TABLE VII

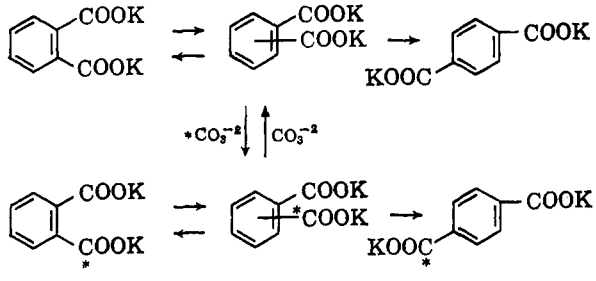
CESIUM 2-NAPHTHOATE WITH CADMIUM CHLORIDE[a]

Temp., °C.	CO_2, p.s.i. Charged	CO_2, p.s.i. Max.	2,6-NDCA, % yield	Naphthalene, mg.	Residue, mg.
400[b]	200	425	76	437	114
400[c]	300	680	82	598	112
425[c]	300	700	76	558	131
450[c]	300	735	66	684	177

[a] Ten mmoles of salt with 5 mole % catalyst. [b] For 0.5 hr. [c] Method YY: heating bomb (300 ml.) bottom to stated temperature and discontinuing heating.

untenable in the light of the intermediate findings. Further, if this suggestion were valid in the naphthalene series, a ring barrier would prevail and the most stable isomer derivable from naphthalene-2,3-dicarboxylate would be naphthalene-1,4-dicarboxylate. This is not the case since the 1,3 isomer and the 2,3 isomer as well as a 1,2–1,4 isomer mixture are converted to the 2,6 isomer.

An important mechanistic scheme is Ogata's intramolecular mode involving π-complexes.[12] This proposal grew out of Ogata's finding that radioactive



terephthalate is formed in small amounts in the *o*-phthalate and the benzoate reactions when radioactive potassium carbonate or cadmium carbonate were in the reaction mixture. These results would argue against a decarboxylation–recarboxylation reaction mode which predicts that radioactivity should have been found to a greater extent in the terephthalate, provided that the carbonates decompose extensively to their oxides and carbon dioxide at reaction conditions. This proviso is incorrect. Cadmium carbonate decomposes at 510° according to differential thermal analysis[16]; potassium carbonate does not decompose to an appreciable extent[17] below 500°. The fact that some radioactivity is found in terephthalate and unreacted *o*-phthalate might be explained by a small amount of such decompositions. For the lack of clear-cut data on this point, the π-complex mechanism might appear to be a solution. In this mechanism, however, no mention is made of the fate of the displaced hydrogen in the position that the carboxyl will occupy. Such an exchange is without precedent. Furthermore, this incompletely delineated proposal ignores the very real possibility that there is a carbonate–gaseous carbon dioxide exchange. That carbonates in general do exchange with gaseous carbon dioxide at a rapid rate between 350 and 400° has been shown by Shushunov and Zateev.[18] The carbon dioxide arises from the decarboxylation of the phthalate and exchanges with the radioactive carbonate. The radioactive gas can then be incorporated by reaction with an aromatic anion formed by decarboxylation. Consequently, the intramolecular reaction mechanism is without valid argumentation.

Acknowledgment.—The author wishes to thank Dr. Charles L. Thomas, Professor Cheves Walling, and Professor Wayland Noland for helpful discussions and Mr. Eugene White for technical assistance.

(16) C. N. R. Rao, S. R. Yoganarasimhan, and M. P. Lewis, *Can. J. Chem.*, **38**, 2359 (1960).
(17) D. Janjic, E. Briner, and H. Pillard, *Helv. Chim. Acta*, **38**, 349 (1955)
(18) V. A. Shushunov and B. G. Zateev, *Zh. Fiz. Khim.*, **30**, 321 (1956).

The Synthesis and Stereochemistry of Octahydrophenanthrenes. II[1,2]

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The addition of ethyl acrylate to the diene I gave, after saponification, 1,2,3,9,10,10aβ-hexahydro-7-methoxy-2α-phenanthrenecarboxylic acid (III). This acid was converted into its isopropyl ester IX, which, upon hydroboration and oxidation, gave the B/C *cis* (XIV) and the B/C *trans* (XXV) octahydro-7-methoxy-4-oxo-2-phenanthrenecarboxylic acids. The B/C *cis* keto acid XIV could be converted into the other possible B/C *cis* stereoisomer XVII. All possible isomeric nonlactonizing and lactonizing acids and lactones of this series were prepared, and their stereochemistry was established. In the B/C *trans* series, the lactones with ring C in the chair and with ring C in the boat conformation, have been prepared (XII and XXVII). N.m.r. spectroscopy provided additional proof for the stereochemistry of the compounds of this series.

In continuation of the work on the octahydrophenanthrene-1-carboxylic acids,[2] the synthesis and stereochemical studies of several new C-2-, C-4-, and C-7-substituted octahydrophenanthrene derivatives is now described.

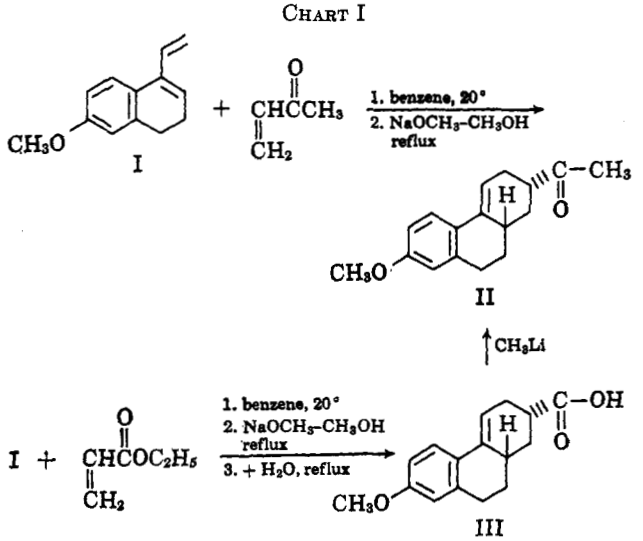
The starting material for the preparation of the derivatives was 3,4-dihydro-6-methoxy-1-vinylnaphthalene (I).[4a,b] The reaction of I with methyl vinyl

(1) Presented before the Organic Chemical Division at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.
(2) Part I: Z. G. Hajos, K. J. Doebel, and M. W. Goldberg, *J. Org. Chem.*, **29**, 2527 (1964).
(3) Deceased Feb. 17, 1964.
(4) (a) P. A. Robins and J. Walker, *J. Chem. Soc.*, 3249 (1956); (b) M. W. Goldberg and W. E. Scott, U. S. Patent No. 2,894,958 (July 14, 1959).

ketone in benzene at room temperature yielded the expected *endo* addition product, 2α-acetyl-1,2,3,9,-10,10aβ-hexahydro-7-methoxyphenanthrene (II).[4b] The methyl ketone II did not change after being refluxed for 2 hr. with 2.6 *N* sodium methoxide in methanol. This treatment actually increased the yield of II from 12 to 32%. This is in accord with the suggested stereochemistry of the compound, because with a $\Delta^{4(4a)}$ double bond, it is the 2α equatorially oriented side chain which allows ring C to be in the semichair formation.

