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Synthesis of Aminohydrophenanthrene Analogs of Morphine[1]

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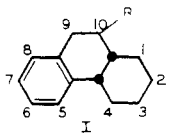
A group of 10-aminohydrophenanthrenes and 10-dimethylaminomethylhydrophenanthrenes, structural analogs of morphine, has been synthesized. The steric relations of the substituent groups on these new aminohydrophenanthrenes has been discussed. A stereoselective Mannich reaction is reported and an unusual epimerization of a benzylic alcohol is presented.

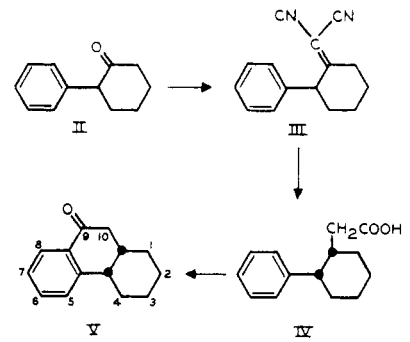
The purpose of the present work was to investigate the hitherto unknown aminohydrophenanthrenes of type I in which R represents an amino group or an aminomethyl group.



I

These phenanthrenes are of interest not only because they retain a large fragment of the morphine molecule but also because they reproduce many of the steric aspects of the natural alkaloid, *i.e.*, in the disposition of the aromatic ring, in the mode of fusion of the alicyclic rings, and in the location of the nitrogen of these substances so that it is close to or identical with that of morphine.

The 10-aminomethyl series. *cis*-1,2,3,4,4a,10a-Hexahydro-9(10H) phenanthrone (V) which had been synthesized by Cook *et al.*[2] appeared to be a highly suitable intermediate for the desired compounds since the carbonyl at position 9 would facilitate modifications at position 10. The stereochemistry of this substance had been corroborated[3,4] by oxidation and nitration to a known diphenic acid derivative. For the preparation of ketone V, 2-phenylcyclohexanone (II) was condensed with malononitrile, a practically quantitative yield of 2-phenylcyclohexylidenemalononitrile (III) being obtained. This unsaturated dinitrile was catalytically reduced, then hydrolyzed, and decarboxylated.



II III IV V

In this way it became possible to secure a 60% yield of the *cis*-acid (IV), which is a marked improvement in yield over the best previously reported procedure (36%[5]). That this reaction sequence led to a satisfactory yield whereas a similar sequence using ethyl cyanoacetate in place of malononitrile gave a low but not specified yield[5] results no doubt from the lower steric requirements of malononitrile for the condensation with 2-phenylcyclohexanone.

Cyclization of the *cis*-acid (IV) to the phenanthrone (V) by heating in sulfuric acid[2] was straightforward. With the phenanthrone (V) at hand, attempts were made to carry out a Mannich reaction. This, under the common reaction conditions of refluxing the components in a solvent[6] failed. Conditions were found (stirring, without solvent, in a 70° bath, under a slow stream of nitrogen) that led to a successful synthesis. In this way it was possible to secure a reproducible 47% yield of the amino ketone (VI). Just as VI was difficult to prepare, so it appeared readily hydrolyzed for it could not be recovered after a relatively short exposure to mineral acid. Although two diastereoisomers of

(1) Abstracted from the Ph.D. thesis of James G. Murphy.

(2) J. W. Cook, C. L. Hewett, and C. A. Lawrence, *J. Chem. Soc.*, 71 (1936).

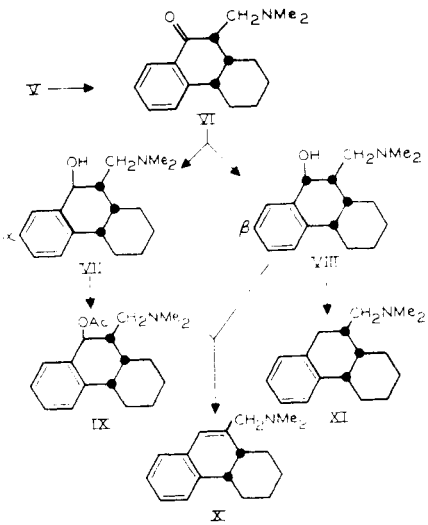
(3) R. P. Linstead, W. E. Doering, S. B. David, P. Levine, and R. R. Whetstone, *J. Am. Chem. Soc.*, **64**, 1985 (1942).

