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Azasteroids II. Approaches to the 13-Azaequilenin System (1,2)

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The synthesis of *N*-[2-(1-naphthyl)ethyl]succinimide, *N*-[2-(1-naphthyl)ethyl]pyrrolidone and the corresponding 3,4-dihydro compounds is described. The pyrrolidones have been converted into 11,12,16,17-tetrahydro-13-azacyclopenta[a]phenanthrene and 6,7,11-12,16,17-hexahydro-13-azacyclopenta[a]phenanthrene. These two compounds were then converted to XIX and XXII. The former compound is a salt of (+) 3-desoxy-17-desoxo-13-azaequilenin.

As part of our program on the synthesis of azasteroids we were interested in preparing 13-azaequilenin and related compounds. Our initial approaches were concerned with the synthesis of a 3-desoxy-13-azaequilenin. In view of the fact that two syntheses of (±)-13-aza-18-norequilenin methyl ether have recently been reported (4,5) we wish to report the synthesis of our closely related 13-aza systems.

N-[2-(1-Naphthyl)ethyl]succinimide (I) was prepared by two methods. Reaction of 1-naphthaldehyde and nitromethane gave 2-(1-naphthyl)-1-nitroethylene (II) in 93.5% yield. Catalytic reduction of II employing ethanol as the solvent and platinum oxide as the catalyst led to the formation of 2-(1-naphthyl)-ethylamine (III) in 42.8% yield. III was also prepared in 20-40% yield by lithium aluminum hydride reduction of 1-naphthylacetonitrile. Heating III in an excess of diethyl succinate gave the amide IV which was converted without further purification to I by refluxing the crude amide in toluene in the presence of *p*-toluenesulfonic acid.

The second method of preparation involved allowing the Grignard reagent prepared from 1-bromonaphthalene to react with ethylene oxide to give 2-(1-naphthyl)ethanol (V) in 62% yield. The alcohol V also was prepared in 30.8% yield by lithium aluminum hydride reduction of ethyl 1-naphthylacetate (VI). The ester VI was prepared from 1-naphthylacetonitrile in 77% yield by solvolysis of the nitrile in absolute ethanol saturated with dry hydrogen chloride gas. The alcohol V was converted to the *p*-toluenesulfonate VII in 98.9% yield. The *N*-substituted succinimide I was obtained in 68% yield by refluxing the *p*-toluenesulfonate VII with the potassium salt of succinimide in absolute methanol.

N-[2-(1-Naphthyl)ethyl]pyrrolidone (VIII) also was prepared by two methods. The first method involved heating 2-(1-naphthyl)ethylamine (III) in an excess of ethyl 4-bromobutyrate to give the amide IX. After washing the crude amide IX thoroughly with ether and drying *in vacuo*, it was added to a slurry of sodium hydride in benzene and refluxed for twenty hours. A 40% yield of VIII was obtained by this method.

The second method of preparation involved the reaction of the *p*-toluenesulfonate VII with the sodium salt of pyrrolidone in refluxing toluene. This method gave a 53% yield of the desired compound.

The dihydro compounds X and XI were prepared by a sequence of reactions employing 1-tetralone as the starting material. Subjecting 1-tetralone to the conditions of the Reformatsky reaction led to the formation of methyl 3,4-dihydro-1-naphthylacetate (XII) in 77.6% yield. Lithium aluminum hydride reduction of XII gave 2-(3,4-dihydro-1-naphthyl)ethanol (XIII) in 85% yield. The alcohol, XIII, was converted to the *p*-toluenesulfonate XIV in 85% yield.

The *N*-substituted succinimide X was prepared in 74% yield by refluxing the *p*-toluenesulfonate XIV with the potassium salt of succinimide in methanol.

The *N*-substituted pyrrolidone XI was prepared in 59% yield by refluxing the *p*-toluenesulfonate XIV with the sodium salt of pyrrolidone in anhydrous toluene.

