

ANALOGUES OF PSILOCIN AND LYSERGIC ACID DIETHYLAMIDE

I. CHLORO, NITRO, AND AMINO DERIVATIVES OF 3-SUBSTITUTED INDOLES

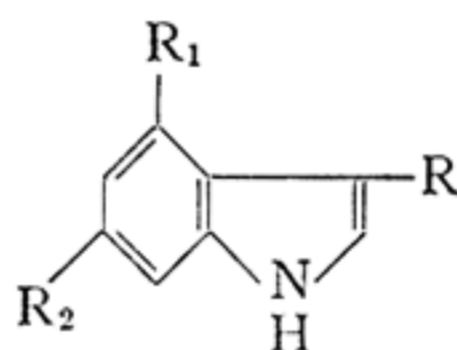
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Received June 5, 1963

ABSTRACT

A number of indole derivatives structurally related to either psilocin or lysergic acid diethylamide (LSD) were synthesized. The following structural analogues of psilocin are reported: 4-chloro-3-dimethylaminoethylindole, 4-nitro-3-dimethylaminoethylindole, 4-nitro-3-aminoethylindole, 4-amino-3-dimethylaminoethylindole, and 4-amino-3-aminoethylindole. Compounds structurally related to LSD that were synthesized are: 3-[β -carboxyethylaminoethyl]-4-nitroindole and 4-nitro-3-[N-methyl-N-(N',N'-diethylcarboxamidoethyl)-aminoethyl]indole. Several 3,5- and 3,6-disubstituted indoles are also reported.

A number of compounds possessing the indole structure have aroused considerable interest because of their hallucinogenic reactions in man. Two of the more potent of these hallucinogens are lysergic acid diethylamide (LSD) and psilocin, 3-dimethylaminoethyl-4-hydroxyindole. Both of these compounds are 3,4-disubstituted indoles. This paper reports the synthesis of a number of 3,4-disubstituted indoles structurally related to psilocin and LSD (1). Also included are several 3,5-disubstituted indoles, used as models for synthesis, and several 3,6-disubstituted indoles which were obtained together with the 3,4-compounds from Fischer ring closures.



(Undesignated R-groups refer to hydrogen)

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|---|---|
| I: R ₁ = Cl | XIII: R ₁ = NO ₂ ; |
| II: R ₁ = Cl; R = COCOCl | R = CH ₂ CH ₂ NHCH ₂ CH ₂ CO ₂ H |
| III: R ₁ = Cl; R = COCON(CH ₃) ₂ | XIV: R ₂ = NO ₂ ; |
| IV: R ₁ = Cl; R = CH ₂ CH ₂ N(CH ₃) ₂ | R = CH ₂ CH ₂ NHCH ₂ CH ₂ CO ₂ H |
| V: R ₁ = NO ₂ ; R = CH ₂ CH ₂ Cl | XV: R ₁ = NO ₂ ; |
| VI: R ₂ = NO ₂ ; R = CH ₂ CH ₂ Cl | R = CH ₂ CH ₂ N(CH ₃)CH ₂ CH ₂ CON(C ₂ H ₅) ₂ |
| VII: R ₁ = NO ₂ ; R = CH ₂ CH ₂ N(CH ₃) ₂ | XVI: R ₂ = NO ₂ ; |
| VIII: R ₂ = NO ₂ ; R = CH ₂ CH ₂ N(CH ₃) ₂ | R = CH ₂ CH ₂ N(CH ₃)CH ₂ CH ₂ CON(C ₂ H ₅) ₂ |
| IX: R ₁ = NO ₂ ; R = CH ₂ CH ₂ NH ₂ | XVII: R ₁ = NH ₂ ; R = CH ₂ CH ₂ N(CH ₃) ₂ |
| X: R ₂ = NO ₂ ; R = CH ₂ CH ₂ NH ₂ | XVIII: R ₂ = NH ₂ ; R = CH ₂ CH ₂ N(CH ₃) ₂ |
| XI: R ₁ = NO ₂ ; R = CH ₂ CH ₃ | XIX: R ₂ = NH ₂ ; R = CH ₂ CH ₂ NH ₂ |
| XII: R ₂ = NO ₂ ; R = CH ₂ CH ₃ | XX: R ₁ = NH ₂ ; R = CH ₂ CH ₂ NH ₂ |