The reaction of the diene I with ethyl acrylate in benzene at room temperature, followed by refluxing for 2 hr. with 2.0 *N* sodium methoxide in methanol and saponification, yielded the *endo* addition product, 1,2,3,9,10,10aβ-hexahydro-7-methoxy-2α-phenanthrenecarboxylic acid III (32.6%). This compound, with methyllithium in tetrahydrofuran, gave the methyl ketone II in good yield (Chart I).

CHART I



The $\Delta^{4(4a)}$ double bond of the acid III rearranges into the thermodynamically more stable $\Delta^{4a(10a)}$ position with acid.[4b] The methyl ester IV was therefore prepared under neutral conditions by causing the acid III to react with diazomethane in ether.

Attempted hydroboration[5] of the methyl ester IV with the theoretical amount of diborane left about 50% of the double bond intact, as determined by ultraviolet spectroscopy. Using 0.5 mole of diborane for 1.0 mole of ester IV, the double bond was saturated but the reaction product consisted of a mixture of diols. Only a small amount of the *cis* V and an even smaller amount of the *trans* VI diol could be isolated from this mixture (Chart II). The stereochemistry of V and VI were established later (Chart V).

The isopropyl ester IX of the unsaturated acid III was then prepared using Staab's imidazolide method.[6a,b] The over-all yield from III to IX was 93% (Chart III).

Hydroboration[5] of the isopropyl ester IX was carried out using 0.5 mole of diborane for 1.0 mole of IX. It was hoped that the bulkiness of the isopropyl group would present enough steric hindrance to protect the

CHART II

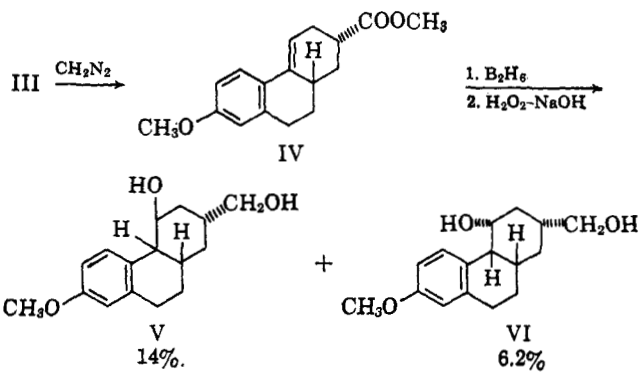
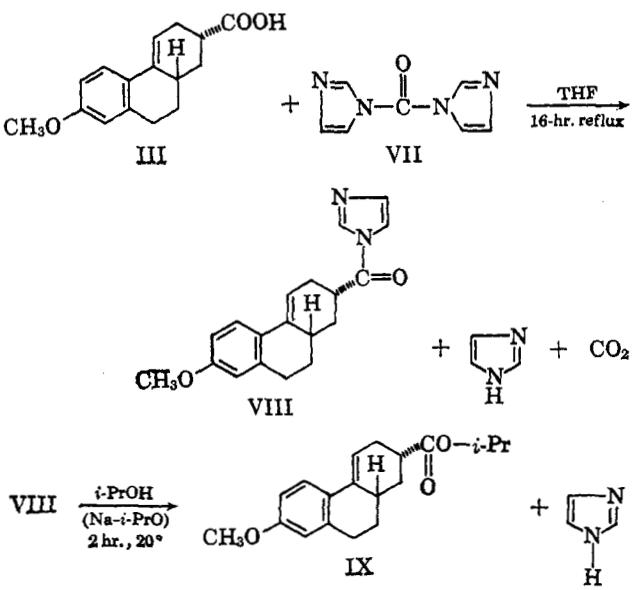


CHART III



ester group during the hydroboration. Oxidation with alkaline hydrogen peroxide yielded a mixture of hydroxy esters and diols which was saponified. Extraction of the basic solution gave the *cis* diol V (7.6%) and the *trans* diol VI (9.3%). The remaining mixture of hydroxy acids X and XI was separated by lactonization. Based on the ester IX, 29.0% of the nonlactonizing acid X and 12.2% of the lactone XII were isolated (Chart IV).

The stereochemistry of the major hydroboration product X is consistent with the *cis* addition[5] of the relatively bulky diborane to the olefinic double bond by attack at the sterically less hindered top side of IX. The lactone XII which is the minor product of the hydroboration, results from *cis* addition of diborane to the double bond from the more hindered bottom side of the molecule IX. Proof for its stereochemistry will be given later (Chart VIII).

The stereochemical relationship of the two diols V and VI to the main hydroboration products X and XII was then determined. The lithium aluminum hydride reduction of the methyl ester XIII of the nonlactonizing acid X gave the diol V in excellent yield, thereby establishing its B/C *cis* configuration and the stereochemistry of the substituents. The reduction of the B/C *trans* lactone XII with a large excess of sodium borohydride in ethanol, on the other hand, yielded the

(5) G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).
(6) (a) H. A. Staab, M. Lüking, and F. H. Dürr, *Ber.*, **95**, 1275 (1962); (b) H. A. Staab and A. Mannschreck, *ibid.*, **95**, 1284 (1962).