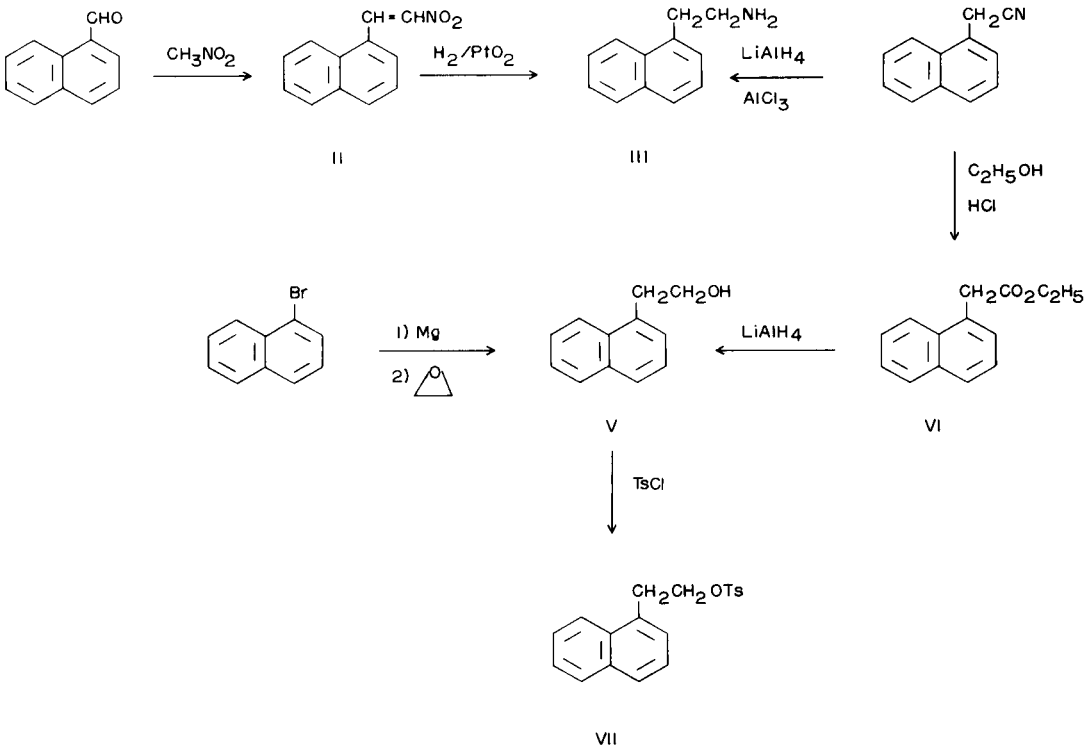
Cyclization of *N*-[2-(1-naphthyl)ethyl]succinimide (I) was attempted employing a number of cyclizing agents. Hydrofluric acid, phosphorus oxychloride in refluxing xylene, phosphorus pentoxide in refluxing xylene, or a mixture of phosphorus pentoxide in phosphoric acid at 145° or 170° had no effect on the *N*-substituted succinimide I. Employing more drastic conditions such as phosphorus pentoxide in boiling tetralin, or commercial polyphosphoric acid at 175-180° resulted in the isolation of a trace amount of solid melting over a wide range. Attempts to purify this solid by recrystallization or chromatography on alumina (elution with benzene) failed. Similar results were obtained when the cyclization of *N*-[2-(3,4-dihydro-1-naphthyl)ethyl]succinimide (X) was attempted employing commercial polyphosphoric acid at 175-180°. S. V. Kessar and co-workers (5) report similar results when the cyclization of *N*-[2-(6-methoxy-1-napthyl)ethyl]succinimide (XV) was attempted, employing polyphosphoric acid at 135-145°. However, Birch and Rao (4) report that XVI was obtained as a gum when the cyclization of XV was carried out employing phosphorus pentoxide in phosphoric acid at 145°.