Conditions which were suitable for reaction of indole (2) with oxalyl chloride gave virtually no product with 4-chloroindole. However, carrying out the reaction in refluxing ether solution for 15 hours yielded 4-chloro-3-indolyglyoxylchloride (II) in 73% yield. Treatment of a suspension of II in ether with dimethylamine for 6 hours gave 4-chloro-3-indolyl-N,N-dimethylglyoxamide (III) in 82% yield. Reduction of III with lithium aluminum hydride in refluxing tetrahydrofuran afforded the desired 4-chlorodimethylaminoethylindole (IV) in 97% yield. Treatment of IV with cuprous cyanide under a wide

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variety of conditions (3), however, failed to yield isolable amounts of 4-cyano-3-dimethylaminoethylindole.

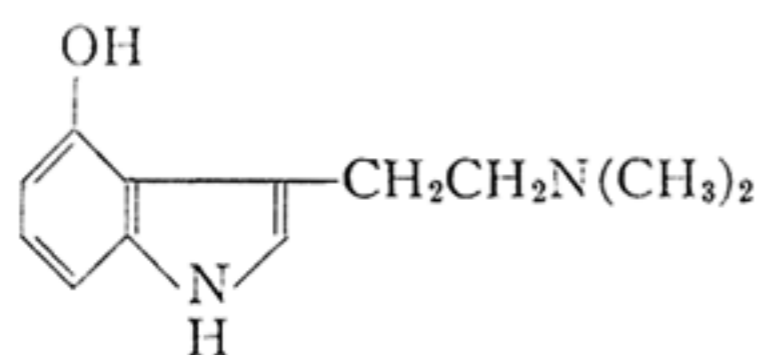
Attempts to utilize 4-bromoindole (4) in the same reaction sequence failed owing to its low reactivity toward oxalyl chloride; steric hindrance may be partly responsible since it was later found that 5-bromoindole reacts readily with oxalyl chloride.

Fischer cyclization (5) of γ -chlorobutyraldehyde gave a mixture of 3-chloroethyl-4-nitroindole (V) and 3-chloroethyl-6-nitroindole (VI). Isomer separation by column chromatography was clean, and isomer identification by n.m.r. was straightforward. Reaction of the separated 3-chloroethyl isomers with dimethylamine yielded 3-dimethylaminoethyl-4-nitroindole (VII) and 3-dimethylaminoethyl-6-nitroindole (VIII), and reaction with ammonium hydroxide yielded 3-aminoethyl-4-nitroindole (IX) and 3-aminoethyl-6-nitroindole (X).

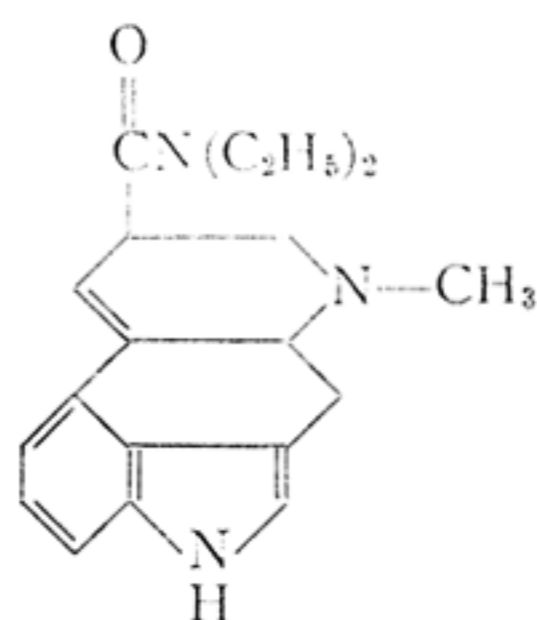
Model studies were carried out on the 3-nitrophenylhydrazone of butyraldehyde, closure of which yielded the readily separated isomers 3-ethyl-4-nitroindole (XI) and 3-ethyl-6-nitroindole (XII).