CHART IV

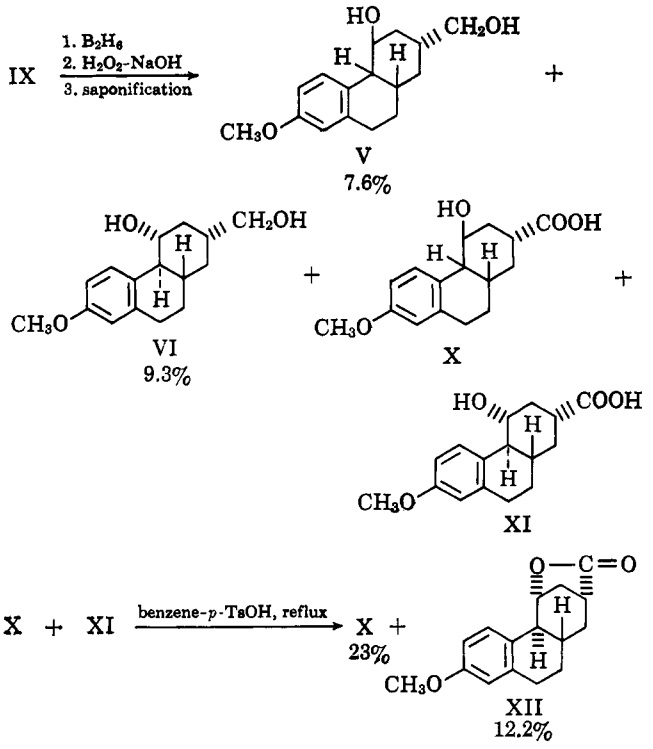
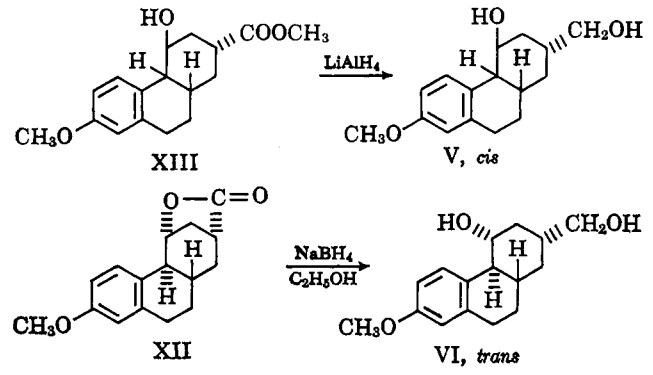


CHART V



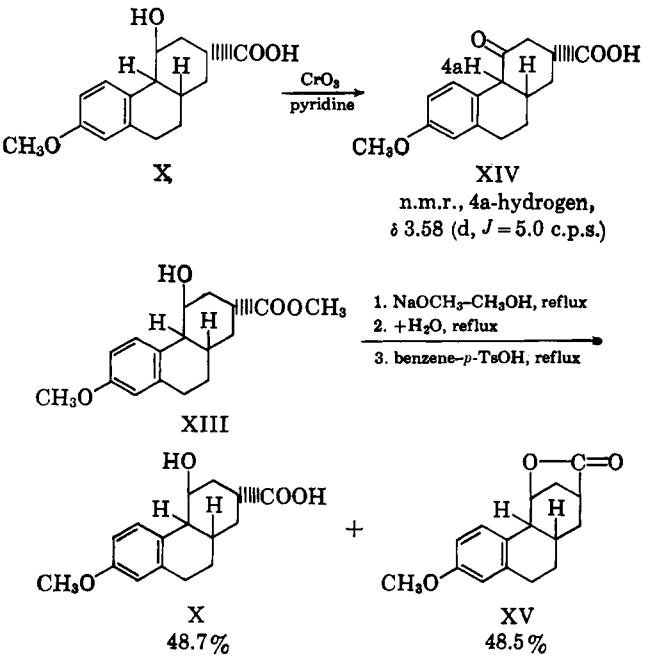
B/C *trans* diol VI in good yield (Chart V). Reduction of lactones with $NaBH_4$ has recently been reported.[7a,b]

The nonlactonizing hydroxy acid X was oxidized with chromium trioxide–pyridine to the corresponding keto acid XIV. The n.m.r. spectrum of XIV was determined at 60 Mc. with tetrahydrofuran-d_8 as the solvent and tetramethylsilane as the internal standard and the signal for the 4a-hydrogen appeared at δ 3.58 (doublet, J = 5.0 c.p.s.). The small coupling constant is in agreement with the assumed B/C *cis* configuration of the major hydroboration product, the nonlactonizing hydroxy acid X (Chart VI).

The methyl ester XIII of the hydroxy acid X was then refluxed for 20 hr. with 2.0 N sodium methoxide in methanol. This was followed by saponification with aqueous base and separation of the mixture of hydroxy acids by lactonization. In this way, 48.7% of the hydroxy acid X and 48.5% of the new lactone XV were obtained (Chart VI). The acid X was formed by saponification of the starting material XIII, whereas

(7) (a) D. M. S. Wheeler and M. M. Wheeler, *J. Org. Chem.*, **27**, 3796 (1962); (b) H. O. House, H. Babad, R. B. Toothill, and A. W. Holtes, *ibid.*, **27**, 4141 (1962).

CHART VI



the new lactone XV had to result from an $\alpha \rightarrow \beta$ inversion of the ester group in XIII. A change in the B/C *cis* configuration could not occur since there is no keto group next to the ring junction.

The lactone XV was saponified to the lactonizing acid XVI which could be reconverted to the lactone XV in excellent yield by refluxing in benzene with a trace of *p*-toluenesulfonic acid. Oxidation of XVI with chromium trioxide–sulfuric acid in acetone gave a new *cis* keto acid XVII. The n.m.r. spectrum of its oxime XVIII was determined at 60 Mc. with perdeuteriopyridine as the solvent and tetramethylsilane as the internal standard and the signal of the 4a-hydrogen of XIV appeared at δ 3.80 (doublet, J = 5.0 c.p.s.). The small coupling constant is in agreement with the assumed B/C *cis* configuration[2] (Chart VII).

The reduction of the new *cis* keto acid XVII with sodium borohydride in 0.1 N sodium hydroxide gave a mixture of hydroxy acids, which were separated by lactonization to give a new *cis* nonlactonizing hydroxy acid XIX in 73% yield along with the previously mentioned lactone XV in 16% yield. Since model studies show a sterically hindered keto group in XVII, the "steric approach control" principle[8a,b] should operate in the reduction. This calls for the formation of the axial alcohol in the reduction of sterically hindered ketones with bulky reducing agents.[7a,9] The nonlactonizing hydroxy acid XIX could be reoxidized to the *cis* keto acid XVII with chromium trioxide–sulfuric acid in acetone (Chart VII).