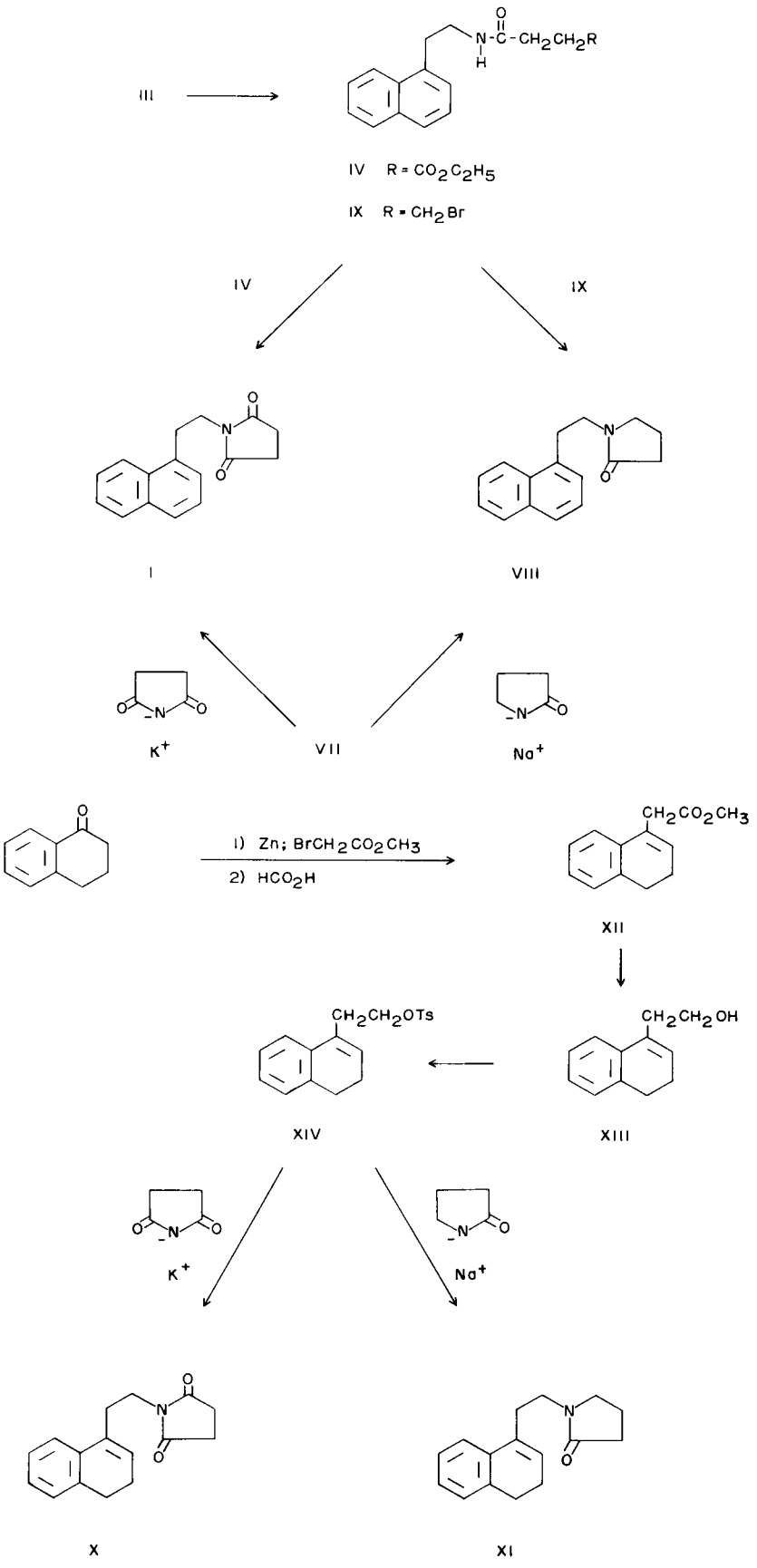
Cyclization of VIII proceeded smoothly when phosphorus pentoxide in boiling tetralin was used, giving a 58% yield of XVII as a light yellow solid. The enamine XVII proved to be unstable, but it could be stored for long periods of time as the perchlorate salt. The infrared spectrum (KBr pellet) of the perchlorate salt contained peaks at 1670, 1618, 1600 and 1570 cm^{-1}. The perchlorate salt of XVII could be reduced catalytically, using ethanol as the solvent and platinum oxide as the catalyst, or with sodium borohydride, using methanol as the solvent to give 11,12,13,14,15,16-hexahydro-13-azacyclopenta[a]-phenanthrene (XVIII). This compound was characterized both as the picrate and the perchlorate. Disappearance of the peaks at 1670, 1618 and 1570 cm^{-1} in the infrared spectrum of the perchlorate of XVIII confirmed the reduction of the C-14,15 double bond. A sample of XVIII was refluxed with methyl iodide in methanol to give the *N*-methyl compound XIX which was characterized as the picrate. This compound can be considered as the picrate of (±) 3-desoxy-17-desoxo-13-azaequilenin.

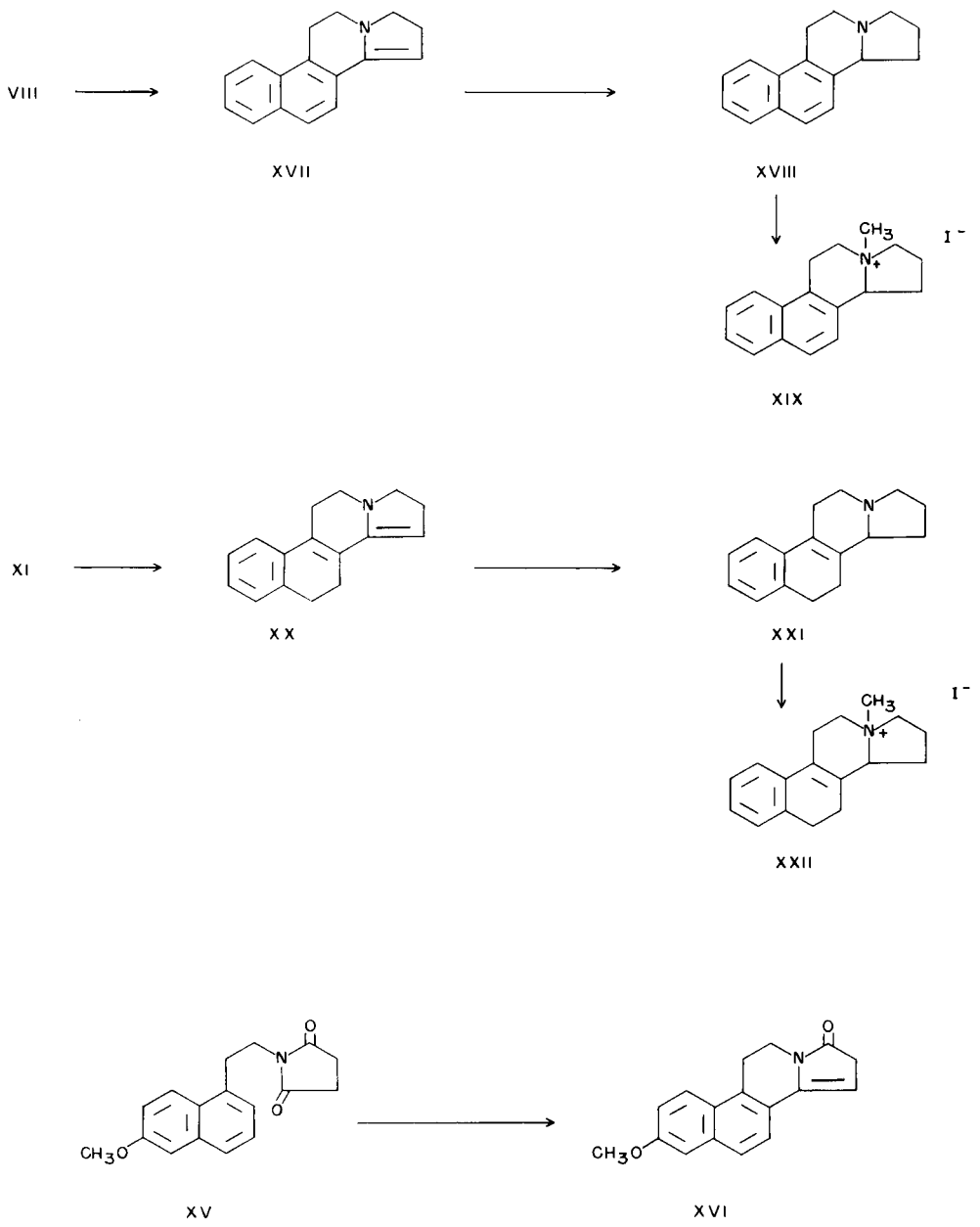
Cyclization of XI also proceeded smoothly when phosphorus pentoxide in boiling tetralin was employed. The crude produce XX proved to be an oil which could be isolated as the perchlorate salt in 69.3% yield. The infrared spectrum (KBr pellet) of the perchlorate of XX contained peaks at 1650, 1598 and 1550 cm^{-1}. Sodium borohydride reduction of XX, employing methanol as the solvent, gave a 99% yield of the octahydro compound XXI, which was characterized as the picrate and the perchlorate salt.