(4) R. P. Linstead, S. B. Davis, and R. R. Whetstone, *J. Am. Chem. Soc.*, **64**, 2009 (1942).

(5) R. P. Linstead, R. R. Whetstone, and P. Levine, *J. Am. Chem. Soc.*, **64**, 2014 (1942).

(6) F. F. Blicke, *Org. Reactions*, I, 327 (1942).

VI are possible, only one was found. The Mannich reaction, for which the mechanism is not yet known,[7] is an equilibrium type, and it is deduced, since this particular synthesis is stereoselective, that the dimethylaminomethyl group in VI has entered in the thermodynamically more stable equatorial position. The entry of the bulky dimethylaminomethyl group is also regarded to have stabilized the conformation of the central ring in the same way, although not to the same degree, as has been shown to be the case for 4-*t*-butylcyclohexanols[8] which are known to be conformationally homogeneous; *i.e.*, each adopts almost completely that form in which the *t*-butyl group is equatorial.



If to the ketone (VI) we assign the thermodynamically favorable chair conformation to ring III and add the restriction that the dimethylaminomethyl group must be equatorial, only two conformations, illustrated in Fig. 1 (R = dimethylaminomethyl-) are possible. Coplanarity due to conjugated aryl and carbonyl resonance exists over that part of the molecule indicated by heavy lines. Scale molecular models (Fisher-Hirschfelder-Taylor) of each conformation were prepared. With the dimethylaminomethyl group in the 10 equatorial position, conformation b is preferred since it offers less nonbonded interaction, or greater freedom of rotation of the new group. Accordingly, the configuration represented by VI making C-10, C-10a and C-4a hydrogens all *cis* is considered the more probable for the product of this Mannich reaction. We recognize that the certainty provided by this approach is not so high as would be obtained by a corresponding analysis of a more rigid fused system.

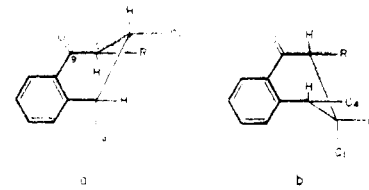
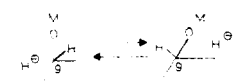


Fig. 1. Preferred conformations of diastereoisomeric aminohydrophenanthrones

Short time exposure of the amino ketone (VI) to excess lithium aluminum hydride in ether permitted the isolation of the α-phenanthrol (VII) in 49% yield, and also a 21% yield of the epimeric β-phenanthrol (VIII). Although the exact mechanism and the importance of steric factors in the reduction of ketones by hydrides are still under discussion,[9,10] the general trend in the absence of pronounced steric hindrance is that lithium aluminum hydride reduction gives rise to a preponderance of the thermodynamically stable (equatorial) alcohol, and the hydroxyl group of VII is assigned this conformation. This inference was strengthened when the experiment was repeated under identical conditions except that reflux time was increased to twenty-four hours. With this longer reaction time, the yield of VII was increased to 78% (with further increased reflux time to seventy-two hours, the yield remained at 78%). Under these conditions lithium aluminum hydride is capable of epimerizing such a benzyl alcohol, thereby increasing the yield of the equatorial alcohol already favored by the short term treatment.

The action of lithium aluminum hydride on ketone VI proceeds in two phases. Addition of hydride can occur from either face of the molecule but the addition proves stereoselective and the formation of the equatorial isomer is preferred. This phase is kinetically controlled. For the second phase of the reaction, we consider a mechanism that permits equilibration of the epimers. Perhaps the simplest one that can be offered is the one illustrated in which hydride exchange occurs with concomitant inversion at C-9. The proposed



mechanism may be more reasonable when it is considered that under the reaction conditions an abundant supply of hydride ion is available and also that the closely related nucleophilic attack of hydride ion on benzylic carbon with replacement of oxygen has already been demonstrated.[11,12]

(7) J. Hine, "Physical Organic Chemistry," p. 256, McGraw-Hill Book Co., Inc., New York, 1956.

(8) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(9) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).

(10) K. D. Hardy and R. J. Wicker, *J. Am. Chem. Soc.*, **80**, 640 (1958).

