Octahydrophenanthrene Analogs of Tetrabenazine

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Acid-catalyzed treatment of 1,9,10,10a-tetrahydro-3(2H)-phenanthrenones with ethylene glycol led to ketalization with accompanying double-bond migration. Catalytic hydrogenation, followed by cleavage of the ketals gave the corresponding B/C-*cis* hexahydrophenanthrenones. Metal in liquid ammonia reduction of the unsaturated ketals followed by hydrolysis gave the B/C-*trans* hexahydrophenanthrenones. Both series of compounds were converted to 2-alkyloctahydro-3-ketophenanthrenes which were of interest as nitrogen-free analogs of tetrabenazine.

In connection with some studies[2] on compounds related to emetine, a series of benzo[*a*]quinolizines was prepared which had interesting pharmacological properties.[3] One compound in this series, tetrabenazine[4a,b] (I), is of interest because of its psychosedative activity. In order to compare the pharmacological activity of the corresponding nitrogen-free analogs of tetrabenazine, we have synthesized a number of octahydrophenanthrene derivatives. Four types of compounds were prepared: (A) monomethoxy-substituted B/C-*cis*-fused octahydrophenanthrenes, (B) the corresponding B/C-*trans*-fused isomers, (C) dimethoxy-substituted B/C-*cis*-fused octahydrophenanthrenes, and (D) the corresponding B/C-*trans*-fused isomers.

The preparation of the monomethoxy B/C-*cis*-fused compounds proceeded from the hydroxymethylene derivative IIa[5] of 6-methoxy-1-tetralone which was condensed with methyl vinyl ketone to give IIIa[6] (see Chart I). This compound has not previously been characterized although it has been obtained as a mixture with IVa.[7] Cyclization of IIIa with potassium hydroxide gave IVa,[5] which on treatment with ethylene glycol gave a ketal lacking an olefinic proton signal in the nmr spectrum. Ketalization was therefore accompanied by migration of the double bond to yield Va. Catalytic hydrogenation of Va over palladium on charcoal gave the *cis* ketal VIa, which was hydrolyzed to the ketone VIIa.[8] Treatment of the latter compound with magnesium methyl carbonate[9] followed by esterification of the intermediate acid gave the β-keto ester VIIIa.[10] This compound was then alkylated with ethyl iodide, *n*-butyl iodide, and isobutyl bromide, respectively, in the presence of potassium *t*-butoxide to give the intermediates of formula IX (R_1 = alkyl). Hydrolysis and decarboxylation with potassium hydroxide[11] gave Xa, Xb, and Xc, respectively.[12]

Since the method of synthesis of these compounds does not allow a definitive assignment of the position of substitution in VIIIa, IXa, and Xa–c, the assignments were substantiated in the following unambiguous manner (see Chart II). The triethylamine-catalyzed reaction of IIa and XI gave crude XIIa which on potassium hydroxide ring closure was converted to XIIIa, although in only 6% over-all yield. Ketalization, catalytic hydrogenation, and hydrolysis gave Xa, identical with the product prepared from the β-keto ester VIIIa.

The synthesis of the monomethoxy B/C-*trans*-fused compounds proceeded from an intermediate obtained in the *cis* series. Thus, the ketal Va was treated with potassium in liquid ammonia to give as the minor product the B/C-*cis*-fused ketal VIa, the major component being the desired B/C-*trans*-fused ketal XIVa. Acid hydrolysis of XIVa gave the ketone XVa[8] which on treatment with sodium hydride and dimethyl carbonate gave the β-keto ester XVIa.[14] This compound was then alkylated with methyl, ethyl, *n*-butyl, and isobutyl iodides to give the intermediates of formula XVIIa. Hydrolysis and decarboxylation of the latter compounds with potassium hydroxide gave the monomethoxy *trans* derivatives XVIIIa, XVIIIb, XVIIIc, and XVIIId,[15] respectively (see Chart III and Table I).

Since the method of synthesis of these compounds does not allow a definitive assignment to the position of alkyl substitution in XVIa, XVIIa, and XVIIIa–d, the structures were confirmed in the following unambiguous manner. Compound XVIIIa was reduced with sodium borohydride to give the corresponding alcohol which was treated with 10% palladium on carbon in *p*-*t*-butyltoluene[16] to yield 2-methyl-7-methoxyphenanthrene, identical with an authentic sample.[17]

The preparation of the B/C-*cis* dimethoxyoctahydrophenanthrenes was achieved by reactions analogous to those already outlined for the monomethoxy analogs. Thus, reaction of methyl vinyl ketone with the hydroxy-

(1) Deceased, Feb 17, 1964.

(2) A. Brossi, H. Lindlar, M. Walter, and O. Schnider, *Helv. Chim. Acta*, **41**, 119 (1958).

(3) A. Pletscher, A. Brossi, and K. F. Gey, *Intern. Rev. Neurobiol.*, **4**, 275 (1962).

(4) Nitoman g.

(5) A. A. Akhrem and I. G. Zavel'skaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1637 (1960).

(6) All compounds prepared in this paper are racemates and for convenience are represented by one enantiomeric series throughout.

(7) G. T. Tatevosyan, P. A. Zagorets, and A. G. Vardanyan, *Zh. Obshch. Khim.*, **23**, 941 (1953); *Chem. Abstr.*, **48**, 7539b (1954).

(8) This compound has been reported in[5] crude form.

(9) M. Stiles, *J. Am. Chem. Soc.*, **81**, 2598 (1959).

(10) The reaction of VIIa and dimethyl oxalate afforded the corresponding glyoxalate (mp 193° dec), which on decarbonylation also gave VIIIa although the over-all yield is much poorer and the procedure more tedious.

(11) W. B. Renfrow, Jr., *J. Am. Chem. Soc.*, **66**, 144 (1944).

(12) The hydrolysis of IXa was attempted by various other procedures, in each case leading to recovery of starting material or tars from which no product could be isolated. Hydrolysis with lithium iodide in collidine[13] did give Xa, although in lower yields than with potassium hydroxide.

(13) F. Elsinger, H. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **43**, 113 (1960).

(14) The conversion of XVa to XVIa could also be accomplished by treatment with magnesium methyl carbonate followed by esterification with diazomethane.

(15) The configuration of the alkyl group in XVIII is assigned by analogy with the work of Y. Mazur and F. Sondheimer, *J. Am. Chem. Soc.*, **80**, 5220 (1958).

(16) H. Rapoport, A. D. Batcho, and J. E. Gordon, *ibid.*, **80**, 5767 (1958).

(17) J. Heer and K. Miescher, *Helv. Chim. Acta*, **21**, 219 (1958).