That only one double bond has been reduced on sodium borohydride reduction of the perchlorate of XX was shown by the catalytic reduction of this salt. When the catalytic reduction of the perchlorate of XX was carried out employing ethanol as solvent and platinum oxide as catalyst, the uptake of hydrogen ceased after the absorption of one mole of hydrogen. The crude perchlorate salt obtained was treated with sodium hydroxide to liberate the free base. A small amount of the free base was converted to the picrate, which proved to be identical in all respects to the picrate of the material obtained on the sodium borohydride reduction of the perchlorate of XX. An examination of the ultraviolet spectra of XII, XIII, XIV, X, and XXI confirms the presence of the double bond in XXI. All of these compounds have very similar ultraviolet spectra and all have a typical styrene type absorption at 265-272 mμ (ϵ = 8,000-10,000). Further evidence that only one double bond had been reduced was obtained from the infrared spectrum of the perchlorate salt of the reduced compound XXI. The infrared spectrum (KBr pellet) contained peaks at 1625 and 1580 cm^{-1}, which would indicate a carbon-carbon double bond conjugated with an aromatic ring. A further examination of the infrared spectrum of XXI indicated the presence of two sharp bands on the low frequency side of the major C-H absorption. These bands (2770 and 2830 cm^{-1}) have been correlated with the presence of at least two α-hydrogens *trans*-diaxial to the unshared pair on the bridgehead nitrogen (6).

The *N*-methyl compound XXII was obtained in 92.5% yield by refluxing a sample of XXI with methyl iodide in methanol. The *N*-methyl compound XXII was characterized as the picrate and perchlorate salt.




III
IV R = $CO_2C_2H_5$
IX R = CH_2Br
IV
IX
I
VIII
VII
K^+
Na^+
1) Zn; $BrCH_2CO_2CH_3$
2) HCO_2H
$CH_2CO_2CH_3$
XII
CH_2CH_2OH
XIII
CH_2CH_2OTs
XIV
K^+
Na^+
X
XI



EXPERIMENTAL (7)

2-(1-Naphthyl)-1-nitroethylene (II).

A mixture of 13.6 ml. (0.1 mole) of 1-napthaldehyde was refluxed with 8 ml. of nitromethane in 50 ml. of acetic acid containing 6.4 g. of ammonium acetate. After 2 hours, the mixture was cooled and poured on 100 ml. of water and ice. The oil that separated soon solidified. The solid was collected, washed with water and dried to give 18.6 g. (93.5%) of the crude product, m.p. 83.5-86°; reported (8) m.p. 87.5°.

2-(1-Naphthyl)ethylamine (III).

Method (a).

A mixture of 1.14 g. (0.0057 mole) of 2-(1-naphthyl)-1-nitroethylene in 50 ml. of ethanol containing 10 ml. of concentrated hydrochloric acid was shaken under 3 to 4 atmospheres of hydrogen in the presence of 0.2 g. of platinum oxide. After the uptake of hydrogen had stopped, the solution was filtered and concentrated, yielding 0.51 g. (42.8%) of the crude hydrochloride, m.p. 240°; reported (8) m.p. 243-8°. A sample of the free base was distilled, b.p. 152°/1.9 mm.