(11) W. H. Hartung, *Org. Reactions*, **VII**, 269 and 301 (1953).

(12) R. F. Nystrom and C. R. A. Berger, *J. Am. Chem. Soc.*, **80**, 2896 (1958).

An alternative to this proposal is to consider epimerization *via* equilibration with some unreduced ketone.[13] Such epimerizations are carried out in such a way that an appreciable concentration of ketone is present (it is frequently deliberately added to an alcohol-alkoxide mixture) and at much higher temperatures (120–200°) than in the present case.

Initial efforts to secure catalytic reduction of VI were indecisive. Since the sample of platinum oxide used liberated base from VI hydrochloride, the addition of acid could be beneficial. On the other hand, strong mineral acid was known to lead to the decomposition of VI. These observations suggested as a compromise an acidic buffer and, using ammonium acetate–acetic acid buffer, a successful reduction was obtained as indicated by smooth consumption of the calculated quantity of hydrogen and the isolation of VIII in good yield.

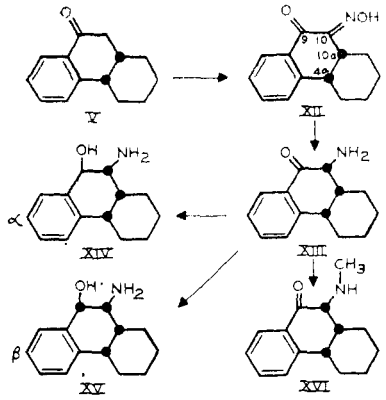
In contrast to the hydride reduction, catalyst (platinum) reduction was stereoselective in the opposite sense, a 72% yield of the β-phenanthrol VIII being obtained. A consideration of a scale model of VI (conformation b, Fig. 1, R = CH_2-$N(CH_3)_2$) reveals that ring III is puckered away from the general plane of rings I and II and following the teaching of Linstead and co-workers,[3] the hydrogen is delivered on the less hindered face of the molecule. This gives rise to an axial alcohol group, which result is congruent with the observations made in the hydride reductions, *i.e.*, that the stereochemical interpretation of either the catalytic reduction or of the hydride reduction leads to the same designation of the epimeric alcohols.

Dehydration of either the α- or β-phenanthrols by means of concentrated hydrochloric acid led to a single substance, the hexahydrophenanthrene X. *In an attempt to obtain the deoxy compound* XI, the first efforts were expended on the catalytic reduction of the hexahydrophenanthrene X.

The absorption of hydrogen was, however, nonselective. This was probably due to stabilization of the C-9-C-10 unsaturation by conjugation with aromatic ring I, a stability reinforced by its interior location rendering nuclear hydrogenation (ring I) more probable. Turning then to the possibility of hydrogenolysis of the β-phenanthrol VIII, we found that this could be accomplished readily using palladium-charcoal in acetic and hydrochloric acids. In this way a smooth uptake of hydrogen occurred and a 72% yield of the deoxy compound XI was readily obtained. The likelihood of migration of unsaturation in XI was ruled out by comparison of its ultraviolet spectrum with that of a model substance, also an *ortho*-disubstituted benzene, 1,2,3,4-tetrahydro-2-naphthoic acid,[14] since they agreed closely not only in the wave lengths of their maxima but also in intensities. Thus XI showed λ_{max} (in ethanol) at 263 and 272 mμ with log ε 2.72 for each peak while the model substance had λ_{max} 268 and 273 mμ with log ε 2.70 and 2.72.

The 10-amino series. In order to secure closer analogs to morphine, attempts were made to secure hydrophenanthrenes bearing the nitrogen at *position 10 on the ring system. Preliminary efforts* to introduce nitrogen at C-10 *via* the pathway of bromination of ketone V followed by nucleophilic attack by an appropriate amine were fruitless, probably because the bromo ketone displayed a much greater tendency for elimination of hydrogen bromide than for substitution. The elimination reaction, already favored in cyclohexane systems is in this instance enhanced by the existing conjugated system. To achieve the goal, again utilizing the phenanthrone(V), sodium ethoxide isonitrosation was employed, giving rise to XII which could be readily crystallized from benzene from which it separated as a solvate. Catalytic reduction of the isonitroso group proved to be selective over that of carbonyl, and a 78% yield of the 10-amino ketone XIII was obtained from XII. When the amino ketone XIII was reduced with lithium aluminum hydride a 56% isolated yield of the α-phenanthrol XIV was obtained while catalytic reduction (platinum) led to an 84% yield of the C-9 epimer, the β-phenanthrol XV.