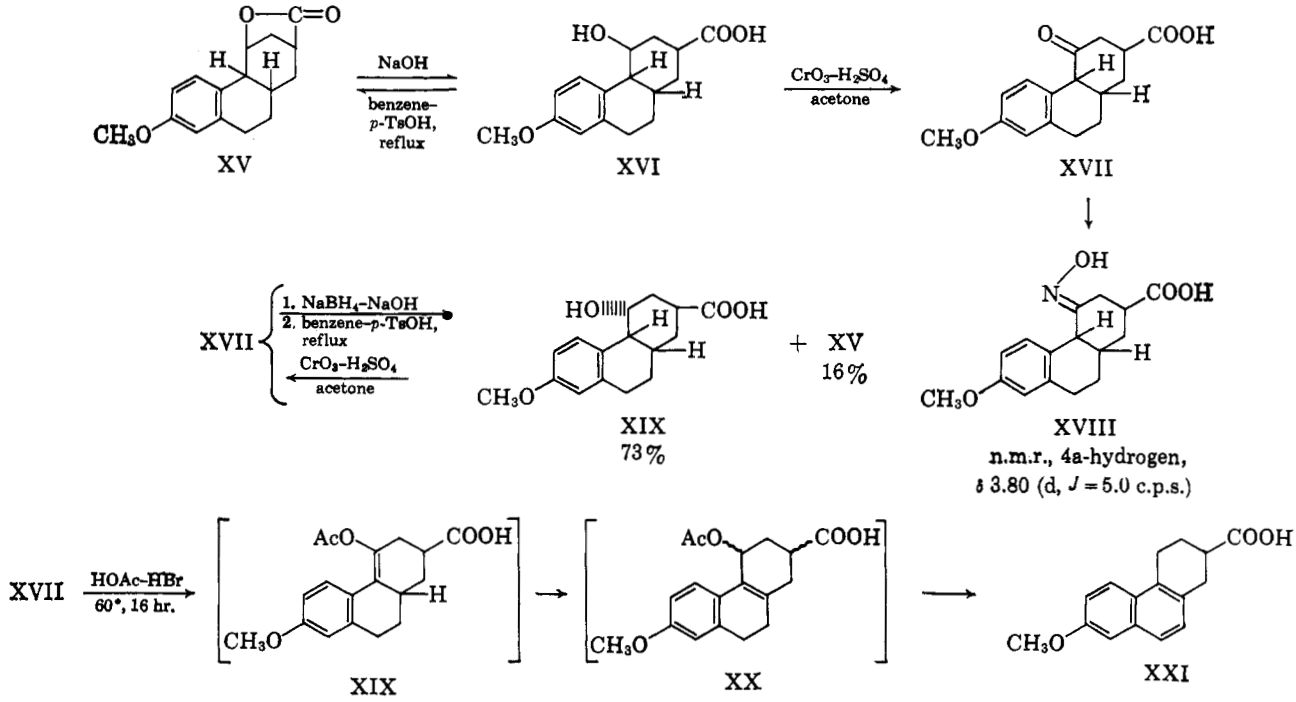
The *cis* keto acid XVII could be converted to the known[10] 1,2,3,4-tetrahydro-7-methoxy-2-phenanthrenecarboxylic acid XXI by treatment at 60° for 16 hr. with acetic acid and a small amount of hydrogen bromide which establishes the position of the carboxyl group. Structures XIX and XX are the postulated

(8) (a) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956); (b) W. G. Dauben, E. J. Blanz, Jr., J. Jiu, and R. A. Micheli, *ibid.*, **78**, 3752 (1956).

(9) K. Heusler, J. Kalvoda, P. Wieland, and A. Wettstein, *Helv. Chim. Acta*, **44**, 179 (1961).

(10) J. Heer and K. Miescher, *ibid.*, **28**, 1506 (1945).

CHART VII



intermediates of the rearrangement. As already mentioned, under acidic conditions, the more stable arrangement in this series has the double bond at the $\Delta^{4a(10a)}$ position. With the 4-acetoxy group, this tendency might be decreased. However, the formation of even a small amount of XX, which involves an allylic hydrogen, would shift the reaction irreversibly toward XXI. The conversion of XX to XXI is very similar to examples already reported in the steroid field.[11a,b]

The sodium borohydride reduction of the isomeric *cis* keto acid XIV in 0.1 *N* sodium hydroxide gave a mixture of hydroxy acids which could be separated by lactonization to give the *cis* lactone XXII in 72% yield and the nonlactonizing *trans* hydroxy acid XXIII in 28% yield. By adding the sodium borohydride after the *cis* keto acid XIV had stood for 45 min. in 1.0 *N* sodium hydroxide, 66.0% of *trans* hydroxy acid XXIII and 20% *cis* lactone XXII were obtained. Upon saponification with aqueous sodium hydroxide, the *cis* lactone XXII gave the *cis* lactonizing hydroxy acid XXIV which, upon oxidation with the chromium trioxide–pyridine complex, yielded the *cis* keto acid XIV. The nonlactonizing *trans* hydroxy acid XXIII, on the other hand, yielded upon oxidation with chromium trioxide–pyridine, a new keto acid XXV which must have the B/C *trans* configuration since the two possible isomeric *cis* keto acids XIV and XVII had already been isolated. The n.m.r. spectrum of the oxime XXVI of the *trans* keto acid XXV was determined at 60 Mc. will perdeuteriopyridine as the solvent and tetramethylsilane as the internal standard and the signal of the 4a-hydrogen appeared at δ 3.53 (doublet, J = 8.0 c.p.s.). This is in agreement with the relationship between the dihedral angle and the coupling constant of vicinal hydrogens.[2]

(11) (a) K. Tsuda, S. Nozoe, and Y. Okada, *Chem. Pharm. Bull.* (Tokyo), **11**, 1271 (1963); (b) M. Heller, R. H. Lenhard, and S. Bernstein, *J. Am. Chem. Soc.*, **86**, 2309 (1964).

Upon reduction with sodium borohydride in 0.1 *N* sodium hydroxide, the B/C *trans* keto acid XXV gave the *trans* nonlactonizing hydroxy acid XXIII in 86% yield (Chart VIII).