Method (b).

A mixture of 9.04 g. (0.054 mole) of 1-napthylacetonitrile in 250 ml. of anhydrous ether was added slowly to a mixture of 6.8 g. of aluminum chloride and 1.93 g. of lithium aluminum hydride in 200 ml. ether. After the addition was complete, the mixture was refluxed 2 hours and then cooled. The excess reducing agent was destroyed by the addition of water dropwise to the reaction mixture. The ether solution was washed thoroughly with dilute hydrochloric acid. The acid washings were made alkaline with sodium carbonate and were extracted with ether. The ether extracts were carefully dried over anhydrous sodium sulfate. Dry hydrogen chloride gas was passed through the ether solution which was cooled in an ice bath. The oil that separated soon solidified. Yields of the hydrochloride ranging from 20 to 40% could be obtained using this method. Omission of the aluminum chloride lowered the yield considerably.

Ethyl 1-naphthylacetate (VI).

A solution of 32.1 g. (0.192 mole) of 1-naphthylacetonitrile in ethanol saturated with dry hydrogen chloride was refluxed overnight. The reaction mixture was concentrated, the salts filtered and the filtrate dissolved in ether. The ether solution was thoroughly dried over anhydrous sodium sulfate and then concentrated. The residue was distilled, b.p. 133-140°/0.58 mm., giving 31.55 g. (77%) of the ester; reported (9) b.p. 176-178°/11 mm.

2-(1-Naphthyl)ethanol (V).

Method (a).

A solution of 31.55 g. (0.148 mole) of ethyl 1-naphthylacetate in 50 ml. of anhydrous ether was added to a slurry of 10 g. of lithium aluminum hydride in 100 ml. of anhydrous ether. The solution turned bright green on the addition of the ester and gradually became brown.

The mixture was refluxed one-half hour after the addition was complete and then cooled. The excess reducing agent was destroyed by the addition of ethyl acetate and subsequently by water. The solution was acidified with dilute hydrochloric acid and the ether layer separated. The aqueous layer was extracted with ether, the ether layers combined, washed, dried over anhydrous sodium sulfate and concentrated. The residue was distilled under reduced pressure to give 7.82 g. (30.8%) of the desired product, b.p. 137-142°/0.63 mm.; reported (10) b.p. 148°/1.5 mm.

Method (b).

To an ice cold solution of the Grignard reagent prepared from 50 g. (0.241 mole) of 1-bromonaphthalene and 6 g. of magnesium turnings in anhydrous ether, was added 12.5 g. (0.285 mole) of ethylene oxide in 50 ml. of anhydrous ether. After stirring two hours at 0°, 1 hour at room temperature and refluxing 3 hours, a mixture of ice and concentrated hydrochloric acid was cautiously added. The ether layer was separated and the aqueous layer extracted with ether. The ether layers were combined, washed with dilute hydrochloric acid, dried over anhydrous sodium sulfate and concentrated. The residue was distilled *in vacuo* to give 25.8 g. (62%) of the desired product, b.p. 140-50°/0.8 mm.

2-(1-Naphthyl)ethyl *p*-toluenesulfonate (VII).

A mixture of 25.8 g. (0.15 mole) of 2-(1-naphthyl)ethanol and 38.1 g. (0.2 mole) of *p*-toluenesulfonyl chloride in 100 ml. chloroform was stirred in an ice bath. Pyridine (50 ml.) was added slowly, keeping the temperature below 20°. After stirring an additional 3 hours in an ice bath, water was added and the chloroform layer separated. The aqueous layer was washed with chloroform, the chloroform solutions were combined and washed with dilute hydrochloric acid, water, and then dried and concentrated. The gummy residue obtained was stirred overnight in ice water, during which time it solidified. The solid was filtered, dried, and recrystallized from methanol to give 48.3 g. (98.9% yield) m.p. 55.5-58°.

Anal. Calcd. for $C_{19}H_{18}O_3S$: C, 69.91; H, 5.56; S, 9.82. Found: C, 69.66; H, 5.63; S, 9.94.

N-[2-(1-Naphthyl)ethyl]succinimide (I).

Method (a).

A mixture of 2-(1-naphthyl)ethylamine [from 9.55 g. (0.038 mole) of the hydrobromide salt] and 47 g. (0.27 mole) of diethyl succinate was heated at 150-160° for 19 hours under a nitrogen atmosphere. The excess diethyl succinate was removed by distillation under reduced pressure to leave a thick gum which was dissolved in 70 ml. of dry xylene (containing a catalytic amount of *p*-toluenesulfonic acid) and refluxed for 19 hours. The solution was concentrated and the clear oil obtained was treated with a hot *n*-hexane-benzene solution. The *n*-hexane-benzene layer was decanted and cooled to give 0.4 g. of a white solid. Repeated treatments gave a total of 1.4 g. (14.5%) (based on 2-(1-naphthyl)ethylamine hydrobromide) of a white solid, m.p. 88-90° from *n*-hexane-benzene.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.95; H, 5.93; N, 5.46.