A brief investigation of the synthesis of γ -chlorobutyraldehyde disclosed that Rosenmund reduction (6) of commercially available γ -chlorobutyryl chloride with sulphur-quinoline poisoned palladium on barium sulphate (3) was the method of choice; the yield was 92%.

Reaction of 3-chloroethyl-4-nitroindole (V) with the sodium salt of β -alanine in aqueous ethanol for 12 days at room temperature gave 3- $[\beta$ -carboxyethylaminoethyl]-4-nitroindole (XIII), isolated as the hydrochloride. Similar treatment of 3-chloroethyl-6-nitroindole (VI) gave 3- $[\beta$ -carboxyethylaminoethyl]-6-nitroindole (XIV). Reaction of V with β -methylamino-*N,N*-diethylpropionamide (from methylamine and diethylacrylamide) gave 4-nitro-3- $[N$ -methyl-*N*-(*N',N'*-diethylcarboxamidoethyl)-aminoethyl]indole (XV), isolated as the picrate. Similar treatment of VI gave 6-nitro-3- $[N$ -methyl-*N*-(*N',N'*-diethylcarboxamidoethyl)-aminoethyl]indole (XVI), isolated as the hydrochloride. The side chain at the 3-position of compounds XIII, XIV, XV, and XVI was designed to resemble part of the molecule of LSD.



Psilocin



Lysergic acid diethylamide (LSD)

Reduction of the nitro group to an amino group with sodium dithionite was studied utilizing the readily prepared model compound (5), 3-ethyl-5-nitroindole. This method of reduction was successfully used for the preparation of 5-amino-3-ethylindole, 4-amino-3-dimethylaminoethylindole (XVII), 6-amino-3-dimethylaminoethylindole (XVIII), and 3-aminoethyl-6-aminoindole (XIX), but failed in the attempted preparation of 3-aminoethyl-4-aminoindole (XX). This latter compound was prepared in excellent yield by catalytic reduction of the corresponding nitro compound with platinum oxide at atmospheric pressure.

Several attempts to replace the diazotized amino group of the model compound, 5-amino-3-ethylindole, with a cyano or a mercapto group demonstrated the lack of utility of the amino compounds as intermediates.

EXPERIMENTAL

4-Chloro-3-indolyl-N,N-dimethylglyoxamide (III)

To a solution of 3.84 g (0.025 mole) of fractionally distilled 4-chloroindole (Aldrich, b.p. 144–145° at 10.5 mm, n_D^{22} 1.6272) in 20 ml ether (distilled from lithium aluminum hydride) stirred at room temperature under nitrogen was added 6.62 g (0.0521 mole) of oxalyl chloride in 30 ml dry ether. After addition, the mixture was refluxed for 15 hours. The yellow precipitate was filtered and washed with ether; it weighed 4.5 g (73%). This product was suspended in 60 ml ether, 6.5 g (0.144 mole) of anhydrous dimethylamine dissolved in 50 ml of ether was added, and the mixture was stirred for 6 hours. The ether and excess dimethylamine were removed under reduced pressure, and the residue was treated with water. This mixture was filtered and the precipitate was washed with water, then dried under reduced pressure at room temperature for 64 hours. It weighed 3.83 g (82%), m.p. 223.5–224.5° corr., $\lambda_{\max}^{\text{Nujol}}$ (μ) 3.25 (NH); 6.05 (C=O, keto); 6.20 (C=O, amide). Anal. Calc. for $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{O}_2$: C, 57.5; H, 4.42; Cl, 14.1; N, 11.2. Found: C, 57.8; H, 4.99; Cl, 13.9; N, 10.9.