The *trans* keto acid XXV was also obtained by oxidizing the *trans* lactonizing hydroxy acid XI with chromium trioxide–pyridine. This acid XI was in turn obtained by saponifying the *trans* lactone XII which had been isolated in the hydroboration–oxidation of the unsaturated isopropyl ester IX (Chart IV). The B/C *trans* configuration of the lactone XII and of the hydroxy acid XI is thus proved.

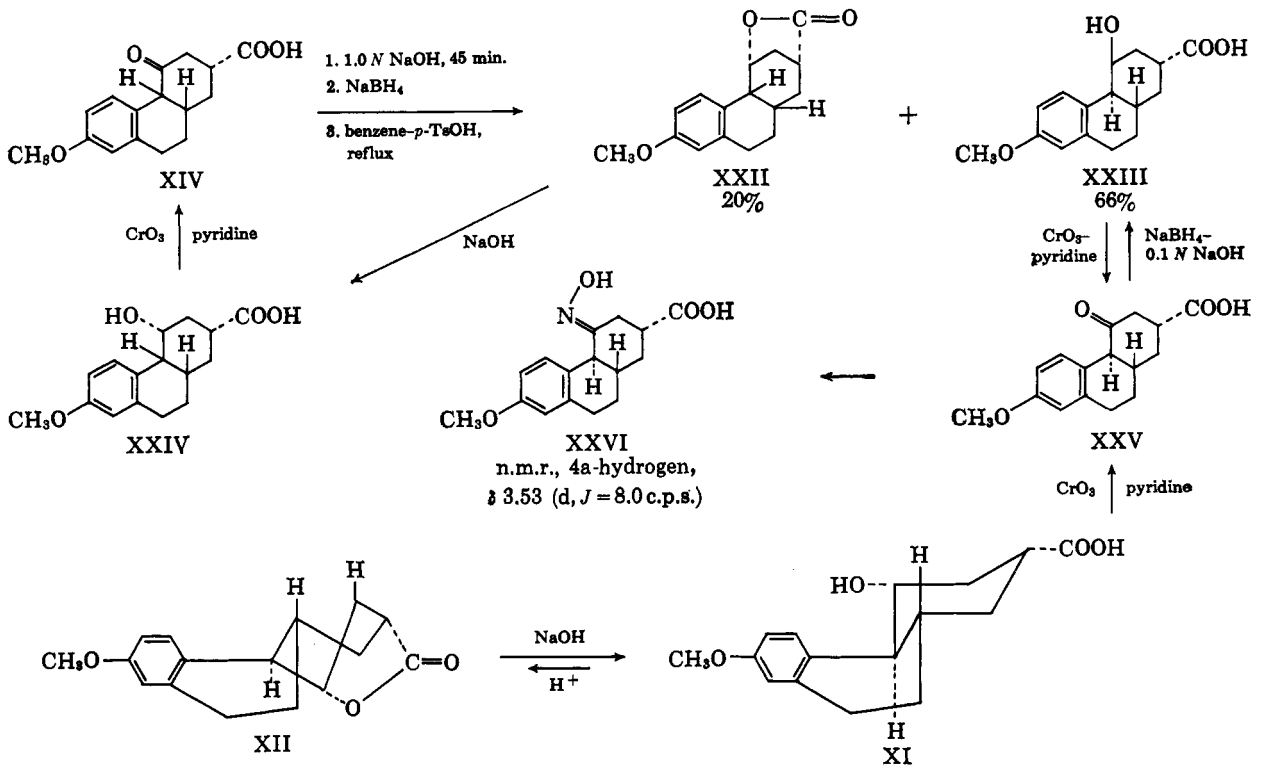
Refluxing the acid XI in benzene with a little *p*-toluenesulfonic acid gave the *trans* lactone XII in a 75% yield. Recovery of 25% of the starting material XI supports the suggested stereochemistry, since the lactonization of the *trans* acid XI requires ring C to flip into the less favorable boat conformation (Chart VIII).

The reduction of the *cis* keto acid XIV with sodium borohydride in sodium hydroxide to give the *cis* XXIV and the *trans* XXIII hydroxy acids can be explained by assuming the presence of a mixture of the *cis* XIV and the *trans* XXV keto acids in the sodium hydroxide solution due to inversion of the B/C *cis* ring junction through enolate formation in the basic solution.

The extent of enolization was determined by ultraviolet spectroscopy in 0.1 *N* sodium hydroxide after standing at 20° for 45 min. (Chart IX). With the *cis* keto acid XVII, the rate of enolization is relatively slow compared with the other *cis* compound XIV. Therefore, the probability of inversion of the B/C *cis* configuration of XVII before the reduction is small.

The amount of the *trans* hydroxy acid XXIII obtained was a function of the normality of the base used and the time which elapsed prior to addition of the reducing agent. Use of more concentrated base and longer exposure time increased the yield of the *trans* acid XXIII from 28 to 66%.

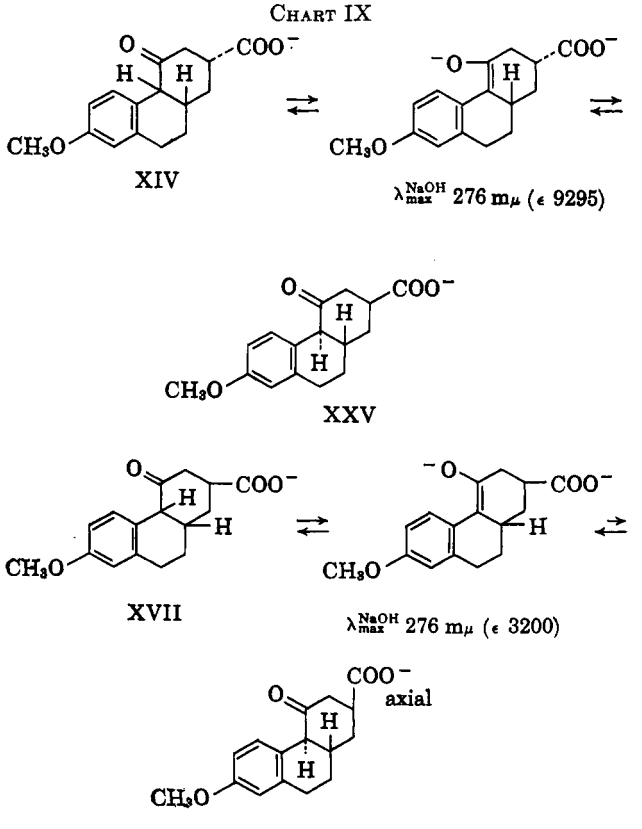
CHART VIII



The sodium borohydride reduction of the isomeric *cis* keto acid XVII gave only *cis* reduction products XVI and XIX because its B/C *trans* partner would have the unfavorable 2β axial side chain, an arrangement which would decrease the probability of its existence in the basic solution (Chart IX).