CHART I

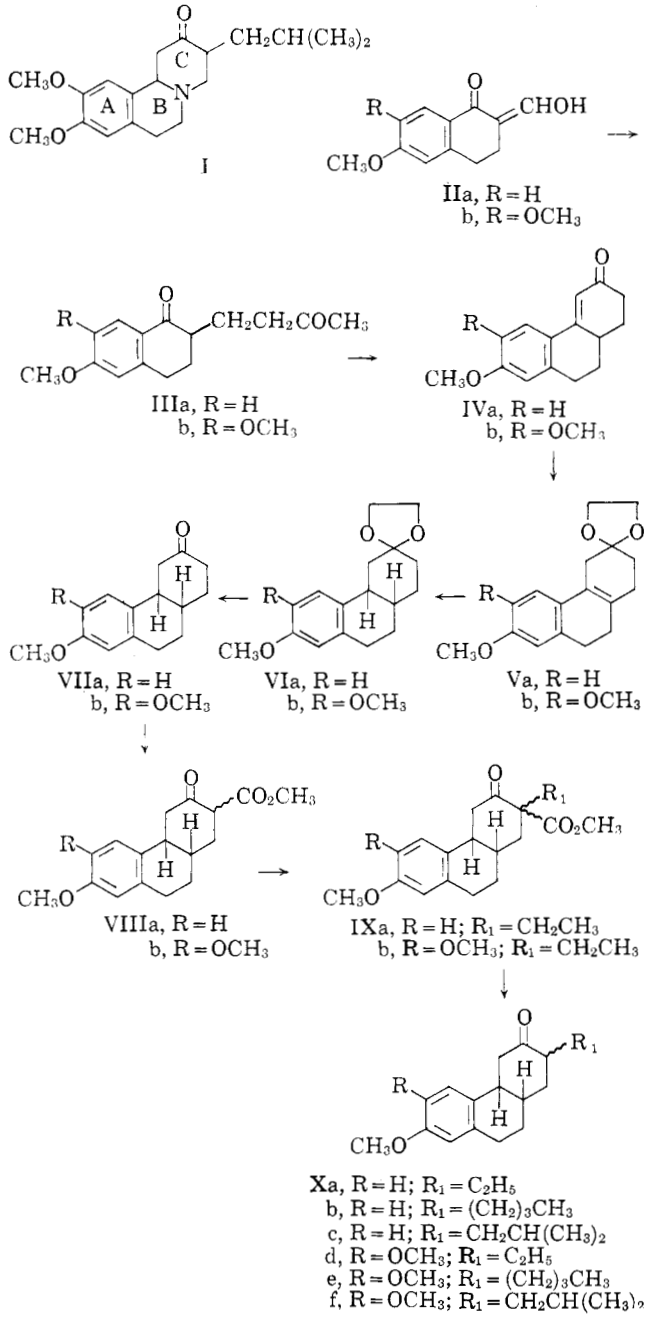


CHART II

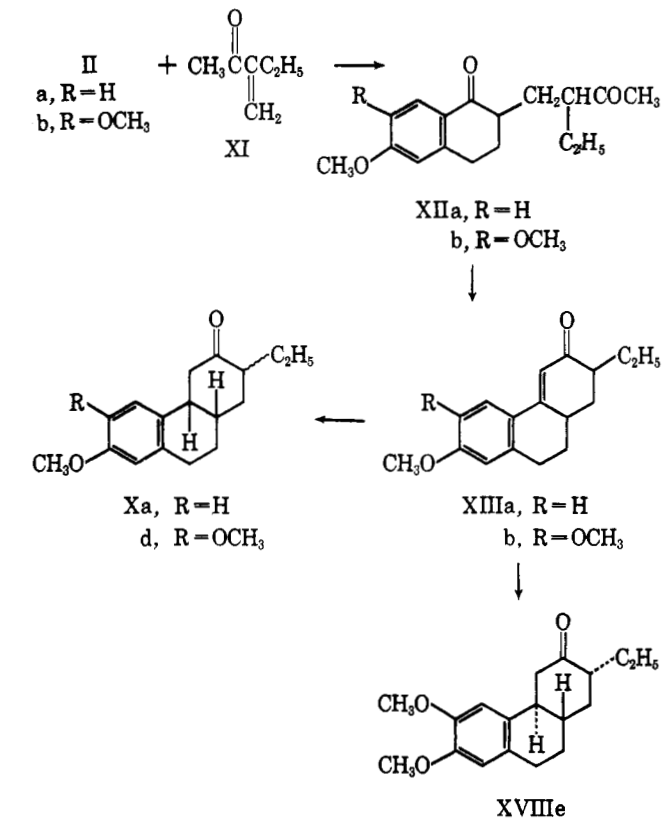
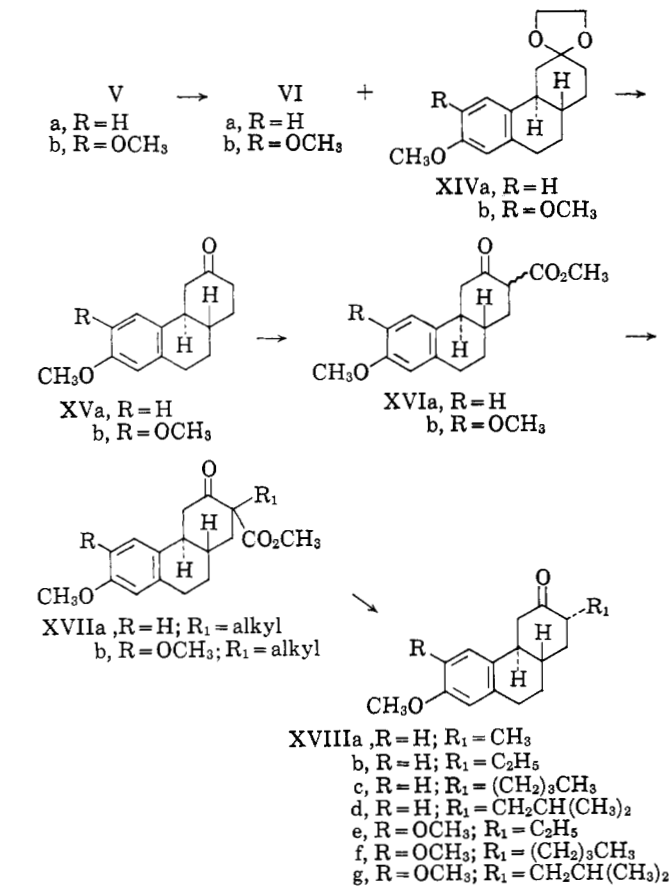


CHART III



methylene derivative IIb[18] of 6,7-dimethoxy-1-tetralone gave IIIb which was cyclized to the ketone IVb.[19] This latter compound was then converted to the ketal Vb in which olefinic proton absorption was absent in the nmr spectrum. Catalytic hydrogenation of the latter compound gave the *cis* ketal VIb which was hydrolyzed to yield the ketone VIIb. Reaction of the latter compound with magnesium methyl carbonate followed by esterification with diazomethane gave the β-keto ester VIIIb.[20] Alkylation of VIIIb with ethyl iodide in the presence of potassium *t*-butoxide gave IXb, which in contrast to the other analogs was obtained crystalline. Analogous alkylation with *n*-butyl and isobutyl iodides, followed by potassium hydroxide hydrolysis then gave Xd, Xe, and Xf, respectively.

Since the position of substitution in VIIIb, IXb, and Xd–f was not definitive, the assignments were confirmed

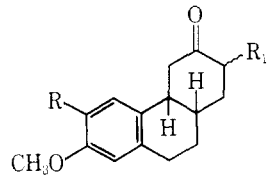
(18) K. N. Campbell, A. Schrage, and B. K. Campbell, *J. Org. Chem.*, **15**, 1135 (1950).

(19) G. N. Walker, *J. Am. Chem. Soc.*, **80**, 645 (1958).

(20) Treatment of VIIb with dimethyl carbonate and sodium hydride did not yield VIIIb, but gave instead a low yield of a product analyzing for the incorporation of two carbomethoxy groups.