Method (b).

A mixture of 6.52 g. (0.02 mole) of 2-(1-naphthyl)ethanol *p*-toluenesulfonate and 3.96 g. (0.04 mole) of succinimide was refluxed in 100 ml. of methanol containing 0.04 mole of potassium methoxide (from 1.56 g. of potassium) for 42 hours. On cooling, potassium *p*-toluenesulfonate precipitated. The salt was filtered and the filtrate concentrated to give 3.46 g. (68%) of the desired product.

N-[2-(1-Naphthyl)ethyl]pyrrolidone (VIII).

Method (a).

A mixture of 3.84 g. (0.0224 mole) of 2-(1-naphthyl)ethylamine and 3.38 g. (0.0224 mole) of ethyl 4-bromobutyrate was heated at 130-140° for 4 hours. The mixture was cooled, washed with ether and the gummy white solid dried under reduced pressure. The gum was taken up in benzene and 1.79 g. (0.0224 mole) of sodium hydride (30% mineral oil dispersion) was added and the mixture refluxed for 20 hours in an oil bath. The mixture was cooled, water was added and the benzene layer separated. The aqueous portion was extracted with benzene, the benzene solutions were combined, dried over anhydrous sodium sulfate, and concentrated to give an oil. The oil was distilled, b.p. 158-190°/0.2 mm. The distillate solidified to a solid, m.p. 73-75°, obtained in 40% yield.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.29; H, 7.16; N, 5.85. Found: C, 80.06; H, 7.26; N, 5.86.

Method (b).

A solution of 2.13 g. (0.025 mole) of freshly distilled pyrrolidone in 5 ml. of toluene was added to a refluxing and stirred mixture of 0.58 g. (0.025 mole) of sodium in 30 ml. of toluene. The thick solution was stirred and refluxed an additional one-half hour, then 6.53 g. (0.02 mole) of 2-(1-naphthyl)ethanol *p*-toluenesulfonate was added, and the mixture was refluxed and stirred for 30 hours. Water was added on cooling, the organic layer separated and the aqueous portion was extracted with benzene. The organic layers were combined, dried over anhydrous sodium sulfate and concentrated. A 53% crude yield of the desired product was obtained.

Methyl 3,4-dihydro-1-naphthylacetate (XII).

A mixture of 12.8 g. (0.0875 mole) of 1-tetralone and 10.4 ml. of methyl bromoacetate was added to 30 g. of zinc shot in a solution consisting of 100 ml. each of anhydrous ether and benzene. A small crystal of iodine was added to initiate the reaction, and the solution brought to reflux. After 2 hours, the reaction mixture was poured into ice water. The solution was acidified with glacial acetic acid and extracted with benzene. The benzene extracts were washed with dilute ammonium hydroxide, water, and then dried over anhydrous sodium sulfate and concentrated. The residue was heated on a steam bath for 0.5 hour with 40 ml. of 90% formic acid. The formic acid was removed by a stream of air and the residue was distilled, b.p. 101-108°/0.17 mm., to give 13.72 g. (77.6%) of the desired product. A sample was distilled for analysis, b.p. 96.5-97°/0.04 mm.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.18; H, 6.94.

2-(3,4-Dihydro-1-naphthyl)ethanol (XIII).

A solution of 13.72 g. (0.068 mole) of methyl 3,4-dihydro-1-naphthylacetate in 24 ml. of anhydrous ether was added to a slurry of 2.62 g. (0.069 mole) of lithium aluminum hydride in 50 ml. of ether. After the addition was complete, the mixture was refluxed for 1 hour. The excess reducing agent was decomposed by the cautious addition of water. The solid was filtered and washed well with ether. The aqueous portion was extracted with ether, the ether solutions were combined, dried over anhydrous sodium sulfate, and concentrated, and the residue distilled to give 10.10 g. (85%) of material, b.p. 125-128°/0.78 mm. A sample was distilled for analysis, b.p. 98.5°/0.03 mm.

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.66; H, 8.11.

2-(3,4-Dihydro-1-naphthyl)ethyl *p*-toluenesulfonate (XIV).

A mixture of 27.60 g. (0.159 mole) of 2-(3,4-dihydro-1-naphthyl)-ethanol and 30.40 g. (0.159 mole) of *p*-toluenesulfonyl chloride was dissolved in 50 ml. of anhydrous chloroform, and the mixture was stirred in an ice bath. Pyridine (50 ml.) was added, keeping the temperature below 20°. After the addition was complete, the mixture was stirred an additional 3 hours while cooled in an ice bath. The reaction mixture was diluted with ice and concentrated hydrochloric acid. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and concentrated. The oil obtained soon solidified (after standing in the ice box) to give 44.37 g. (85%) of the desired product, m.p. 51.5-53° from methanol.

Anal. Calcd. for $C_{19}H_{20}O_3S$: C, 69.48; H, 6.14; S, 9.76. Found: C, 69.50; H, 6.24; S, 9.92.