It should be mentioned that the stereochemistry of the hydroxyl group in the reduction products XXIII and XXIV is in agreement with the principles of the sodium borohydride reduction. Model studies show an unhindered keto group in the *cis* keto acid XIV. The 4α-equatorial hydroxyl group in XXIV is, therefore, in agreement with the "product development control" principle,[8a,b] which calls for the formation of the equatorial alcohol in the reduction of an unhindered ketone. The keto group in the *trans* keto acid XXV, on the other hand, is shielded by the aromatic ring. The β axial hydroxyl group in the *trans* acid XXIII is, therefore, also in agreement with the "steric approach control" principle.[8a,b]

CHART IX



The nonlactonizing hydroxy acid XXIII was also obtained in small quantities in the reduction of the *cis* keto acid XVII with sodium isopropoxide in isopropyl alcohol, the system used by Verley in his original procedure.[12] A small amount of a new γ-lactone XXVII was also isolated from the reaction mixture after refluxing in benzene with *p*-toluenesulfonic acid. Since the two *cis* γ-lactones XV and XXII and the *trans* γ-lactone XII with ring C in the boat conformation are already known, this new γ-lactone XXVII must, by exclusion, have the B/C *trans* configuration with ring C in the chair conformation. Chair and boat lactone isomers have previously been described.[13]

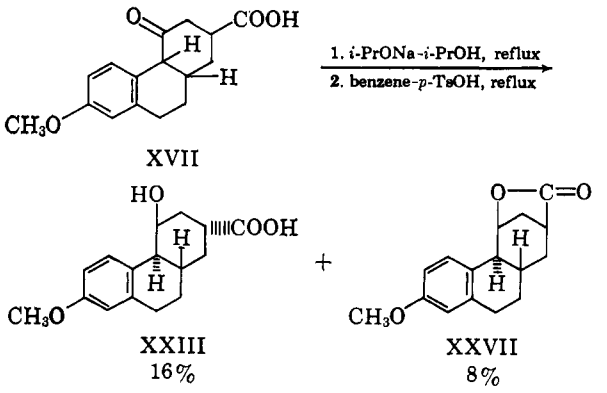
The formation of *trans* compounds XXIII and XXVII in the Verley-type reduction of the *cis* keto acid XVII is due to equilibration of the B/C *cis* ring junction with or without a change in the β-orientation of the substituent in the 2-position (Chart X).

The axial orientation of the hydroxyl groups in the reduction products XXIII and XXVII is consistent with hydride attack from the less hindered equatorial

(12) M. A. Verley, *Bull. soc. chim. France*, **37**, 817 (1925).

(13) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. M. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).

CHART X



direction through a cyclic intermediate, as postulated for Verley reductions.[14]

All compounds described in this paper are racemates. As a matter of convenience, only one enantiomeric series (10aβ-hydrogen) has been pictured.

Experimental[15]

3,4-Dihydro-6-methoxy-1-vinylnaphthalene (I).—The diene I was prepared according to the method described in the literature[4a] from crude 1,2,3,4-tetrahydro-1-hydroxy-6-methoxy-1-vinylnaphthalene by refluxing in benzene with a small amount of iodine and quinoline using the Dean–Stark apparatus to separate the water. After the theoretical amount of water was collected, the benzene solution was cooled to about 10° and extracted with a dilute NaCl solution, then with a dilute $NaHCO_3$ solution, and again with a dilute NaCl solution. It was then dried with Na_2SO_4 and filtered and this benzene solution of the diene I was used in the preparation of the methyl ketone II and the acid III.

2α-Acetyl-1,2,3,9,10,10aβ-hexahydro-7-methoxyphenanthrene (II).—The preparation of this compound II has already been described.[4b] An improved preparation is given here. To 1 l. of a benzene solution of the crude diene I prepared from 204 g. (1 mole) of crude 1,2,3,4-tetrahydro-1-hydroxy-6-methoxy-1-vinylnaphthalene was added, with stirring under nitrogen and with external cooling, 160 ml. of methyl vinyl ketone. The cooling bath was then removed and the reaction mixture was allowed to stand for 72 hr. at 20° under nitrogen. NaOMe (1 *N*) in methanol (10 ml.) was then added, and the solvents and excess methyl vinyl ketone were removed *in vacuo*. NaOMe (2 *N*) in methanol (400 ml.) was added and the solution was refluxed for 2 hr. under nitrogen with stirring. It was then cooled to 20°, poured into 1 l. of ice–water, and extracted first with ethyl acetate then with ether. The combined extract was washed with water, dried with $MgSO_4$, and evaporated *in vacuo*. The remaining oil crystallized upon the addition of a mixture of 50 ml. of ether and 50 ml. of petroleum ether (b.p. 30–60°) to give 90.25 g. of the crude ketone II. This material was recrystallized from 1500 ml. of ligroin (b.p. 90–120°) and gave 82.20 g. (32.1%) of the pure methyl ketone II: m.p. 87.5–89°, λ_{max} 263 mμ (ε 21,200) and 296 mμ (ε 3600), ν_{max}^{KBr} 1715 cm.$^{-1}$ (keto carbonyl).

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.35; H, 8.09.

1,2,3,9,10,10aβ-Hexahydro-7-methoxy-2α-phenanthrenecarboxylic Acid (III).—To 1 l. of a benzene solution of the crude diene I prepared from 204 g. (1 mole) of crude 1,2,3,4-tetrahydro-1-hydroxy-6-methoxy-1-vinylnaphthalene was added, with stirring under nitrogen, 300 ml. of ethyl acrylate. The mixture was allowed to stand for 72 hr. under nitrogen at 20°. The solvent and the excess ethyl acrylate were removed *in vacuo*, 1 l. of 2 *N* NaOMe in methanol was added, and the solution was stirred and refluxed under nitrogen for 16 hr. Water (200 ml.) was added to the cooled solution, and the mixture was saponified by stirring and refluxing under nitrogen for 2 hr. It was then cooled, 3 l. of ice–water was added, and the solution was acidified slowly, while stirring, with 2 *N* HCl to pH 5. After stirring for 1 hr. in the cold, the crystalline precipitate was filtered and dried *in vacuo* at 60° for 16 hr. Recrystallization from acetone gave 84.0 g. (32.6%) of the unsaturated acid III: m.p. 184–186°, λ_{max} 263 mμ (ε 20,400) and 298 mμ (ε 3280), $\nu_{max}^{CHCl_3}$ 3500 and 2540–2700 (OH of acid) and 1700 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.23; H, 7.18.