4-Chloro-3-dimethylaminoethylindole (IV)

To a slurry of 13.00 g (0.344 mole) of LiAlH_4 in 150 ml of tetrahydrofuran (THF), freshly distilled from LiAlH_4 , was added a solution of 14.2 g (0.0568 mole) of 4-chloro-3-indolyl-N,N-dimethylglyoxamide (III) in 1 liter of dry tetrahydrofuran (THF). The mixture was refluxed for 3 hours, then cooled, and 110 ml of methyl alcohol – THF 1:1 mixture was added, followed by 30 ml of saturated sodium sulphate. The mixture was concentrated under reduced pressure almost to dryness, then dissolved in 200 ml of ether. This solution was extracted three times with 20-ml portions of 5% HCl solution, dried over anhydrous sodium sulphate, and evaporated to dryness under reduced pressure. The residue of nonbasic material weighed less than 0.4 g. The combined acid extracts were made basic with cold 50% sodium hydroxide and extracted with chloroform. The combined chloroform extracts were dried over sodium sulphate and evaporated to dryness under reduced pressure. The residue of crude basic product weighed 12.25 g (97%). Repeated recrystallization from cyclohexane afforded an analytical sample, m.p. 136.5–138° corr., $\lambda_{\max}^{\text{Nujol}}$ (μ) 3.30 (NH); absence of C=O bands at 6.06, 6.20. Anal. Calc. for $\text{C}_{12}\text{H}_{15}\text{ClN}_2$: C, 64.7; H, 6.79; N, 12.6; Cl, 15.9. Found: C, 64.7; H, 6.75; N, 12.6; Cl, 15.9.

3-Ethyl-4- and -6-nitroindoles (XI and XII)

A solution of 10 g (0.0484 mole) of *n*-butyraldehyde-3-nitrophenylhydrazone in 200 ml of concentrated hydrochloric acid and 200 ml of benzene was stirred for 3 hours at room temperature. The benzene was replaced with fresh benzene for another 3 hours. The combined benzene fractions were washed with water, dried over sodium sulphate, and chromatographed on acid-washed Merck alumina (3×25 cm).

The first major fraction from the column, an orange crystalline solid, m.p. 109.5–112°, was found to be the 3-ethyl-4-nitroindole by its n.m.r. spectrum.

The second major fraction, yellow needles, melting at 87–89°, was found to be the 6-isomer. The overall yields were about 0.55 g (6%) and 0.18 g (2%), respectively.

The infrared absorption spectra of the 4- and 6-nitro isomers were very similar. 3-Ethyl-4-nitroindole: $\lambda_{\max}^{\text{Nujol}}$ (μ) 2.95 (NH); 6.63, 7.60 (NO_2); 7.91, 8.86, 9.36, 10.2, 10.4, 12.1, 12.6, 13.8. 3-Ethyl-6-nitroindole: $\lambda_{\max}^{\text{Nujol}}$ (μ) 2.95 (NH); 6.63, 7.65 (NO_2); 8.15, 9.05, 9.40, 11.4, 11.9, 12.3, 12.7, 13.3, 13.7.

The n.m.r. spectra made possible assignment of structures to the two isomers. 3-Ethyl-4-nitroindole: CH_3 (triplet, 8.80 τ); CH_2 (quartet, 7.15 τ); 2 H and 6 H (2.78 τ); 7 H (2.36 τ); 5 H (doublet, 2.24 τ , additional meta coupling); 1 H (1.43 τ). 3-Ethyl-6-nitroindole: CH_3 (triplet, 8.65 τ); CH_2 (quartet, 7.23 τ); 2 H (2.63 τ); 4 H (doublet, 2.40 τ); 5 H (doublet, 1.98 τ , additional meta coupling); 7 H (doublet, 1.65 τ); 1 H (1.40 τ).

3-Ethyl-4-nitroindole: $\lambda_{\max}^{\text{EtOH}}$ 2400 Å, $\epsilon = 8650$; 3-ethyl-6-nitroindole: $\lambda_{\max}^{\text{EtOH}}$ 2525 Å, $\epsilon = 8930$; 2680 Å, $\epsilon = 8530$.

Anal. Calc. for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2$: C, 63.1; H, 5.31; N, 14.7. Found 4- NO_2 : C, 63.5; H, 5.57; N, 14.6. Found 6- NO_2 : C, 62.9; H, 5.20; N, 14.7.