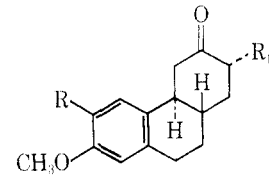
TABLE I

2-ALKYL-1,4,4a,9,10,10a-HEXAHYDRO-3(2H)-PHENANTHRENONES



X

or



XVIII

Compd	R	R_1	Prepn[a]	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
Xa	H	C_2H_5	A + B	48	86–88[b]	$C_{17}H_{22}O_2$	79.03	8.58	79.04	8.58
Xb	H	$(CH_2)_3CH_3$	A + B	26	84–85[c]	$C_{19}H_{26}O_2$	79.68	9.15	80.04	9.07
Xc	H	$CH_2CH(CH_3)_2$	A + B	12	110–111.5[c]	$C_{19}H_{26}O_2$	79.68	9.15	79.90	9.28
Xd	OCH_3	C_2H_5	A + B	27	128–129[b]	$C_{18}H_{24}O_3$	74.97	8.39	75.13	8.73
Xe	OCH_3	$(CH_2)_3CH_3$	A + B	32	96–98[b]	$C_{20}H_{28}O_3$	75.91	8.92	75.96	9.08
Xf	OCH_3	$CH_2CH(CH_3)_2$	A + B	17.5	141–141.5[d]	$C_{20}H_{28}O_3$	75.91	8.92	76.06	9.19
XVIIIa	H	CH_3	A + B	76	133.5–134.5[b]	$C_{16}H_{20}O_2$	78.65	8.25	78.65	8.16
XVIIIb	H	C_2H_5	A + B	24	95.5–97[b]	$C_{17}H_{22}O_2$	79.03	8.58	78.97	8.76
XVIIIc	H	$(CH_2)_3CH_3$	A + B	26	97.5–99[b]	$C_{19}H_{26}O_2$	79.68	9.15	79.62	9.42
XVIIId	H	$CH_2CH(CH_3)_2$	A + B	11.6	88.5–91.5[b]	$C_{19}H_{26}O_2$	79.68	9.15	79.49	9.07
XVIIIe	OCH_3	C_2H_5	A + C	44	145–146[b]	$C_{18}H_{24}O_3$	74.97	8.39	74.70	8.51
XVIIIf	OCH_3	$(CH_2)_3CH_3$	A + C	32	109–110[b]	$C_{20}H_{28}O_3$	75.91	8.92	75.72	8.89
XVIIIg	OCH_3	$CH_2CH(CH_3)_2$	A + C	8.3	140–141[b]	$C_{20}H_{28}O_3$	75.91	8.92	75.85	8.95

[a] The letters denoting the method of preparation refer to the general methods outlined in the Experimental Section. [b] Recrystallization from methanol. [c] Recrystallization from hexane. [d] Recrystallization from ether.

by the following unambiguous method. Reaction of IIb with 2-ethyl-3-oxobutyl-1-trimethylammonium iodide (the precursor of XI) in the presence of sodium methoxide[21] gave XIIb, which was then cyclized with potassium hydroxide to XIIIb. The latter compound, upon ketalization, catalytic hydrogenation, and hydrolysis, was converted to Xd, identical with the product obtained from the β-keto ester VIIIb.

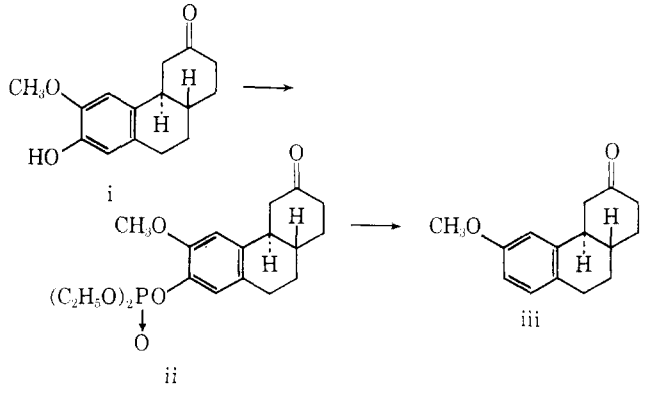
The dimethoxy B/C-*trans*-fused compounds were also prepared in a manner similar to the monomethoxy analogs. Thus treatment of Vb with lithium[22] in liquid ammonia gave the B/C-*cis*-fused ketal VIb as the minor component and the desired B/C-*trans*-fused ketal XIVb as the major component. Acid hydrolysis of XIVb gave the ketone XVb which was converted to the β-keto ester XVIb[24] on treatment with sodium hydride and dimethyl carbonate. Alkylation of XVIb with ethyl, *n*-butyl, and isobutyl iodides gave intermediates of formula XVIIb. Hydrolysis and decarboxylation with potassium carbonate then gave the B/C-*trans* dimethoxy derivatives XVIIIe, XVIIIf, and XVIIIg, respectively.

Since the position of alkyl substitution in XVIb, XVIIb, and XVIIIe–g was not definitive, the structures were proven by the following unambiguous method. Ketalization of XIIIb followed by reduction with potassium in liquid ammonia and subsequent acid hydrolysis gave XVIIIe, identical with the product prepared from the β-keto ester XVIb.

Biological Data.[25]—None of the compounds in series VII, X, XV, or XVIII exhibit any tetrabenazine-like sedation when administered to rats in the continuous avoidance test,[26] although XVIIIa showed weak stimulant activity in rats. Also, the compounds in series VII, X, XV, and XVIII have no significant depressant activity as measured in either the inclined screen procedure[27] or the foot shock test.[28] None of these compounds have any significant stimulant activity as measured in the norepinephrine potentiation test (in dogs) or by the prevention of tetrabenazine ptosis.[29] Compound VIIa has moderate blood pressure lowering activity (in the dog), whereas VIIb and the compounds of series X, XV, and XVIII are inactive. However, XVa does have some blood pressure lowering activity when administered to hypertensive rats.

(21) A. L. Wilds and C. H. Shunk, *J. Am. Chem. Soc.*, **72**, 2388 (1950).

(22) Treatment of Vb with potassium in liquid ammonia gave the B/C-*cis* ketal VIb and also a noncrystalline residue. Mild acid hydrolysis of the latter material gave a low yield of the phenol (i), which was methylated with dimethyl sulfate to give the B/C-*trans* dimethoxy ketone XVb. On the other hand, treatment of i with diethyl phosphite[23] gave crude ii which was cleaved with sodium in liquid ammonia to yield iii. The latter compound was similar to, but not identical with XVa, thus establishing the position of the methoxy group in i.



i ii iii

(23) S. W. Pelletier and D. M. Locke, *J. Org. Chem.*, **23**, 131 (1958).

(24) The conversion of XVb to XVIb could also be effected by the use of magnesium methyl carbonate followed by diazomethane esterification. This procedure in practice is limited to small-scale reactions, because of the low solubility of the intermediate acid.

(25) We are indebted to Dr. L. O. Randall and his staff for these results.

(26) G. A. Heise and E. Boff, *Psychopharmacologica*, **3**, 264 (1962).

(27) L. O. Randall, *J. Pharm. Exptl. Therap.*, **129**, 163 (1960).

(28) R. E. Tedeschi, D. H. Tedeschi, A. Mucha, L. Cook, P. A. Mattis, and E. J. Fellows, *ibid.*, **125**, 28 (1959).

(29) L. O. Randall and R. E. Bagdon, *Diseases Nervous System*, **19**, 539 (1958).

These results indicate that the presence of a basic function in the tricyclic nucleus seems to be a prerequisite for tetrabenazine-like activity.

Experimental Section[30]

3,4-Dihydro-6-methoxy-2-(3-oxobutyl)-1(2H)-naphthalenone (IIIa).—To a cold (0–5°) suspension of 92.5 g (0.45 mole) of 6-methoxy-3,4-dihydro-2-hydroxymethylene-1(2H)-naphthalenone[5] in 200 ml of methanol and 48.5 g (0.69 mole) of methyl vinyl ketone was added with stirring over 20 min a solution of 6.7 g of triethylamine in 34 ml of methanol. After a short time the reaction became homogeneous and was stirred at room temperature for 3 days. The reaction was diluted with 1 l. of ether and was extracted with 10% Na_2CO_3 solution to remove unreacted starting material. Concentration of the organic layer gave a red oil which was taken up in benzene and filtered through a column of alumina. The eluate was evaporated to dryness and the residue was crystallized from methanol to give 101 g (91%) of IIIa as yellow crystals, mp 66–68°. Recrystallization from ethanol gave the analytical sample: mp 68.5–69.5°; $\lambda_{max}^{C_2H_5OH}$ 224 mμ (ε 13,300) and 274 mμ (ε 17,900); $\nu_{max}^{CHCl_3}$ 1713 and 1672 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.27; H, 7.36.