Preparation of the Methyl Ketone II from the Unsaturated Acid III.—The acid III (7.8 g.) was dissolved in 100 ml. of dry THF. The solution was stirred under nitrogen and 45 ml. of a 2 *N* CH_3Li solution in ether was added within 1 hr. at 20°. After all the CH_3Li was added, stirring was continued for 1 hr. at 20°. The solution was then added slowly to ice–water, and the ether and most of the THF were evaporated *in vacuo*. The aqueous phase was extracted with ethyl acetate and then with ether. The combined extract was washed with a dilute $NaHCO_3$ solution and then with water, dried with $MgSO_4$, and evaporated *in vacuo*. The residual oil crystallized from ether–petroleum ether, and gave 5.38 g. of the methyl ketone II, which was in every respect identical with the sample prepared from the diene I.

1,2,3,9,10,10aβ-Hexahydro-7-methoxy-2α-phenanthrenecarboxylic Acid Methyl Ester (IV).—The acid II (12.4 g.) was esterified with about 4.4 g. of diazomethane in ether. After evaporation of the ether *in vacuo*, 13.0 g. of the crude methyl ester was obtained. Recrystallization from ligroin (b.p. 90–120°) gave 11.0 g. of the pure ester IV: m.p. 71–72°, λ_{max} 263 mμ (ε 19,800) and 296 mμ (ε 3220), $\nu_{max}^{CHCl_3}$ 1720 cm.$^{-1}$ (ester carbonyl).

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.08; H, 7.52.

Preparation of the Diborane Solution.—A solution of B_2H_6 in THF was prepared by adding 73 ml. of boron trifluoride etherate in 200 ml. of diglyme to a stirred solution of 17.1 g. of $NaBH_4$ in 400 ml. of diglyme, and driving the B_2H_6 gas with the help of a stream of dry nitrogen over a period of 16 hr. into a receiver containing 400 ml. of THF, which was stirred at −70°. A trap containing 2.2 g. of $NaBH_4$ in 100 ml. of diglyme was placed between the generator and the receiving flask to capture any BF_3 that might have been entrained.

The B_2H_6 contents of the solution was determined by taking an aliquot, converting the B_2H_6 into H_3BO_3, and by titrating the latter using the standard procedure.[16] The concentration was found to be 5.25 g. of B_2H_6 in the 400 ml. of THF solution.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4β-hydroxy-2-α-hydroxymethyl-7-methoxyphenanthrene (V) and 1,2,3,4,4aα,9,10,10aβ-Octahydro-4α-hydroxy-2α-hydroxymethyl-7-methoxyphenanthrene (VI).—Ester IV (5.0 g.) was dissolved in 25 ml. of anhydrous THF. The solution was stirred under nitrogen at 20–23° and 22 ml. of the previously described B_2H_6 solution in THF (5.25 g. of B_2H_6 in 400 ml. of THF) was added over a period of 1 hr. This amount corresponds to 0.5 mole of B_2H_6 for 1 mole of the ester XIV. After standing for 2 hr. at 20°, the solution was cooled in an ice bath, and ice was added carefully to destroy the excess diborane.

NaOH (3 *N*, 20 ml.) was added to the stirred, ice-cold THF solution, and 20 ml. of 30% H_2O_2 was added over a period of 5 min. The solution was stirred for 30 min. at 0° and for 1 hr. at 20°. Most of the THF was then removed *in vacuo*. The water solution was extracted with ethyl acetate and with ether and the extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 4.5 g. of a mixture of diols.

Fractional crystallization from acetone gave 0.7 g. (14%) of diol V and 0.3 g. (6.2%) of diol VI. Recrystallization of the crude V from ether gave the analytical sample of V: m.p. 148–148.5°; λ_{max} 221 mμ (ε 8500), 278 (1950), and 285 (1850); ν_{max}^{KBr} 3200–3400, 1000–1100, and 1250–1300 cm.$^{-1}$ (OH bands).

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.26; H, 8.24.

Recrystallization of the crude diol VI from 80% ethanol gave analytically pure diol VI: m.p. 177–178°; λ_{max} 224 mμ (ε 9000),

(14) M. Balasubramanian and N. Padma, *Tetrahedron*, **19**, 2135 (1963).

(15) All melting points were determined in a Thomas–Hoover melting point apparatus and are corrected. All ultraviolet spectra were taken in ethanol.

(16) W. W. Scott, "Standard Methods of Chemical Analysis," Vol. 1, 5th Ed., N. H. Furman, Ed., D. Van Nostrand Co., Inc., New York, N. Y., 1939, p. 70.

276 (1880), and 283 (1680); ν_{max}^{KBr} 3375, 3300, 1025–1090, and 1250–1300 cm.$^{-1}$ (OH bands).

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.91; H, 8.60.

1-(1,2,3,9,10,10aβ-Hexahydro-7-methoxy-2α-phenanthrylcarbonyl)imidazole (VIII).—Sixty grams of N,N′-carbonyl diimidazole[16a] was stirred in 840 ml. of anhydrous tetrahydrofuran at 60°. A solution of 77.7 g. of unsaturated acid III in 1300 ml. of anhydrous THF was added over a period of 45 min. Evolution of CO_2 was observed throughout the addition. The solution was then refluxed with stirring for 16 hr. The solution was concentrated to about one-third of its original volume *in vacuo*, and the crystalline imidazolide VIII, m.p. 154–155°, was filtered off. By repeating this procedure, two more crops were obtained, m.p. 154–155°. Altogether, 89.2 g. of VIII was isolated (96.3%), which could be used without further purification in the following step. A small sample was recrystallized from acetone to give analytically pure VIII: m.p. 155.5–156°; λ_{max} 214 mμ (ε 29,450), 264 (20,400), and 297 (3550); $\nu_{max}^{CHCl_3}$ 1735 cm.$^{-1}$ (carbonyl).