γ -Chlorobutyraldehyde by Rosenmund Reduction

A mixture of 153 g (1.085 moles) of γ -chlorobutyryl chloride, 16 g palladium on barium sulphate catalyst, 1.66 ml of sulphur-quinoline poison (7), and 900 ml of toluene was refluxed and vigorously stirred while hydrogen was passed through; the effluent gas was bubbled through water. After 6.5 hours, the evolution of hydrogen chloride ceased. The mixture was filtered and the filtrate washed with water, sodium bicarbonate solution, and water. After drying over sodium sulphate, the toluene was removed by distillation under reduced pressure through a Vigreux column. The yield of crude product was 99.7 g (92%), b.p. 28–29° at 2.0 mm; 2,4-dinitrophenylhydrazone, m.p. 130–131°, lit. 130–131°.

γ -Chlorobutyraldehyde-3-nitrophenylhydrazone

A solution of 10 g (0.1 mole) of crude γ -chlorobutyraldehyde and 20 g (0.132 mole) of 3-nitrophenylhydrazine dissolved in a minimum amount of hot ethanol containing 10% of acetic acid was allowed to stand on the steam bath for 1 hour. The mixture was cooled, and water was added until a dark red oil started to separate out. Because attempts to crystallize this oil failed, the alcohol was evaporated *in vacuo*, the water was decanted off, and the crude oil used directly in the next step.

3-[β -Chloroethyl]-4- and -6-nitroindoles (V and VI)

A solution of 29 g of the crude 3-nitrophenylhydrazone of γ -chlorobutyraldehyde in 300 ml of concentrated hydrochloric acid and 200 ml of benzene was stirred rapidly for 3 hours. The benzene was replaced with fresh benzene, and stirring was continued for another 4 hours. The combined benzene fractions were washed with water, dried over anhydrous sodium sulphate, and evaporated *in vacuo* to about 35 ml. The solution was placed on a column of alumina (3 \times 25 cm) and eluted with benzene. The two major fractions were 3-[β -chloroethyl]-4-nitroindole, 1.89 g (7%), and 3-[β -chloroethyl]-6-nitroindole, 2.19 g (8%). Several recrystallizations from benzene - petroleum ether gave products which melted at 134-135°, golden yellow plates, in the case of the 4-nitro, and 108-110°, canary yellow needles, in the case of the 6-nitro compound.

The infrared absorption spectra of the two isomers were similar. 3-[β -Chloroethyl]-4-nitroindole: $\lambda_{\max}^{\text{Nujol}}$ (μ) 3.00 (NH); 6.60, 7.60 (NO₂); 8.95, 10.03, 10.2, 12.4, 12.6, 13.7. 3-[β -Chloroethyl]-6-nitroindole: $\lambda_{\max}^{\text{Nujol}}$ (μ) 2.90 (NH); 6.25 (aryl); 6.55, 7.45 (NO₂); 9.10, 9.45, 11.3, 13.3, 13.7, 14.0.

3-[β -Chloroethyl]-4-nitroindole: CH₂CH₂Cl (triplet, 6.62 τ); CH₂CH₂Cl (triplet, 6.25 τ); 2 H (2.80 τ); 6 H (2.63 τ); 7 H (doublet, 2.34 τ , *m*-coupled); 5 H (doublet, 2.09 τ , *m*-coupled); 1 H (1.40 τ). 3-[β -Chloroethyl]-6-nitroindole: CH₂CH₂Cl (triplet, 6.73 τ); CH₂CH₂Cl (triplet, 6.22 τ); 2 H (2.57 τ); 4 H (doublet, 2.39 τ); 5 H (doublet with additional *m*-coupling, *J* \sim 2 c.p.s., 1.97 τ); 7 H (doublet 1.62 τ); 1 H (1.22 τ).

3-[β -Chloroethyl]-4-nitroindole: $\lambda_{\max}^{\text{EtOH}}$ 2375 Å, $\epsilon = 7480$. 3-[β -Chloroethyl]-6-nitroindole: $\lambda_{\max}^{\text{EtOH}}$ 2525 Å, $\epsilon = 8290$; 2650 Å, $\epsilon = 7900$.