1,9,10,10a-Tetrahydro-7-methoxy-3(2H)-phenanthrenone (IVa) was prepared by the procedure of Akhrem and Zavel'skaya[5] to give yellow crystals: mp 118–119° (lit.[5] mp 115–115.5°); $\lambda_{max}^{C_2H_5OH}$ 243 mμ (ε 9900) and 330 mμ (ε 24,600); $\nu_{max}^{CHCl_3}$ 1652, 1609, 1583 cm^{-1}; nmr ($CDCl_3$) τ 2.30 (1 proton doublet, J = 8 cps, 5 H split by 6 H), 3.21 (1 proton doublet of doublets, J = 8 and 3 cps, 6 H split by 5 H and 8 H), 3.30 (1 proton singlet, 4 H) and 3.48 (1 proton doublet, J = 3 cps, 8 H split by 6 H).

7′-Methoxy-1′,4′,9′,10′-tetrahydrospiro[1,3-dioxolane-2,3′-(2′H)-phenanthrene] (Va).—A solution of 175 g (0.77 mole) of IVa in 1.5 l. of benzene containing 130 ml of ethylene glycol and 1.0 g of *p*-toluenesulfonic acid was heated under reflux (Dean–Stark trap) for 48 hr. The cooled reaction mixture was then poured into 2 l. of water containing 5 g of KOH. The benzene layer and three ether extracts of the aqueous layer were washed with water, dried (Na_2SO_4), and evaporated to give a solid residue. Crystallization from ether gave 182 g (87%) of Va as yellow crystals, mp 75–77°. Recrystallization from ether gave the analytical sample: mp 76–77°; $\lambda_{max}^{C_2H_5OH}$ 273 mμ (ε 15,800); $\nu_{max}^{CHCl_3}$ 1608, 1570 cm^{-1}; nmr ($CDCl_3$) τ 2.96 (1 proton doublet, J = 9 cps, 5 H split by 6 H), 3.4 (2 proton multiplet, 6 H and 8 H).

Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.08; H, 7.76.

7′-Methoxy-1′,4′,4′aβ,9′,10′,10′aβ-hexahydrospiro[1,3-dioxolane-2,3′(2′H)-phenanthrene] (VIa).—A solution of 50.0 g (0.184 mole) of Va in 1000 ml of ethyl acetate was hydrogenated at room temperature and pressure over 10 g of 10% Pd–C. One mole of hydrogen was absorbed in 15 min whereupon the rate of hydrogenation markedly decreased and the reaction was stopped. Colorless crystals were observed in the hydrogenation flask. The catalyst was filtered and washed repeatedly with hot ethyl acetate. Concentration of the solution gave 43 g (85%) of VIa as colorless crystals, mp 139–140°. Recrystallization from dichloromethane gave the analytical sample: mp 139–140.5°; $\lambda_{max}^{C_2H_5OH}$ 220 mμ (ε 8300), 278 (2000), and 287 (1860); $\nu_{max}^{CHCl_3}$ 1611 cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.23; H, 8.27.

1,4,4aβ,9,10,10aβ-Hexahydro-7-methoxy-3(2H)-phenanthrenone (VIIa).—A mixture of 75 g (0.274 mole) of VIa in 400 ml of methanol and 100 ml of 3 N HCl was heated on the steam bath for 1 hr. The cooled solution was filtered, and the filtrate was diluted with 500 ml of water. The resulting precipitate was filtered to give a total of 60.5 g (96%) of VIIa as colorless crystals, mp 82–85°. Recrystallization from a mixture of ether and hexane gave the analytical sample: mp 88–89°;[31] $\lambda_{max}^{C_2H_5OH}$ 225 (infl) mμ (ε 7500), 279 (1900), and 287 (1770); $\nu_{max}^{CHCl_3}$ 1708 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.46; H, 7.96.

The 2,4-dinitrophenylhydrazone of VIIa (prepared in 73% yield) crystallized from ethanol as orange red crystals, mp 167–180°. Further recrystallization from a mixture of dichloromethane and ethanol did not improve the melting point, and the analytical sample had mp 168–178°;[31] $\lambda_{max}^{C_2H_5OH}$ 220 mμ (ε 24,000), 229 (23,800), 260–270 (infl) (12,200), 287 (infl) (5000), 365 (24,000); ν_{max}^{KBr} 1615 and 1590 cm^{-1}.

Anal. Calcd for $C_{21}H_{22}N_4O_5$: C, 61.45; H, 5.40; N, 13.65. Found: C, 61.49; H, 5.14; N, 13.64.

Hydrolysis[32] of the 2,4-Dinitrophenylhydrazone of VIIa.—A solution of 200 mg (0.5 mmole) of the dinitrophenylhydrazone and 1 ml of concentrated HCl in 50 ml of acetone was heated under reflux for 20 min. The resulting orange-yellow solution was added to a solution of 1.0 g of $SnCl_2$ in 4 ml of concentrated HCl and 6 ml of water, and the mixture was heated under reflux for 45 min. The acetone was removed under vacuum at room temperature, and the residue was diluted with water and extracted with benzene. The organic layer was repeatedly washed with 1 N HCl, and the organic layer was evaporated to give 100 mg (91%) of VIIa as colorless crystals, mp 88–89°, undepressed on mixing with VIIa prepared from VIa.

Methyl 1,2,3,4,4aβ,9,10,10aβ-Octahydro-7-methoxy-3-oxo-2-phenanthrenecarboxylate (VIIIa).—A solution of 18.4 g (0.08 mole) of VIIa in 160 ml of a 2.0 M solution of magnesium methyl carbonate[9] in dimethylformamide was heated at 125–130° (nitrogen atmosphere) for 2 hr. The cooled reaction mixture was poured with stirring into a mixture of ice and HCl and extracted with ether until all the solid had dissolved, excess ice being present at all times. The ether solution was dried (Na_2SO_4) in the refrigerator and then treated with an excess of diazomethane (prepared from nitrosomethylurea). Concentration of the ether solution gave a yellow oil which crystallized from acetone to give in several batches a total of 15.36 g (74%) of VIIIa as pale yellow crystals, mp 145–155°, homogeneous and identical with pure material by thin layer chromatography. This material is probably a mixture of tautomers. Recrystallization from ethanol gave the analytical sample: mp 166–168°; $\lambda_{max}^{C_2H_5OH}$ immediately 225 mμ (ε 7700), 276 (2500), and 285 (2000); 48 hr later 220 (infl) mμ (ε 8800), 257 (7300), and 285 (infl) (ε 2350); $\lambda_{max}^{0.1\ N\ KOH}$ 286 mμ (ε 11,850); $\nu_{max}^{CHCl_3}$ 1746 and 1716 cm^{-1}.

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.78; H, 7.17.

Preparation of IX and XVII. General Method A.—A slurry of 0.03 mole of ester VIII or XVI and 0.06 mole of potassium *t*-butoxide in 300 ml of *t*-butyl alcohol was heated under reflux for 30 min. Alkyl halide (30 ml) was added and heating was continued overnight. The reaction mixture was acidified with acetic acid and concentrated under vacuum. The residue was diluted with water and extracted (CH_2Cl_2). The extracts were dried (Na_2SO_4) and concentrated under vacuum to give crude IX or XVII in the form of an oil which was used directly for the preparation of X or XVIII (see Table I).

Preparation of 6-Substituted 2-Alkyl-1,4,4a,9,10,10a-hexahydro-7-methoxy-3(2H)-phenanthrenones (X and XVIII). General Method B.—The crude IX or XVII from 0.03 mole of VIII or XVI was heated under reflux with 15 ml of methanol and 5 ml of water containing 0.03 mole of KOH. After 4 hr another 0.015 mole of solid KOH was added, and heating was continued overnight. The cooled reaction mixture was diluted with water and extracted (CH_2Cl_2). The extracts were dried (Na_2SO_4) and concentrated under vacuum to give an oil from which X or XVIII could be crystallized (see Table I).

