (30 cc.) was refluxed for 0.5 hr. Filtration of the hot solution separated the yellow-orange solid precipitate (0.06 g., 3%), m.p. 348–354° dec., reported m.p. 131°.[4]

The cooled filtrate yielded unchanged 2-methyl-5-nitroindole (0.81 g., 81%), m.p. 175–176°, which gave no depression in mixture melting point with starting material.

2-Methyl-5-nitrogramine (XIII).[3]—A solution of 2-methyl-5-nitroindole (0.95 g., 0.00539 mole) in acetic acid (20 cc.) was added dropwise, with stirring, to a solution of formalin (0.50 g. of 37% CH_2O, 0.0062 mole) and dimethylamine (0.90 g. of aqueous 25% solution, 0.0050 mole) in acetic acid (15 cc.) at 0° over a period of 30 min. The mixture, in which an orange solid had precipitated, was stirred at 0° for an additional 30 min., then at room temperature for 45 min., and finally at 100° for 15 min. The acetic acid was neutralized to pH 7 with aqueous 20% potassium hydroxide solution, and the mixture was filtered, giving **2,2′-dimethyl-5,5′-dinitro-3,3′-methylenediindole** (XIIa) as an orange-yellow solid (0.50 g., 51%). Recrystallization from acetone gave a sample, m.p. 348–354° dec., having an infrared spectrum in Nujol identical with that of the sample prepared from the formaldehyde reaction.

The aqueous filtrate was basified to pH 10 with aqueous 20% potassium hydroxide solution and extracted with ether. The ether extract was treated with charcoal, dried over anhydrous sodium sulfate, and evaporated to a small volume. Addition of petroleum ether (b.p. 40–75°) caused precipitation of **2-methyl-5-nitrogramine (XIII)** as yellow crystals (0.21 g., 18% from dimethylamine), m.p. 173–175°; λ_{max} mμ (log ϵ) in 95% ethanol: 267 (4.23), 331 (3.87); ν_{NH} no well defined peaks except for a weak peak in Nujol at 2700 cm.$^{-1}$, with a broad tailing out of absorption toward lower frequencies, ν_{NO_2} 1527 m, 1333 s in Nujol, 1338 cm.$^{-1}$ in chloroform.

Anal. Calcd. for $C_{12}H_{15}N_3O_2$ (233.26): C, 61.78; H, 6.48; N, 18.02. Found: C, 61.71; H, 6.69; N, 17.96.

Equilibration of the sample with deuterium oxide in homogeneous methanol solution produced a sample containing, in addition to the weak peak at 2690, three broad medium weak peaks at 2340, 2190, and 2060 cm.$^{-1}$ attributed to the ND group, and also minor changes elsewhere in the infrared spectrum in Nujol.[14b]

Reaction of 2-Methyl-5-nitroindole with Nitroethylene.[3]—A solution of 2-methyl-5-nitroindole (2.3 g., 0.0130 mole) and nitroethylene[31] (7.0 g., 0.096 mole) in benzene (20 cc.) was kept at room temperature for 12 hr. The liquids were distilled under reduced pressure (0.7 mm.) and the residue was dissolved in acetone, producing a dark brown solution. Two treatments with liberal amounts of charcoal did not appreciably diminish the color of the solution. Addition of successive portions of petroleum ether (b.p. 40–75°) caused separation first of a quantity of dark brown tar, then a large amount of an amorphous tan solid, and finally a *1:2 adduct,* believed to be **3-(2,4-dinitro-1-butyl)-2-methyl-5-nitroindole (XIV)**, as a bright yellow crystalline solid (0.35 g., 8%), m.p. 215–217°; λ_{max} mμ (log ϵ) in 95% ethanol: 271 (4.32), 330 (4.09); ν_{NH} 3400 s in potassium bromide and Nujol, ν_{NO_2} 1546 s, 1506 m, 1327 s in potassium bromide, 1545 s, 1510 m, 1330 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{13}H_{14}N_4O_6$ (322.27): C, 48.45; H, 4.38; N, 17.39. Found: C, 49.52, 49.31; H, 4.61, 4.80; N, 16.88.

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Acylation *vs.* Conjugate Addition of Dipotassio β-Diketones with Cinnamic Esters. Synthesis of Unsaturated 1,3,5-Triketones and *t*-Butyl 5,7-Dioxoalkanoates[1]

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The dipotassio salts of benzoylacetone and certain related β-diketones, prepared by means of two molecular equivalents of potassium amide in liquid ammonia, were acylated with phenyl cinnamate to form unsaturated 1,3,5-triketones. These products were cyclized by means of sulfuric acid to give unsaturated 4-pyrones. Several dipotassio-β-diketones were condensed with *t*-butyl cinnamate to afford the conjugate addition products, certain of which were cleaved to produce appropriate derivatives. Methyl cinnamate exhibited, toward dipotassiobenzoylacetone, both acylation and conjugate addition. Studies were made on the influence of variations in the molecular ratios of β-diketone to ester on the yields of triketones from acylations of certain β-diketones with phenyl cinnamate and with phenyl and methyl benzoates.

Recently such β-diketones as benzoyl- and acetylacetones were shown to undergo alkylation,[2,3] acylation,[2,4,5] and the aldol type condensation[2,6] at their terminal methyl group through their dicarbanions, which were prepared by means of two molecular equivalents of an alkali amide (equation 1).

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