In XII resonance between the aromatic ring, the carbonyl group and the isonitroso groups leads to coplanarity of rings I and II while ring III is puckered away from this general plane. Again following Linstead and co-workers,[3] catalyst hydrogen will be added on the less hindered face of the molecule resulting in the hydrogen at C-10 in XIII being *cis* to those at C-10a and C-4a. Further catalytic reduction to the β-phenanthrol (XV) will introduce the C-9 hydrogen *cis* to the three previously mentioned giving the configuration indicated. The α-phenanthrol XIV is, of course, the C-9 epimer.



(13) W. E. Doering and T. C. Aschner, *J. Am. Chem. Soc.*, 71, 838 (1949).

(14) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," Spectrum 23, John Wiley and Sons, Inc., New York, 1951.

Alternatively one may consider that since the formation of XIII has led to a *cis* arrangement of the C-10 amino group and the C-4–C-4a bond, the molecule will, in order to minimize 1,3-diaxial interaction of these groups, adopt that conformation (conformation b, R = —NH_2, Fig. 1) which permits these bonds to be equatorially arranged. Lithium aluminum hydride reduction of XIII would then be expected to produce a preponderance of the thermodynamically favored isomer, *i.e.*, the newly generated hydroxyl group will be equatorial and *trans* to the amino group, the configuration indicated by XIV. Thus this approach leads to the same stereochemical conclusion as the one discussed above.

Attempts to obtain methylation of XIII using the formic acid–formaldehyde method[15] were unsuccessful, only resin being produced. The next method attempted was that of reductive alkylation using formaldehyde and catalyst (platinum). The rate of hydrogen uptake showed no indications of selectivity but it was found to be possible to isolate, in good yield, the *N*-monomethyl phenanthrone (XVI).

EXPERIMENTAL[16]

Unless otherwise noted, all evaporations were conducted at 55° under aspirator vacuum and all melting points were taken on a micro hot stage and are corrected.

1-Dicyanomethylene-2-phenylcyclohexane (III). A mixture of 86.6 g. of 2-phenylcyclohexanone,[17] 33.0 g. of malononitrile, 7.7 g. of ammonium acetate, 4.6 ml. of glacial acetic acid and 100 ml. of benzene was refluxed with stirring for 12 hr., the water of condensation being collected in a Dean-Stark trap. The solution was washed with water and 1.0*M* sodium carbonate, then evaporated to dryness. The residue, which crystallized on cooling, gave, after air drying, 107.6 g. (97%) of III, m.p. 59–65°. The analytical sample, crystallized from alcohol and evaporatively distilled at 130°, melted at 67–68°.

Anal. Calcd. for $C_{15}H_{14}N_2$: C, 81.1; H, 6.4. Found: C, 80.8; H, 6.4.

cis-2-Phenylcyclohexyl-1-acetic acid (IV). Catalytic reduction of III, 50 g., using 5.00 g. of platinum oxide and 500 ml. of methanol at room temperature and atmospheric pressure was allowed to proceed until the calculated amount of hydrogen was absorbed (1.5 hr.). The mixture was filtered and the filtrate evaporated to dryness. The residue in 75 ml. of 38% hydrochloric acid and 113 ml. of glacial acetic acid was heated for three days on the steam bath. Cooling, filtration, washing with 50% acetic acid and water followed by vacuum drying at 90° gave 29.6 g. (60%) of IV, m.p. 161–164°, which was raised by recrystallization (carbon tetrachloride) to 168–169.5° (reported[2] m.p., 168–170°).

10-Dimethylaminomethyl-cis-1,2,3,4,4a,10a-hexahydro-9(10H)phenanthrone (VI) *hydrochloride.* A mixture of 14.00 g. of V, 5.71 g. of dimethylamine hydrochloride, and 2.10 g. of paraformaldehyde was stirred in a 70° bath under a slow stream of nitrogen for 22 hr. The reaction mixture was taken up in absolute alcohol and filtered. The filtrate was evaporated and the resulting residue made alkaline with molar sodium carbonate. The oil that separated was taken up in ether and neutralized with alcoholic hydrochloric acid. (Excess should be avoided since the compound is unstable under acid conditions. Stoichiometry is readily attained by following the titration with a *p*H meter.) Evaporation and crystallization from acetone gave 9.4 g. (46%) of VI hydrochloride, m.p. 147–148° dec. The analytical sample (from methanol-acetone), m.p. 151.5–152° dec. when heated at the rate of 2°/min.