2-Ethyl-1,9,10,10a-tetrahydro-7-methoxy-3(2H)-phenanthrenone (XIIIa).—To a cold (0–5°) suspension of 20.4 g (0.10 mole) of 6-methoxy-3,4-dihydro-2-hydroxymethylene-1(2H)-naphthalenone (IIa)[5] in 500 ml of methanol and 9.81 g (0.10 mole) of 3-methylene-2-pentanone was added slowly a solution of 2.1 ml of triethylamine in 20 ml of methanol. After a short time the mixture became homogeneous and was stirred at room temperature for 3 days. It was diluted with 2 l. of ether and was extracted repeatedly with 10% Na_2CO_3 solution. The ether

(30) All melting points were taken in glass capillaries and are corrected. The infrared spectra were determined using a Beckman IR-9 spectrophotometer. The ultraviolet spectra were determined using a Cary 14 spectrophotometer. The nmr spectra were determined using a Varian A-60 spectrometer.

(31) This ketone has been reported[5] as an oil which gave a 2,4-dinitrophenylhydrazone with mp 162–164°, $\lambda_{max}^{alcohol}$ 364 mμ (saturated ketone); no analyses given.

(32) J. Demaecker and R. H. Martin, *Nature*, **173**, 266 (1954).

layer was dried (Na_2SO_4) and concentrated to give a black oil, which was heated under reflux for 8 hr with a solution of 10 g of KOH in 250 ml of water and 250 ml of ethanol. The reaction mixture was cooled and filtered to give gummy orange crystals which on recrystallization from methanol gave 1.50 g (6%) of XIIIa as pale yellow crystals, mp 172–175°. Further recrystallization from methanol gave the analytical sample as colorless crystals: mp 177–178°; $\lambda_{max}^{C_2H_5OH}$ 242 mμ (ε 11,600) and 328 mμ (ε 29,400); $\nu_{max}^{CHCl_3}$ 1645, 1610, and 1585 cm^{-1}.

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 80.04; H, 7.73.

2-Ethyl-1,4,4aβ,9,10,10aβ-hexahydro-7-methoxy-3(2H)-phenanthrenone (Xa) from XIIIa.—A solution of 1.0 g (0.0039 mole) of XIIIa in 50 ml of benzene containing 2.0 ml of ethylene glycol and 2 mg of *p*-toluenesulfonic acid was heated under reflux (Dean–Stark trap) for 40 hr. The cooled reaction mixture was poured into 0.1 *N* NaOH and extracted three times (CH_2Cl_2). The extracts were dried (Na_2SO_4) and then concentrated to a colorless oil which was dissolved in 100 ml of ethyl acetate and hydrogenated at room temperature and pressure in the presence of 100 mg of 10% Pd–C. One molar equivalent of hydrogen was absorbed in 30 min whereupon the rate of hydrogenation markedly decreased. The catalyst was removed by filtration, and the filtrate was evaporated to yield a colorless oil. The oil was treated with 50 ml of ethanol and 50 ml of 3 *N* HCl and was heated on the steam bath for 30 min. The cooled solution was diluted with water and was extracted with dichloromethane. The extracts were dried (Na_2SO_4) and evaporated to give a colorless oil. Two crystallizations from methanol gave 0.40 g (40%) of Xa as colorless crystals, mp 88–90°. Further recrystallization from methanol gave the pure product, mp 90–91°, undepressed on mixing with a sample of Xa prepared from VIIIa. In addition, the two samples had identical infrared spectra in chloroform solution and were not separated on thin layer chromatography.

7′-Methoxy-1′,4′,4′aα,9′,10′,10aβ-hexahydrospiro[1,3-dioxolane-2,3′(2′H)-phenanthrene] (XIVa).—A solution of 50.0 g (0.18 mole) of Va in 250 ml of tetrahydrofuran was added over 30 min to a stirred and refluxing solution of 80 g (2.05 g-atoms) of potassium in 1.5 l. of liquid NH_3 (distilled through a tower filled with KOH pellets). After the reaction had stirred for an additional 30 min, excess NH_4Cl was added to discharge the blue color, and the ammonia was allowed to evaporate. The residue was diluted with 2 l. of water and extracted (CH_2Cl_2). The extracts were dried (Na_2SO_4) and concentrated to a yellow oil which on mixing with ether gave 5.3 g (10.6%) of crude B/C-*cis* ketal VIa. The mother liquors were concentrated, and the residue was crystallized from methanol to give 37.0 g (74%) of the B/C-*trans* ketal XIVa as colorless crystals, mp 73–75°. Recrystallization from methanol gave the analytical sample: mp 77–78°; $\lambda_{max}^{C_2H_5OH}$ 218 mμ (ε 8900), 278 (2200), and 287 (2020).

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.54; H, 7.71.

1,4,4aα,9,10,10aβ-Hexahydro-7-methoxy-3(2H)-phenanthrenone (XVa).—A solution of 14.5 g (0.053 mole) of XIVa in 450 ml of methanol and 75 ml of 3 *N* HCl was allowed to stand at room temperature for 30 min. The reaction mixture was diluted with 450 ml of water and was then filtered to give 10.2 g (84%) of XVa as colorless crystals, mp 136–137°. Recrystallization from ethanol gave the analytical sample: mp 137–138°;[33] $\lambda_{max}^{C_2H_5OH}$ 220 (infl) mμ (ε 8400), 278 (2050), and 287 (1900); ν_{max}^{KBr} 1708 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.20; H, 7.85.

The 2,4-dinitrophenylhydrazone of XVa (prepared in 82% yield) crystallized from ethanol as orange-red crystals, mp 203–206°. Recrystallization from a mixture of ethyl acetate and ethanol gave the analytical sample: mp 205.5–208.5°;[33] $\lambda_{max}^{C_2H_5OH}$ 229 mμ (ε 24,800); ν_{max}^{KBr} 1615 and 1590 cm^{-1}.

Anal. Calcd for $C_{21}H_{22}N_4O_5$: C, 61.45; H, 5.40; N, 13.65. Found: C, 61.58; H, 5.59; N, 13.61.

Hydrolysis of the 2,4-Dinitrophenylhydrazone of XVa.—A solution of 200 mg (0.5 mmole) of the 2,4-dinitrophenylhydrazone of XVa in 1 ml of concentrated HCl and 50 ml of acetone was heated under reflux for 30 min. The reaction mixture was then poured into a solution of 1.0 g of $SnCl_2$ in 4 ml of concentrated HCl and 6 ml of water, and the mixture was heated under reflux for an additional 30 min. The acetone was removed under vacuum at room temperature and the residue was diluted with water and extracted with benzene. The organic layer was repeatedly washed with 1 *N* HCl, dried (Na_2SO_4), and concentrated to a colorless crystalline residue. Recrystallization from ethanol gave 82 mg (73%) of the B/C-*trans* ketone XVa, mp 137–138°, undepressed upon admixture with XVa prepared from XIVa.