N-[2-(3,4-Dihydro-1-naphthyl)ethyl]succinimide (X).

A solution of 6.57 g. (0.02 mole) of 2-(3,4-dihydro-1-naphthyl)-ethyl *p*-toluenesulfonate in 5 ml. of methanol was added to a refluxing solution of 0.021 mole of the potassium salt of succinimide [obtained from 0.82 g. (0.021 mole) of potassium and 2.08 g. (0.021 mole) of succinimide] in methanol. After refluxing for 42 hours, the mixture was cooled and the potassium *p*-toluenesulfonate that separated was filtered. The filtrate was concentrated giving 3.77 g. (74%) of the desired product, m.p. 88-89° from *n*-hexane-benzene.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.06; H, 6.64; N, 5.48.

N-[2-(3,4-Dihydro-1-napthyl)ethyl]pyrrolidone (XI).

A solution of 9.80 g. (0.0299 mole) of 2-(3,4-dihydro-1-naphthyl)-ethyl *p*-toluenesulfonate in 5 ml. of toluene was added to a refluxing solution of 0.03 mole of the sodium salt of pyrrolidone [from 0.69 g. (0.03 mole) of sodium and 2.55 g. (0.03 mole) of pyrrolidone] in toluene. After refluxing for 42 hours, the mixture was cooled and water added. The aqueous portion was separated and extracted

thoroughly with benzene. The benzene and toluene solutions were combined, washed with water, dried over anhydrous sodium sulfate, and concentrated. The residue was distilled, b.p. 174-178°/0.15 mm., giving 4.27 g. (59%) of a light yellow oil. A sample was distilled for analysis, b.p. 166°/0.10 mm.

Anal. Calcd. for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.81. Found: C, 79.43; H, 7.82; N, 5.58.

11,12,16,17-Tetrahydro-13-azacyclopenta[a]phenanthrene (XVII).

A solution of 2.93 g. (0.0123 mole) of *N*-[2-(1-naphthyl)ethyl]pyrrolidone in 5 ml. of tetralin was added to a refluxing mixture of 6.1 g. of phosphorus pentoxide in 30 ml. of tetralin. After refluxing one-hour, an additional 10.2 g. of phosphorus pentoxide was added and the mixture was refluxed for 45 minutes. The mixture was cooled, the tetralin removed by decantation, and the solid decomposed by the addition of ice. The resulting aqueous solution was washed with ether, made alkaline with 10% potassium hydroxide, and the oil that separated was extracted with ether. The ether was dried and concentrated to give 1.57 g. (58%) of an unstalbe white solid. From *n*-hexane, m.p. 110-112° (sintered at 98°).

Anal. Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 87.17; H, 6.73; N, 6.11.

The perchlorate was prepared by dissolving a small sample in concentrated perchloric acid and diluting with water. A portion was recrystallized from ethanol, m.p. 187-188.5°.

Anal. Calcd. for $C_{16}H_{16}ClNO_4$: C, 59.72; H, 5.01; N, 4.35; Cl, 11.20. Found: C, 59.59; H, 5.04; N, 4.37; Cl, 11.01.

11,12,13,14,15,16-Hexahydro-13-azacyclopenta[a]phenanthrene (XVIII).

Method (a).

To a stirred suspension of 1.23 g. (0.0038 mole) of 11,12,15,16-tetrahydro-13-azacyclopenta[a]phenanthrene perchlorate in 40 ml. of anhydrous methanol was added 4.0 g. of sodium borohydride over a 10 minute period. After the addition was complete, the mixture was refluxed for 1 hour, then poured into a mixture of 100 g. of crushed ice and 20 ml. of 50% (by weight) sodium hydroxide solution. The aqueous alkaline solution was extracted thoroughly with ether. The ether extracts were combined and washed with water, dried over anhydrous sodium sulfate and concentrated to give 0.70 g. (82%) of the desired product as a low melting solid. The perchlorate was prepared by dissolving a small sample of the amine in concentrated perchloric acid and diluting with water. A portion was recrystallized from ethanol, m.p. 146.5-149.5°.

Anal. Calcd. for $C_{16}H_{18}ClNO_4$: C, 59.35; H, 5.60; N, 4.33; Cl, 10.95. Found: C, 59.48; H, 5.59; N, 4.24; Cl, 10.78.

The picrate was prepared by adding a few drops of a concentrated solution of picric acid in ethanol to a solution of the amine in ethanol. A portion was recrystallized from ethanol, m.p. 183-185°.

Anal. Calcd. for $C_{22}H_{20}N_4O_7$: C, 58.40; H, 4.46; N, 12.39. Found: C, 58.12; H, 4.53; N, 12.12.

Method (b).

A solution of 1.35 g. (0.0042 mole) of 11,12,15,16-tetrahydro-13-azacyclopenta[a]phenanthrene perchlorate in 30 ml. of ethanol was shaken under 3 to 4 atmospheres of hydrogen in the presence of 0.10 g. of platinum oxide. After 2 hours, the catalyst was filtered and the filtrate was concentrated to give 1.07 g. (79%) of the desired product as its perchlorate, m.p. 145-146°.