Anal. Calcd. for $C_{17}H_{24}ONCl$: C, 69.5; H, 8.2. Found: C, 69.4; H, 8.4.

α-10-Dimethylaminomethyl-cis-1,2,3,4,4a,9,10,10a-octahydrophenanthr-9-ol (VII) *hydrochloride.* A solution of VI base in 30 ml. of ether was prepared from 1.00 g. of the hydrochloride by addition of 0.5 *M* sodium carbonate, extraction, and drying with calcium hydride. This ether solution was added to a stirred refluxing solution of 0.40 g. of lithium aluminum hydride in 20 ml. of absolute ether. Within 15 min. a gray precipitate formed which persisted to the end of the reflux period (24 hr.). Water was added cautiously to decompose hydride and precipitate aluminum hydroxide. The ether solution was decanted and dried with sodium sulfate. After acidifying with alcoholic hydrochloric acid, evaporating to dryness, and crystallizing from ethanol-ethyl acetate, there was obtained 0.79 g. (78% yield) of VII hydrochloride, m.p. 189–191°. The analytical sample (from methyl ethyl ketone), m.p. 191–192°.

Anal. Calcd. for $C_{17}H_{26}ONCl$: C, 69.0; H, 8.9. Found: C, 69.0; H, 9.1.

α-9-Acetoxy-10-dimethylaminomethyl-cis-1,2,3,4,4a,9,10,-10a-octahydrophenanthrene (IX) *hydrochloride.* To a stirred solution of 1.60 ml. of acetic anhydride in 6.4 ml. of pyridine there was added 1.59 g. of VII hydrochloride. At the end of 2 hr. the volume of acetylating reagent was doubled to facilitate stirring. After a total of 22 hr. the pure microcrystalline IX hydrochloride was filtered, washed with ether and dried (1.23 g., 68% yield, m.p. 216.5–217°). An additional 0.28 g., m.p. 203–205°, could readily be recovered from the mother liquor.

Anal. Calcd. for $C_{19}H_{28}O_2NCl$: C, 67.5; H, 8.4. Found: 67.8; H, 8.4.

β-10-Dimethylaminomethyl-cis-1,2,3,4,4a,9,10,10a-octahydrophenanthr-9-ol (VIII) *hydrochloride.* (a). *Via hydride reduction.* The phenanthrone VI hydrochloride (4.00 g.) was converted to the base using *M* sodium carbonate. The mixture was extracted with 30 ml. of ether, and the extract was dried with sodium sulfate, then with calcium hydride. This extract was added over a 10-min. period to a refluxing mixture of 1.60 g. of commercial lithium aluminum hydride in 80 ml. of ether. Refluxing was continued 15 min. after the addition. Water was added cautiously until the formation of aluminum hydroxide gel was completed. After decanting and washing, the combined ether solutions were acidified with alcoholic hydrochloric acid and evaporated. The solid residue was fractionally crystallized using hot ethyl acetate (in which the β-phenanthrol is preferentially soluble). In this way there was obtained 1.96 g. (49% yield) of pure VII hydrochloride, m.p. 192°, and 0.85 g. (21% yield) of VIII hydrochloride, nacreous plates, m.p. 171–171.5° at a heating rate of 1°/min. (It showed a solid phase change at *ca.* 100°), analytically pure after drying at 100° in vacuum.

Anal. Calcd. for $C_{17}H_{26}ONCl$: C, 69.0; H, 8.9. Found: C, 69.1; H, 8.9.

(b) *Via catalytic reduction.* To a mixture of 1.02 g. of VI hydrochloride and 0.10 g. of platinum oxide in 10 ml. of methanol, there was added 0.057 ml. of glacial acetic acid and 0.08 g. of ammonium acetate. Shaking with hydrogen at room temperature and 1 atm. was allowed to proceed until the calculated amount was absorbed (*ca.* 85 min.). The platinum was filtered, and the filtrate evaporated. After

(15) H. T. Clarke, H. B. Gillespie, and S. Z. Weisshaus, *J. Am. Chem. Soc.*, 55, 4571 (1933).