Anal. Calc. for C₁₀H₉ClN₂O₂: C, 53.5; H, 4.04; Cl, 15.8; N, 12.5. Found 4-NO₂: C, 53.3; H, 4.26; Cl, 15.5; N, 12.4. Found 6-NO₂: C, 53.5; H, 4.28; Cl, 15.9; N, 12.5.

3-Dimethylaminoethyl-4-nitroindole (VII)

A solution of 356.8 mg (1.59 mmoles) of 3-[β -chloroethyl]-4-nitroindole in 20 ml of alcohol and 20 ml of 34.3% aqueous dimethylamine was left at room temperature for 7 days. The alcohol was removed *in vacuo*, and the orange-yellow crystalline material was filtered; the crude yield was 300 mg (81%). The material was dissolved in dilute hydrochloric acid, filtered, and precipitated with dilute sodium hydroxide. Recrystallization from alcohol-water mixtures gave orange needles melting at 115-116°. Anal. Calc. for C₁₂H₁₅N₃O₂: C, 61.8; H, 6.48; N, 18.0. Found: C, 61.6; H, 6.39; N, 18.3.

3-Dimethylaminoethyl-6-nitroindole (VIII)

A solution of 485.7 mg (2.16 mmoles) of 3-[β -chloroethyl]-6-nitroindole in 20 ml of ethanol was treated with aqueous dimethylamine as in the case of the 4-isomer above. The crude yield was 423 mg (85%). The recrystallized product appeared as yellow plates melting at 171.5-172.5°. Anal. Calc. for C₁₂H₁₅N₃O₂: C, 61.8; H, 6.48; N, 18.0. Found: C, 61.2; H, 6.47; N, 17.8.

3-Aminoethyl-4-nitroindole (IX)

A solution of 1.0 g (4.46 mmoles) of 3-[β -chloroethyl]-4-nitroindole, 50 ml of concentrated NH₄OH, and 75 ml of ethyl alcohol was kept in a stoppered flask for 10 days. The alcohol was removed under reduced pressure, and the precipitate was filtered. The crude product was dissolved in hydrochloric acid and the solution filtered with Celite. After precipitation with dilute sodium hydroxide, the product was collected and recrystallized from ethanol-water; yield, 0.587 g (64.5%), m.p. 145-147°. Anal. Calc. for C₁₀H₁₁N₃O₂: C, 58.5; H, 5.40; N, 20.5. Found: C, 58.0; H, 5.61; N, 20.1.

3-Aminoethyl-6-nitroindole (X)

A solution of 2.0 g (8.92 mmoles) of 3-[β -chloroethyl]-6-nitroindole, 150 ml of concentrated ammonia, and 150 ml of ethyl alcohol was kept at room temperature for 9.5 days. The solvent was evaporated under reduced pressure, and the residue was dissolved in 10% hydrochloric acid. The acid solution was filtered with Celite, made basic, and the precipitated amine was filtered and recrystallized from ethyl acetate - petroleum ether (60-110°). Yield 1.37 g (71.5%). Another recrystallization yielded an analytical sample, m.p. 185-186° (decomp.). Anal. Calc. for C₁₀H₁₁N₃O₂: C, 58.5; H, 5.4; N, 20.5. Found: C, 58.5; H, 5.5; N, 20.4.

3-[β -Carboxyethylaminoethyl]-4-nitroindole Hydrochloride (XIII)

A solution of 1.0 g (4.46 mmoles) of 3-[β -chloroethyl]-4-nitroindole, 0.15 mole of β -alanine sodium salt in 75 ml of water, and 75 ml of ethyl alcohol was kept in a stoppered flask at room temperature for 12 days. The solvent was removed under reduced pressure and the residue triturated with benzene. The benzene-insoluble precipitate was dissolved in water, precipitated with HCl, and the crude product was collected and recrystallized from water; yield 3-[β -carboxyethylaminoethyl]-4-nitroindole, 0.20 g (28.6%), m.p. 210°. The hygroscopic orange product was dried *in vacuo* to constant weight. Anal. Calc. for C₁₃H₁₅ClN₃O₄: C, 49.8; H, 5.14; Cl, 11.3; N, 13.4. Found: C, 49.8; H, 5.35; Cl, 11.3; N, 13.5.