11,12,13,14,15,16-Hexahydro-13-azacyclopenta[a]phenanthrene methiodide (XIX).

A solution of 0.70 g. (0.00314 mole) of 11,12,13,14,15,16-hexahydro-13-azacyclopenta[a]phenanthrene in 10 ml. of methanol containing 5 ml. of methyl iodide was refluxed for 5 hours. The solution was cooled and poured into 50 ml. of ether. The oil that separated soon solidified. The solid was filtered, washed with ether and dried to give 0.97 g. (84.5%) of the desired product. The picrate was prepared by adding a few drops of a concentrated solution of picric acid in ethanol to a solution of the methiodide in ethanol. A portion was recrystallized from ethanol, m.p. 145-147°.

Anal. Calcd. for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75; N, 12.01. Found: C, 58.97; H, 4.95; N, 11.83.

6,7,11,12,16,17-Hexahydro-13-azacyclopenta[a]phenanthrene (XX).

A solution of 6.85 g. (0.028 mole) of *N*-[2-(3,4-dihydro-1-naphthyl)-ethyl]pyrrolidone in 15 ml. of tetralin was added to a refluxing solution of 13.0 g. of phosphorus pentoxide in 70 ml. of tetralin. After refluxing for 0.5 hour, an additional 25 g. of phosphorus pentoxide was added, and the mixture was refluxed for 45 minutes. The mixture was cooled, the tetralin removed by decantation, and the solid decomposed by the addition of ice. The aqueous solution was washed with ether, made alkaline with 10% potassium hydroxide and the basic solution extracted thoroughly with ether. The ether extracts were dried over anhydrous sodium sulfate and concentrated to a volume of 100 ml. Concentrated perchloric acid was added, and the precipitate that separated was filtered, washed with ether and dried to give 6.36 g. (69.3%) of the desired product as its perchlorate. A small portion was recrystallized from ethanol, m.p. 150-152°.

Anal. Calcd. for $C_{16}H_{18}ClNO_4$: C, 59.35; H, 5.60; N, 4.33; Cl, 10.95. Found: C, 59.44; H, 5.48; N, 4.42; Cl, 11.04.

6,7,11,12,13,14,15,16-Octahydro-13-azacyclopenta[a]phenanthrene (XXI).

To a stirred suspension of 1.29 g. (0.0040 mole) of 6,7,11,12,15,16-hexahydro-13-azacyclopenta[a]phenanthrene perchlorate in 40 ml. of anhydrous methanol was added 4.0 g. of sodium borohydride over a 10 minute period. After the addition was complete, the mixture was refluxed for 1 hour, then poured into a mixture of 100 g. of crushed ice and 20 ml. of 50% (by weight) sodium hydroxide solution. The aqueous alkaline solution was extracted thoroughly with ether. The ether extracts were combined, washed with water, dried over anhydrous sodium sulfate, and concentrated to give 0.90 g. (99%) of the desired product as an oil. The picrate was prepared by adding a few drops of a concentrated solution of picric acid in ethanol to a solution of the amide in ethanol. A portion was recrystallized from ethanol, m.p. 178-179°.

Anal. Calcd. for $C_{22}H_{22}N_4O_7$: C, 58.14; H, 4.88; N, 12.33. Found: C, 57.99; H, 4.80; N, 12.19.

The perchlorate was prepared by adding a few drops of concentrated perchloric acid to a solution of the crude amine. A portion was recrystallized from ethanol, m.p. 187-188°.

Anal. Calcd. for $C_{16}H_{20}ClNO_4$: C, 58.98; H, 6.19; N, 4.30; Cl, 10.88. Found: C, 58.95; H, 6.51; N, 4.33; Cl, 10.72.

6,7,11,12,13,14,15,16-Octahydro-13-azacyclopenta[a]phenanthrene methiodide (XXII).

A solution of 0.90 g. (0.0033 mole) of 6,7,11,12,13,14,15,16-octahydro-13-azacyclopenta[a]phenanthrene in 10 ml. of methanol containing 5 ml. of methyl iodide was refluxed for 5 hours. The solution was cooled and poured into 50 ml. of ether. The solid that separated was filtered, washed with ether and dried to give 1.11 g. (92.5%) of the desired product. The picrate was prepared by adding a few drops of a concentrated solution of picric acid in ethanol to a solution of the methiodide in ethanol. A portion was recrystallized from ethanol, m.p. 179-180°.

Anal. Calcd. for $C_{23}H_{24}N_4O_7$: C, 58.97; H, 5.16; N, 11.96. Found: C, 58.97; H, 5.10; N, 11.84.

The perchlorate was prepared by adding a few drops of concentrated perchloric acid to a solution of the crude methiodide in water. A portion was recrystallized from ethanol, m.p. 157-159°.

Anal. Calcd. for $C_{17}H_{22}ClNO_4$: C, 60.08; H, 6.53; N, 4.12; Cl, 10.43. Found: C, 60.12; H, 6.28; N, 4.20; Cl, 10.49.

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