Methyl 1,2,3,4,4aα,9,10,10aβ-Octahydro-7-methoxy-2-oxo-2-phenanthrenecarboxylate (XVIa).—Dimethyl carbonate (10 ml) was distilled under nitrogen from NaH into a flask containing the NaH obtained by repeatedly washing with dry xylene [420 mg (0.0087 mole) of 50% NaH in mineral oil dispersion]. A slurry of 1.00 g (0.0043 mole) of XVa in 10 ml of xylene was added, and the reaction mixture was heated under reflux for 3 hr. The mixture was cooled and poured onto crushed ice, acidified with acetic acid, and extracted with ether. The extracts were dried (Na_2SO_4) and concentrated under vacuum to yield a colorless oil which was crystallized from methanol to give 1.13 g (90%) of XVIa, mp 114–138°. Recrystallization from methanol gave the analytical sample: mp 113–144° (the melting point varied erratically with the rate of heating and with the solvent used for crystallization); $\lambda_{max}^{C_2H_5OH}$ immediately 220 (infl) mμ (ε 8900), 258 (9400), and 285 (infl) (2300); 24 hr later 220–228 (infl) mμ (ε 9100), 258 (9900), and 286 (infl) (2400); $\lambda_{max}^{0.1\ N\ HCl}$ 225 mμ (ε 8700); λ_{max} 258 mμ (ε 9300); $\lambda_{max}^{0.1\ N\ KOH}$ 284 mμ (ε 14,900); $\nu_{max}^{CHCl_3}$ 1748, 1713, 1660, and 1616 cm^{-1}.

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 71.04; H, 6.79.

2-Methyl-7-methoxyphenanthrene from XVIIIa.—One drop of 6 *N* NaOH was added to a solution of 177 mg (0.73 mmole) of XVIIIa in 25 ml of methanol, followed by an excess of solid $NaBH_4$. The reaction mixture was allowed to stand at room temperature for 90 min. At the end of this time excess acetone was added and the solution was concentrated under vacuum at room temperature. The residue was diluted with water and extracted (CH_2Cl_2). The extracts were dried (Na_2SO_4) and concentrated to a colorless residue, $\nu_{max}^{CHCl_3}$ 3630 cm^{-1}, no carbonyl absorption. This residue was mixed with 60 mg of 10% Pd–C in 6 ml of *p*-*t*-butyltoluene[16] and was heated under reflux overnight. The cooled solution was filtered from the catalyst and the filtrate was concentrated under vacuum to give an orange oil. This oil was dissolved in benzene and filtered through a short column of alumina (grade III). Concentration of the eluates gave 74 mg of yellow gummy crystals which, after repeated recrystallization from methanol, gave 4 mg (4%) of product as yellow crystals, mp 140–142°, undepressed upon admixture with an authentic sample.[17] In addition, the infrared (KBr) and ultraviolet (C_2H_5OH) spectra were identical with those of the authentic sample.

3,4-Dihydro-6,7-dimethoxy-2-(3-oxobutyl)-1(2H)-naphthalenone (IIIb).—To a cold (0–5°) suspension of 117 g (0.50 mole) of 3,4-dihydro-2-hydroxymethylene-6,7-dimethoxy-1(2H)-naphthalenone[18] in 2 l. of methanol and 54 g (0.77 mole) of methyl vinyl ketone was added (over 20 min) a solution of 10 g of triethylamine in 200 ml of methanol. The reaction was carried out and worked up as described under the preparation of IIIa to to give, after crystallization from ethanol, 118 g (85%) of IIIb, mp 82–83°. Further recrystallization from ethanol gave the analytical sample as colorless crystals: mp 83–84°; $\lambda_{max}^{C_2H_5OH}$ 233 mμ (ε 18,600), 275 (12,400), and 314 (8400); $\nu_{max}^{CHCl_3}$ 1713 and 1668 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.84; H, 7.46.

1,9,10,10a-Tetrahydro-6,7-dimethoxy-3(2H)-phenanthrenone[19] (IVb).—A mixture of 118 g (0.43 mole) of IIIb in 1 l. of methanol and 100 g of KOH in 1 l. of water was heated under reflux for 15 min, cooled to room temperature, and filtered to give 100 g (91%) of IVb as yellow crystals, mp 208–210°. Recrystallization from ethanol gave the pure product as colorless crystals: mp 213–214°; $\lambda_{max}^{C_2H_5OH}$ 242 mμ (ε 10,400), 310 (13,000), and 346 (20,400); $\nu_{max}^{CHCl_3}$ 1639 cm^{-1}; nmr ($CDCl_3$) τ 2.81 (1 proton singlet, 5 H), 3.27 (1 proton singlet, 8 H), 3.50 (1 proton doublet, J = 2 cps, 4 H split by 10a H).

6′,7′-Dimethoxy-1′,4′,9′,10′-tetrahydrospiro[1,3-dioxolane-2,3′(2′H)-phenanthrene] (Vb).—A solution of 100 g (0.39 mole) of IVb in 2 l. of benzene containing 90 ml of ethylene glycol and 100 mg of *p*-toluenesulfonic acid was heated under reflux (Dean–Stark trap) for 3 days. The reaction mixture was worked up as

(33) This ketone has been reported[5] as colorless crystals with mp 123–125° (from benzene), ν_{max} 1717 cm^{-1}, forming an orange 2,4-dinitrophenylhydrazone with mp 193–195°; no analyses given.

described for the preparation of Va to give an oil which crystallized on mixing with ether. Filtration gave 106 g (91%) of Vb as tan crystals, mp 110–112°. Crystallization from ether gave the analytical sample of colorless crystals: mp 111–113°; $\lambda_{max}^{C_2H_5OH}$ 217 mμ (ε 25,000), 276 (10,200), 300 (7650), and 310 (infl) (6200); $\nu_{max}^{CHCl_3}$ 1608 and 1581 cm^{-1}; nmr ($CDCl_3$) τ 3.29 and 3.32 (2 protons, 5 H and 8 H).

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.46; H, 7.25.

6′,7′-Dimethoxy-1′,4′,4′aβ,9′,10′,10′aβ-hexahydrospiro[1,3-dioxolane-2,3′(2′H)-phenanthrene] (VIb).—A solution of 40 g (0.133 mole) of Vb in 500 ml of ethyl acetate was hydrogenated at room temperature and pressure in the presence of 4.0 g of 10% Pd-C. Uptake stopped, with 1 equiv of hydrogen being absorbed, after 1 hr. The catalyst was removed by filtration, and the filtrate was evaporated to give 37.1 g (93%) of VIb as colorless crystals, mp 165–167°. Recrystallization from ethyl acetate gave the analytical sample: mp 167–168°; $\lambda_{max}^{C_2H_5OH}$ 223 mμ (ε 8200), 282 (4000), 286 (4000), and 291 (infl) (3300).

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 71.40, 71.04; H, 8.03, 7.71.

1,4,4aβ,9,10,10aβ-Hexahydro-6,7-dimethoxy-3(2H)-phenanthrenone (VIIb).—A solution of 30.4 g (0.10 mole) of VIb in 500 ml of methanol, 500 ml of water, and 10 ml of 6 *N* HCl was heated under reflux for 1 hr and then concentrated to about 500 ml under vacuum. The cooled solution was filtered to give 24.0 g (92%) of VIIb as colorless crystals, mp 105–107°. Recrystallization from methanol[34] gave the analytical sample, mp 108–109°, which 2 weeks later had mp 107–114°. On other preparations the product had mp 107–114° which occasionally, after resolidification, had mp 106–108°; $\lambda_{max}^{C_2H_5OH}$ 230 (infl) mμ (ε 8600), 282 (4600), 286 (4600), and 292 (infl) (3800); $\nu_{max}^{CHCl_3}$ 1705 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.62; H, 7.61.

The 2,4-dinitrophenylhydrazone of VIIb (prepared in 82% yield) after two recrystallizations from benzene had mp 239–241.5°. Further recrystallization from benzene gave the analytical sample of orange crystals: mp 242–243°; $\lambda_{max}^{C_2H_5OH}$ 229 mμ (ε 20,900), 270 (10,600), and 365 (21,400); ν_{max}^{KBr} 1608 and 1592 cm^{-1}.

Anal. Calcd for $C_{22}H_{24}N_4O_6$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.07; H, 5.64; N, 12.63.