(16) Microanalyses were performed by the staff of the Institute's Service Analytical laboratories under the direction of Dr. William C. Alford. Mrs. Anne H. Wright supplied the ultraviolet spectra.

(17) M. S. Newman and M. D. Farbman, *J. Am. Chem. Soc.*, 66, 1550 (1944).

crystallizing from ethyl acetate, there was obtained 0.71 g. (70% yield) of VIII hydrochloride, m.p. 166–167°. A portion of this was converted to the picrate (platelets from acetone), m.p. 203.5–204°.

Anal. Calcd. for $C_{23}H_{28}O_8N_4$: C, 56.6; H, 5.8. Found: C, 56.5; H, 5.8.

Occasionally a higher melting (181°) variety of VIII hydrochloride was obtained. Either dimorph when recrystallized from water gave a crystalline hydrate (needles) which melted at (sealed capillary, 3°/min. heating rate) 141–142° alone or in admixture.

10-Dimethylaminomethyl-cis-1,2,3,4,4a-10a-hexahydrophenanthrene (X) *hydrochloride.* A mixture of 1.20 g. of VII hydrochloride and 12 ml. of 38% hydrochloric acid was placed in a stoppered flask. After standing overnight at room temperature, the solution was evaporated to dryness at 100° in vacuum. Crystallization of the residue from aqueous acetone gave 0.85 g. (76% yield) of X hydrochloride, nacreous plates, m.p. 246° (capillary).

Anal. Calcd. for $C_{17}H_{24}NCl$: C, 73.5; H, 8.7. Found: C, 73.2; H, 8.4.

Proceeding in a similar way from 0.54 g. of the β-phenanthrol (VIII) hydrochloride, there was obtained 0.46 g. (90% yield) of X hydrochloride, melting at 246° (capillary), not depressed by admixture of analytical sample.

10-Dimethylaminomethyl-cis-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XI) *hydrochloride.* To 0.20 g. of 10% palladium on charcoal there was added 0.61 g. of VIII hydrochloride, 25 ml. of glacial acetic acid and 0.8 ml. of 38% hydrochloric acid. Hydrogenolysis was carried out at room temperature and atmospheric pressure until the calculated amount of hydrogen gas was absorbed (about 80 min.). The mixture was filtered and the filtrate was evaporated at 100° *in vacuo*. The residue was taken up in methanol-acetone, 0.03 g. of by-product filtered off, again evaporated to dryness, then crystallized from acetone–ethyl acetate yielding 0.42 g. (72%) of XI hydrochloride, m.p. 206.5°. Further crystallization from the same solvent mixture gave the analytical sample, needles, m.p. 206–206.5°.

Anal. Calcd. for $C_{17}H_{26}NCl$: C, 73.0; H, 9.4. Found: C, 72.8; H, 9.5.

10-Isonitroso-cis-1,2,3,4,4a,10a-hexahydro-9-phenanthrone (XII). To a solution of 0.52 g. of sodium in 16 ml. of absolute alcohol cooled in an ice bath and maintained in a nitrogen atmosphere, there was added, with stirring, a solution of 4.00 g. of phenanthrone V in 8 ml. of absolute alcohol followed by 5.00 ml. of isoamyl nitrite. The mixture was let stand overnight, ice cooled, then diluted with 60 ml. of water, then acidified by addition of glacial acid, followed by ether extraction. The extract was evaporated and the residue crystallized from petroleum ether (b.p. 30–60°). Yield, 2.44 g. (53%) of XII, m.p. 160.5–163° dec. The analytical sample crystallized from benzene as a solvate, m.p. 173.5–174° dec. (heating rate, 2°/min.) and was dried for analysis at 95° in vacuum.

Anal. Calcd. for $C_{14}H_{15}O_2N$: C, 73.3; H, 6.6. Found: C, 73.7; H, 6.7.