3-[β-Carboxyethylaminoethyl]-6-nitroindole Hydrochloride (XIV)

A solution of 374 mg (1.67 mmoles) of 3-[β-chloroethyl]-6-nitroindole in 25 ml of alcohol and a solution of 0.1 mole of β-alanine sodium salt in 25 ml of water were mixed and allowed to stand at room temperature for 10 days. Evaporation of the alcohol and addition of hydrochloric acid caused the precipitation of a green solid weighing 300 mg (57%). The infrared spectrum of this material shows a strong band at 5.80 μ. The light green hydrochloride was recrystallized from water four times, dried to constant weight, m.p. 220° (decomp.). Anal. Calc. for C₁₃H₁₆ClN₃O₄: C, 49.8; H, 5.14; Cl, 11.3; N, 13.4. Found: C, 49.6; H, 5.84; Cl, 11.2; N, 13.3.

β-Methylamino-N,N-diethylpropionamide

To a solution of 26 g (0.84 mole) of methylamine in 80 ml of absolute ethyl alcohol was added, with cooling, 25.5 g (0.20 mole) of diethylacrylamide. The solution was allowed to stand in a freezer (-15°) for 45 hours. The solvent and excess methylamine were removed under reduced pressure, and the residue was distilled. One fraction was collected, b.p. 76–80° at 0.6 mm, n_D^{20} 1.4617. This material was redistilled through a spinning band column; one fraction of b.p. 62–63° at 0.40 mm, weight 16.6 g, n_D^{23} 1.4609 was collected. The hydrochloride was precipitated from ether with anhydrous HCl; m.p. 84.5–86°. Anal. Calc. for C₈H₁₉ClN₂O: C, 49.3; H, 9.84; Cl, 18.2; N, 14.4. Found: C, 49.1; H, 9.74; Cl, 17.3; N, 13.9.

6-Nitro-3-[N-methyl-N-(N',N'-diethylcarboxamidoethyl)-aminoethyl]indole (XVI)

A solution of 0.5 g (2.23 mmoles) of 3-β-chloroethyl-6-nitroindole in 3.0 ml of β-methylamino-N,N-diethylpropionamide was allowed to stand at room temperature for 10 days. The solution was poured into water, and the insoluble oil was isolated by centrifugation. The oil was dissolved in dilute acid, filtered with Celite, the solution made basic, and the product extracted into chloroform. The solution was dried (MgSO₄), and the solvent was removed under reduced pressure. The residue crystallized on scratching. Yield 0.67 g (87%). An analytical sample was obtained by repeated recrystallization from benzene-petroleum ether mixture; m.p. 93–94°. Anal. Calc. for C₁₈H₂₆N₄O₃: C, 62.4; H, 7.56; N, 16.2. Found: C, 62.3; H, 7.46; N, 16.2.

4-Nitro-3-[N-methyl-N-(N',N'-diethylcarboxamidoethyl)-aminoethyl]indole (XV)

A solution of 0.290 g (1.29 moles) of 3-[β-chloroethyl]-4-nitroindole in 6 ml of β-methylamino-N,N-diethylpropionamide was allowed to stand at room temperature for 14 days. The solution was poured into water and the oil which formed was isolated by centrifugation. The oil was dissolved in dilute hydrochloric acid, filtered, the solution made basic, and the product extracted into chloroform. The chloroform extracts were dried over anhydrous magnesium sulphate, and the solvent was removed under reduced pressure. Because the residue (0.187 g, 58%) could not be crystallized, the picrate was made. An analytical sample of the picrate was obtained by recrystallization from ethyl acetate; m.p. 205–208°. Anal. Calc. for C₂₄H₂₉N₇O₁₀: C, 50.1; H, 5.08; N, 17.0. Found: C, 50.0; H, 4.98; N, 16.7.