Hydrolysis of the 2,4-Dinitrophenylhydrazone of VIIb.—The above 2,4-dinitrophenylhydrazone (226 mg, 0.5 mmole) was hydrolyzed as described for the hydrolysis of the 2,4-dinitrophenylhydrazone of VIIa to give 137 mg of solid. Crystallization from methanol gave 74 mg (55%) of VIIb as pale yellow crystals, mp 105–111°, undepressed on mixing with VIIb prepared from VIb.

Methyl 1,2,3,4,4aβ,9,10,10aβ-Octahydro-6,7-dimethoxy-3-oxo-2-phenanthrenecarboxylate (VIIIb).—A solution of 3.90 g (0.067 mole) of VIIb in 45 ml of a 1.88 *M* solution of magnesium methyl carbonate in dimethylformamide was heated at 130° (nitrogen atmosphere) for 1 hr. The reaction mixture was worked up as described in the preparation of VIIIa. After esterification with diazomethane, the solution was concentrated to an oil which crystallized from methanol to give 2.24 g (47%) of VIIIb as colorless crystals, mp 144–146°. Recrystallization from methanol gave the analytical sample: mp 147–149°; $\lambda_{max}^{C_2H_5OH}$ immediately 230 (infl) mμ (ε 9700), 282 (5400), 286 (5350), and 292 (infl) (4300); after 48 hours 230 (infl) mμ (ε 11,800), 257 (9070), 280 (infl) (7050), 285 (infl) (6200), and 290 (infl) (5000); $\lambda_{max}^{0.1\ N\ KOH}$ 287 mμ (ε 16,300); $\nu_{max}^{CHCl_3}$ 1746 and 1717 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.07; H, 6.90.

Methyl 2-Ethyl-1,2,3,4,4aβ,9,10,10aβ-octahydro-6,7-dimethoxy-3-oxo-2-phenanthrenecarboxylate (IXb).—A slurry of 2.65 g (0.083 mole) of VIIIb and 2.40 g (0.19 mole) of potassium *t*-butoxide in 100 ml of *t*-butyl alcohol was heated under reflux for 1 hr. Ethyl iodide (10 ml) was then added and heating was continued overnight. The reaction mixture was cooled, acidified with acetic acid, and concentrated under vacuum. The residue was diluted with water and extracted with dichloromethane. The extracts were dried (Na_2SO_4) and concentrated to a yellow oil which crystallized from methanol. Recrystallization from methanol gave 835 mg (29%) of the analytical sample of IXb as colorless crystals: mp 145–148°; $\lambda_{max}^{C_2H_5OH}$ 230 (infl) mμ (ε 7600), 282 (4000), 287 (4200), 291 (infl) (3600); no change on standing 48 hr; $\nu_{max}^{CHCl_3}$ 1735 (infl), 1705 cm^{-1}.

Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.49; H, 7.34.

3,4-Dihydro-6,7-dimethoxy-2-(2-ethyl-3-oxobutyl)-1(2H)-naphthalenone (XIIb).—To a cooled solution of sodium methoxide, prepared from 0.23 g (0.01 g-atom) of sodium and 20 ml of methanol, was added 2.34 g (0.01 mole) of IIb. The solution was cooled thoroughly in an ice bath and 8.55 g (0.03 mole) of 2-ethyl-3-oxobutyl-1-trimethylammonium iodide was added, followed by 20 ml of methanol. After stirring at room temperature overnight the slurry was poured onto ice containing an excess of HCl. The resulting mixture was extracted with dichloromethane and the extracts were dried (Na_2SO_4) and concentrated to give an oil (strong ferric chloride test). The oil was dissolved in benzene and extracted three times with cold 10% Na_2CO_3 solution. The benzene solution was filtered through a short column of alumina. The benzene and ether eluates were concentrated to give 1.20 g (39%) of XIIb as a colorless oil (suitable for the next step). Crystallization and recrystallization of 200 mg of this material from methanol gave 87 mg of the analytical sample: mp 79–86° (probably a mixture of stereoisomers); $\lambda_{max}^{C_2H_5OH}$ 233 mμ (ε 17,700), 275 (12,000), and 314 (8150); $\nu_{max}^{CHCl_3}$ 1700 and 1664 cm^{-1}.

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.90; H, 7.75.

2-Ethyl-1,9,10,10a-tetrahydro-6,7-dimethoxy-3(2H)-phenanthrenone (XIIIb).—A mixture of 1.00 g (3.3 mmoles) of XIIb, 10 ml of methanol, 10 ml of water, and 1.0 g of KOH was heated under reflux for 1 hr. The solution was cooled thoroughly and filtered to give 0.477 g (51%) of XIIIb as pale yellow crystals, mp 142–148°. Recrystallization from methanol gave the analytical sample as colorless crystals: mp 152–153.5°; $\lambda_{max}^{C_2H_5OH}$ 224 mμ (ε 9600), 242 (9800), 309 (13,100), and 344 (20,500); $\nu_{max}^{CHCl_3}$ 1645 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.29; H, 7.81.

2-Ethyl-1,4,4aβ,9,10,10aβ-hexahydro-6,7-dimethoxy-3(2H)-phenanthrenone (Xd). From XIIIb.—A solution of 95 mg (0.33 mmole) of XIIIb, 50 ml of benzene, and 2 ml of ethylene glycol containing 10 mg of *p*-toluenesulfonic acid was heated under reflux (Dean–Stark trap) overnight. The cooled reaction mixture was poured into water containing an excess of Na_2CO_3 and extracted three times with dichloromethane. The extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a light tan oil. This was dissolved in 25 ml of ethyl acetate and hydrogenated at room temperature and pressure in the presence of 25 mg of 10% Pd–C. One molar equivalent of hydrogen was absorbed in 30 min, whereupon the rate of hydrogenation markedly decreased. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo* to a colorless oil. This was refluxed for 30 min with 5 ml of methanol and 5 ml of 3 N HCl. The cooled solution was filtered to give a gummy solid which, after crystallization from methanol, gave 15 mg (16%) of Xd as colorless crystals, mp 125–128°, undepressed on mixing with a sample of Xd prepared from VIIIb. In addition the two samples had identical infrared spectra in chloroform solution.

6′,7′-Dimethoxy-1′,4′,4′aα,9′,10′,10′aβ-hexahydrospiro[1,3-dioxolane-2,3′(2′H)-phenanthrene] (XIVb).—A solution of 50.0 g (0.166 mole) of Vb in 500 ml of tetrahydrofuran was added over 1 hr to a stirred and refluxing solution of 13.0 g (1.9 g-atoms) of lithium in 4 l. of liquid NH_3 (distilled through a tower filled with KOH pellets). The reaction was carried out and worked up as described under the preparation of XIVa to yield an oil which on crystallization and recrystallization from ethyl acetate gave 6.5 g (13%) of the B/C-*cis* ketal VIb. The mother liquors were concentrated and crystallized from methanol to give 37.0 g (74%) of the B/C-*trans* ketal XIVb as colorless crystals, mp 99–102°. Recrystallization from methanol gave the analytical sample: mp 102–103°; $\lambda_{max}^{C_2H_5OH}$ 223 mμ (ε 7500), 282 (3700), 286 (3650), 291 (infl) (3100).

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.66; H, 7.77.