10-Amino-cis-1,2,3,4,4a,10a-hexahydro-9(10H)phenanthrone (XIII) *hydrochloride.* A mixture of 2.80 g. of XII, 0.25 g. of platinum oxide, 30 ml. of methanol, and 0.99 ml. of 38% hydrochloric acid was hydrogenated at room temperature and 1 atm. The initial uptake of hydrogen was very rapid and exothermic. The reduction was stopped after 20 min. at which point hydrogen consumption had dropped to a rate of 1 ml./min., and 610 ml. had been absorbed. The catalyst was filtered and the filtrate evaporated. The residue (crystalline) was triturated with acetone, filtered, and dried to give 2.38 g. (78% yield) of XIII hydrochloride, m.p. 199.5–201° dec. The analytical sample, clusters of needles from water-acetone, melted at 211–212° dec. (evacuated capillary). (Solutions exposed to air are unstable and gradually discolor).

Anal. Calcd. for $C_{14}H_{18}ONCl$: C, 66.8; H, 7.2. Found: C, 66.8; H, 7.1.

α-10-Amino-cis-1,2,3,4,4a,9,10,10a-octahydro-9-phenanthrol (XIV) *hydrochloride.* To a mixture of 0.25 g. of XIII hydrochloride and 2.5 ml. of dry ether, there was added 0.11 g. of lithium aluminum hydride in 2 ml. of dry ether. After refluxing for 15 min. the mixture was evaporated, mixed with a solution of 1.41 g. of sodium potassium tartrate tetrahydrate in 2.5 ml. of water and with 12 ml. of 25% potassium hydroxide. After brief heating on the steam bath and cooling, the solid was filtered and air dried. The solid was then sublimed at 150° *in vacuo* and the sublimate was converted to the hydrochloride (alcoholic hydrogen chloride) which was evaporated to a solid residue. This, crystallized from water-acetone gave 0.14 g. (56% yield) of XIV hydrochloride, m.p. 282–283° (evacuated capillary). The analytical sample, plates from water, melted at 293–293.5° (evacuated capillary) which melting point is depressed by admixture of the corresponding β-phenanthrol (XV) hydrochloride.

Anal. Calcd. for $C_{14}H_{20}ONCl$: C, 66.3; H, 7.9. Found: C, 66.5; H, 7.9.

β-10-Amino-cis-1,2,3,4,4a,9,10,10a-octahydro-9-phenanthrol (XV) *hydrochloride.* A mixture of 0.20 g. of XIII hydrochloride, 0.10 g. of platinum oxide, and 10 ml. of methanol was shaken with hydrogen at room temperature and 1 atm. until the absorption of hydrogen ceased (2 hr.). Catalyst was filtered and the filtrate was evaporated to a solid residue. Crystallization from acetone gave 0.17 g. (84% yield) of XV hydrochloride, m.p. 260–261° (evacuated capillary). Recrystallization from absolute ethanol gave clusters of needles, m.p. 268° (evacuated capillary).

Anal. Calcd. for $C_{14}H_{20}ONCl$: C, 66.3; H, 7.9. Found: C, 66.5; H, 7.9.

10-Methylamino-cis-1,2,3,4,4a,10a-hexahydro-9-(10H)phenanthrone (XVI) *hydrochloride.* A mixture of 0.39 g. of XIII hydrochloride, 0.30 ml. of 40 g./100 ml. formaldehyde, 0.10 g. of platinum oxide and 10 ml. of methanol was shaken at room temperature and 1 atm. for reductive methylation. After about 6 hr., 83 ml. of hydrogen had been absorbed. At this point 0.30 ml. of 3*N* hydrochloric acid was added and shaking was continued for an additional 20 min. in which time an additional 8 ml. of hydrogen was consumed. Catalyst was filtered and the filtrate was evaporated. Crystallization from acetone gave 0.25 g. (61% yield) of XVI hydrochloride, m.p. 213–214° (evacuated capillary). Crystallization from *t*-butyl alcohol gave micro-crystals, m.p. 217° (evacuated capillary).

Anal. Calcd. for $C_{15}H_{20}ONCl$: C, 67.8; H, 7.6. Found: C, 67.7; H, 7.7.

The picrate, needles from ethyl acetate, m.p. 150° dec. capillary.

Anal. Calcd. for $C_{21}H_{22}O_8N_4$: C, 55.0; H, 4.8. Found: C, 55.0; H, 4.8.

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