6-Amino-3-dimethylaminoethylindole (XVIII)

To a solution of 1.0 g (4.3 mmoles) of 3-dimethylaminoethyl-6-nitroindole in 75 ml of alcohol and 20 ml of *N* sodium hydroxide at 50° was added a solution of 6 g of sodium dithionite in 30 ml of 0.2 *N* sodium hydroxide. The mixture was filtered hot and the filtrate evaporated to dryness. The residue was dissolved in 5% hydrochloric acid solution, filtered, and made basic with cold 30% sodium hydroxide. The basic solution was extracted with ether, and the light purple ether solution was evaporated to dryness. The purple solid residue weighed 0.66 g (75%), m.p. 93–96°. Two sublimations at 110° at 0.1 mm gave a white crystalline product; m.p. 98–99°. Anal. Calc. for C₁₂H₁₇N₃: C, 70.9; H, 8.43; N, 20.7. Found: C, 70.5; H, 8.95; N, 20.5.

4-Amino-3-dimethylaminoethylindole (XVII)

To a solution of 0.52 g (2.2 mmoles) of 3-dimethylaminoethyl-4-nitroindole in 35 ml of ethyl alcohol and 10 ml of *N* sodium hydroxide at 50° was added a solution of 3 g of sodium dithionite in 15 ml of 0.2 *N* sodium hydroxide. The mixture was filtered hot and the filtrate evaporated to dryness. The residue was dissolved in acid, filtered, made basic, and extracted into ether. The residue from evaporation of the ether weighed 0.21 g (47.5%), m.p. 129–131°, and sublimed at 125–130° at 0.1 mm. The sublimate weighed 0.182 g, m.p. 130.5–131.5°. Anal. Calc. for C₁₂H₁₇N₃: C, 70.9; H, 8.43; N, 20.7. Found: C, 71.4; H, 7.72; N, 20.8.

3-Aminoethyl-6-aminoindole (XIX)

A solution of 3.0 g of sodium dithionite in 15 ml of 0.5 *N* sodium hydroxide solution was added to a solution of 0.50 g of 3-aminoethyl-6-nitroindole in 35 ml ethyl alcohol and 10 ml *N* sodium hydroxide solution at 50° C. The mixture was then filtered hot, and the filtrate was evaporated to dryness, 0.27 g (63.5% yield). The viscous oil residue was sublimed at 130° at 0.1 mm. The noncrystalline sublimate was partially dissolved in ether and cooled in a dry ice-acetone bath. Crystallization was induced by scratching with a glass rod. The ether was removed under reduced pressure and the residue, m.p. 102–105°, was sublimed twice at 110–120° at 0.015 mm, m.p. 105.5–107.5°. Anal. Calc. for C₁₀H₁₃N₃: C, 68.5; H, 7.48; N, 24.0. Found: C, 68.0; H, 7.54; N, 24.0.

3-Aminoethyl-4-aminoindole (XX)

A mixture of 0.232 g (1.13 mmole) of 3-aminoethyl-4-nitroindole, 0.0165 g (0.07 mmole) of platinum oxide, and 25 ml of absolute ethanol was stirred in an atmospheric hydrogenation apparatus. The reaction ceased after 50 minutes at 95% completion. The solution was filtered and the filtrate evaporated to dryness under reduced pressure. The oily residue was crystallized by cooling an ether solution in a dry ice - acetone bath and scratching the flask wall with a glass rod. The ether was removed under reduced pressure. The light purple product (0.18 g, 90%, m.p. 106-113°) was sublimed twice (100° at 0.01 mm, m.p. 116°). Anal. Calc. for $C_{10}H_{13}N_3$: C, 68.5; H, 7.48; N, 24.0. Found: C, 68.2; H, 7.81; N, 24.1.

ACKNOWLEDGMENT

The authors wish to express their appreciation to the United States Army Chemical Center Research and Development Command for support of this research under contract RFP-147, DA 18-108-405-CML-839.

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