Reduction of Vb with Potassium in Liquid Ammonia.—A solution of 20.0 g (0.066 mole) of Vb in 300 ml of tetrahydrofuran was added over 1 hr to a stirred and refluxing solution of 30 g (0.77 g-atom) of potassium in 1500 ml of liquid ammonia. After the reaction had stirred for an additional hour, excess NH_4Cl was

(34) Recrystallization of the ketone VIIb from methanol containing traces of acid gave the corresponding dimethyl ketal, mp 114–115°.

added to discharge the blue color, and the ammonia was allowed to evaporate. The residue was diluted with 1.5 l. of water and filtered to give 2.59 g (13%) of the B/C-*cis* ketal VIb as a colorless solid, mp 155–160°. The filtrate was extracted with dichloromethane, and the extracts were dried (Na_2SO_4) and concentrated under vacuum. The resulting oil was dissolved in 250 ml of methanol, mixed with 100 ml of 1.5 *N* HCl, and allowed to stand at room temperature overnight. The mixture was diluted with water and extracted with dichloromethane, and the organic extracts were extracted with 1 *N* NaOH. The basic extracts were acidified and extracted with dichloromethane. Removal of the solvent gave 7.3 g of the crude phenol as a gummy solid. The latter material could be crystallized (see the preparation of i) or converted into XVb as follows. The crude phenolic material was dissolved in 650 ml of 1 *N* NaOH, 130 ml of dimethyl sulfate was added, and the reaction mixture was stirred at room temperature overnight. Filtration, followed by recrystallization from methanol gave 4.8 g (28%) of the B/C-*trans* dimethoxy ketone XVb as colorless crystals, mp 154–156°, undepressed upon admixture with a sample of XVb prepared from XIVb.

1,4,4aα,9,10,10aβ-Hexahydro-6-methoxy-7-hydroxy-3(2H)-phenanthrenone (i).—The mixture of crude phenolic material obtained from the potassium in liquid NH_3 reduction of 20.0 g (0.066 mole) of Vb was recrystallized from dichloromethane to give 0.90 g (5.5%) of the phenol (i) as colorless crystals, mp 170–174°. Further recrystallization from dichloromethane gave the analytical sample: mp 175–176°; $\lambda_{max}^{C_2H_5OH}$ 225 (infl) mμ (ϵ 7200), 288 (3920), and 295 (infl) (3100); $\nu_{max}^{CHCl_3}$ 3555 and 1712 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.33; H, 7.59.

Preparation of XVb from i.—To a solution of 200 mg (0.8 mmole) of i in 20 ml of 1 *N* NaOH was added 4 ml of dimethyl sulfate. The reaction mixture was stirred at room temperature overnight and then filtered to give 186 mg (88%) of XVb as colorless crystals, mp 156–158°, undepressed upon admixture with the sample of XVb prepared from the B/C-*trans* dimethoxy ketal XIVb.

1,4,4aα,9,10,10aβ-Hexahydro-6-methoxy-3(2H)-phenanthrenone (iii).—To a stirred suspension of 625 mg (0.0024 mole) of i in 8.0 ml of CCl_4 was added enough tetrahydrofuran to affect complete solution at room temperature (15.6 ml), 0.35 ml of diethyl phosphite,[23] and 0.38 ml of triethylamine. After standing at room temperature for 4 days, the reaction mixture was diluted with chloroform, washed with water then with dilute HCl, and then extracted with dilute NaOH. Acidification of the basic extracts gave 224 mg of recovered starting material. The original chloroform solution was dried (Na_2SO_4) and concentrated to a colorless oil. The latter material was dissolved in 3.0 ml of tetrahydrofuran and the resulting solution was cooled in a Dry Ice bath. Liquid ammonia (10 ml) (distilled over KOH pellets) was added, and the solution was allowed to warm to reflux temperature. To this mixture was added 76 mg (3.3 mg-atoms) of sodium, which gave a momentary blue color followed by the appearance of a yellow precipitate. After the reaction mixture had stirred for an additional 10 min at reflux temperature, 3 ml of ethanol was added. The ammonia was allowed to evaporate and the residue, after dilution with benzene, was washed with dilute HCl, water, dilute NaOH, and finally with water. The organic layer was dried (Na_2SO_4) and concentrated to a colorless oil which after crystallization and recrystallization from methanol gave 55 mg (15%) of the analytical sample of iii: mp 97.5–99°; $\lambda_{max}^{C_2H_5OH}$ 225 (infl) mμ (ϵ 6000), 281 (2170), and 289 (1920); $\nu_{max}^{CHCl_3}$ 1710 cm^{-1}.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.59; H, 7.90.

6,7-Dimethoxy-1,4,4aα,9,10,10aβ-hexahydro-3(2H)-phenanthrenone (XVb).—A solution of 41.5 g (0.136 mole) of XIVb in 1 l. of methanol was mixed with 200 ml of 3 *N* HCl. After standing at room temperature for 30 min, the mixture was filtered to give 24.35 g of colorless crystals of XVb, mp 156–157°. An additional 7.48 g (mp 156–157°) was recovered from the filtrate (total yield of 31.83 g, 90%). Recrystallization from methanol gave the analytical sample: mp 157.5–158.5°; $\lambda_{max}^{C_2H_5OH}$ 230 (infl) mμ (ϵ 7300), 283 (3900), 287 (3900), and 292 (infl) (3250); $\nu_{max}^{CHCl_3}$ 1717 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.01; H, 7.84.

Methyl 1,2,3,4,4aα,9,10,10aβ-Octahydro-6,7-dimethoxy-3-oxo-2-phenanthrenecarboxylate (XVIb).—Dimethyl carbonate (150 ml) was distilled under nitrogen from NaH into a flask containing the NaH obtained by repeatedly washing with xylene [6.5 g (0.135 mole) of 50% NaH in mineral oil dispersion]. A solution of 15.0 g (0.058 mole) of XVb in 100 ml of dry xylene was added to the mixture, and the reaction was carried out and worked up as described for the preparation of XVIa. The resulting oil was crystallized from methanol to give 16.5 g (90%) of XVIb as colorless crystals, mp 127–132°. Recrystallization from methanol gave the analytical sample: mp 131–137° (a mixture of tautomeric forms); $\lambda_{max}^{C_2H_5OH}$ 232 mμ (ϵ 9500), 257 (9000), 281 (infl) (5600), and 292 (infl) (3600); $\nu_{max}^{CHCl_3}$ 1745, 1716, 1660, and 1617 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.81; H, 7.05.

Preparation of 2α-Alkyl-1,4,4aα,9,10,10aβ-hexahydro-6,7-dimethoxy-3(2H)-phenanthrenones (XVIIIe–g). General Method C.—The crude XVIIb (general method A) from 0.03 mole of XVIb was mixed with 40 ml of water, 80 ml of methanol, and 0.075 mole of K_2CO_3, and the resulting solution was heated under reflux overnight. The cooled reaction mixture was diluted with water and extracted with dichloromethane. The extracts were dried (Na_2SO_4) and concentrated under vacuum to give a residue from which XVIIIe–g could be crystallized (see Table I).

2α-Ethyl-1,4,4aα,9,10,10aβ-hexahydro-6,7-dimethoxy-3(2H)-phenanthrenone (XVIIIe). From XIIIb.—A solution of 300 mg (1.05 mmoles) of XIIIb, 100 ml of benzene, and 5 ml of ethylene glycol containing 25 mg of *p*-toluenesulfonic acid was heated under reflux (Dean–Stark trap) overnight. The cooled reaction mixture was then poured into water containing an excess of Na_2CO_3 and was extracted (CH_2Cl_2). The extracts were dried (Na_2SO_4) and concentrated to an oil. The latter mixture, dissolved in 5 ml of tetrahydrofuran, was added over 10 min to a stirred and refluxing solution of 1.0 g (25 mg-atoms) of potassium in 20 ml of liquid ammonia (distilled through a tower filled with KOH pellets). The mixture was stirred for an additional 30 min whereupon an excess of NH_4Cl was added to discharge the blue color. The ammonia was allowed to evaporate, and the residue was diluted with water and extracted with dichloromethane. The extracts were dried and concentrated to an oil, which was dissolved in 10 ml of methanol and mixed with 2 ml of 3 *N* HCl. The resulting solution was allowed to stand at room temperature for 3 days and then diluted with 10 ml of water. The resulting precipitate was collected and recrystallized twice from methanol to give 4 mg of XVIIIe, mp 144–145°, undepressed upon admixture with a sample of XVIIIe prepared from XVIb.

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