Anal. Calcd. for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.09. Found: C, 74.26; H, 6.53; N, 8.97.

1,2,3,9,10,10aβ-Hexahydro-7-methoxy-2α-phenanthrenecarboxylic Acid Isopropyl Ester (IX).—Imidazolide VIII (89.2 g.) was suspended in 250 ml. of anhydrous isopropyl alcohol; 0.1 *N* sodium isopropoxide in isopropyl alcohol (140 ml.) was added to the stirred suspension at 20°, and stirring was continued for 2 hr. The slurry was then poured into 1 l. of ice–water, and the pH of the solution was adjusted to about 7.5 by the addition of 2 *N* HCl. The crystalline material was filtered off, washed with ice–water, and dried *in vacuo* at 20° for 16 hr. to give 85.49 g. (98.4%) of the isopropyl ester IX, m.p. 82–83.5°. The ester could be used without further purification in the next step of the synthesis. A small sample was recrystallized from isopropyl alcohol, and gave analytically pure IX: m.p. 83–83.5°, λ_{max} 264 mμ (ε 20,600) and 298 mμ (ε 3400), $\nu_{max}^{CHCl_3}$ 1720 cm.$^{-1}$ (ester carbonyl).

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.92; H, 7.81.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid (X) and 1,2,3,4,4aα,9,10,10aβ-Octahydro-4α-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid Lactone (XII).—The isopropyl ester IX (35.3 g.) was dissolved in 1400 ml. of anhydrous THF. The solution was stirred under nitrogen at 20–23°, and 125 ml. of the previously described B_2H_6 in THF solution (5.25 g. of B_2H_6 in 400 ml. of THF) was added over a period of 1 hr. This amount corresponds to 0.5 mole of B_2H_6 per mole of the ester IX. After an additional 1 hr. of stirring at 20°, the solution was cooled with an ice bath and ice was added carefully to destroy the excess diborane.

NaOH (3 *N*, 156 ml.) was added to the stirred ice-cold THF solution, and 156 ml. of 30% H_2O_2 was then added over a period of 15 min. The ice bath was removed, and the mixture was stirred at 20° for 1 hr. The pH was checked periodically, and more NaOH was added if necessary to adjust the pH to about 10. At the end of the hour, a freshly prepared solution of 142 g. of $NaHSO_3$ in 500 ml. of H_2O was added dropwise to destroy the excess peroxide. At the end of the addition, the pH was adjusted to 7.0 with 3 *N* NaOH.

The THF was then removed *in vacuo*, the oil which separated was taken up in ethyl acetate, and the aqueous solution was extracted with ethyl acetate and with ether. The combined extract was washed with water, dried over $MgSO_4$, and evaporated *in vacuo* to yield 34.5 g. of an oil which consisted of a mixture of hydroxy esters and diols.

The mixture was saponified by stirring and refluxing in 600 ml. of 1 *N* NaOH for 5 hr. under nitrogen. The mixture of diols (10.15 g.) was removed by extraction with $CHCl_3$. Fractional crystallization from acetone gave 2.7 g. (9.3%) of the *trans* diol VI and 2.2 g. (7.6%) of the *cis* diol V. Both V and VI were identical with the previously described samples of the same compounds.

The basic solution was cooled in an ice bath, stirred, and acidified slowly with 2 *N* HCl to pH 3.0. The mixture was stirred at ice-bath temperature for 3 hr. and the crystalline precipitate was filtered and dried at 55° for 16 hr. *in vacuo*. A mixture of hydroxy acids X and XI obtained.

The 18.2 g. of the crude mixture of hydroxy acids X and XI was suspended in 900 ml. of benzene, 0.4 g. of *p*-toluenesulfonic acid monohydrate was added, and the mixture was stirred and refluxed for 3 hr., using the Dean–Stark apparatus to separate the water. The mixture was then cooled to 20°, and stirred at this temperature for 1 hr. Filtration gave 7.3 g. of the hydroxy acid X, m.p. 190–192°. Recrystallization from acetone yielded the analytically pure nonlactonizing hydroxy acid X: m.p. 192.5–193.5°; λ_{max} 221 mμ (ε 8280), 279 (1970), and 287 (1750); ν_{max}^{KBr} 3430 (OH), 2570–2700 (associated OH of acid), and 1710 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.72; H, 7.09.

After the nonlactonizing hydroxy acid X had been removed by filtration, the benzene solution was dried over Na_2SO_4 and evaporated *in vacuo* to give 4.15 g. of the crude lactone XII. Recrystallization from methylene chloride–hexane gave the analytically pure lactone XII: m.p. 165–166°, λ_{max} 222 mμ (ε 8680) and 278 mμ (ε 1850), $\nu_{max}^{CHCl_3}$ 1780 cm.$^{-1}$ (carbonyl of γ-lactone).

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.34; H, 6.72.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid Methyl Ester (XIII).—The *cis* nonlactonizing hydroxy acid X (1.5 g.) was refluxed under nitrogen in 1 *N* methanolic sulfuric acid for 5 hr. It was cooled to 20°, and poured onto ice. The pH was adjusted to 7.0 with $NaHCO_3$ in water. After the methanol was removed *in vacuo*, the aqueous fraction was extracted with ether. The extract in turn was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 1.6 g. of the hydroxy ester XIII, m.p. 107–109°. Recrystallization from hexane gave the analytical sample of XIII: m.p. 111–111.5°; λ_{max} 221 mμ (ε 8100), 278 (1830), and 287 (1650); ν_{max}^{KBr} 3200–3450 (OH band) and 1733 cm.$^{-1}$ (ester carbonyl).

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.29; H, 7.50.

Reduction of the *cis* Hydroxy Ester XIII to the *cis* Diol V.—$LiAlH_4$ (260 mg.) was suspended in 8 ml. of anhydrous ether; 700 mg. of *cis* hydroxy ester XIII was dissolved in 15 ml. of anhydrous ether, and this was added to the stirred lithium aluminum hydride suspension within 20 min. It was refluxed for 1 hr., then it was cooled in an ice bath. Ethyl acetate and 5 ml. of saturated Na_2SO_4 solution were added carefully, and the mixture was filtered. The salts were extracted with hot ethyl acetate and the combined extracts were dried over $MgSO_4$, evaporated *in vacuo*, and gave 520 mg. (82%) of the diol V, m.p. 146–147.5°. Recrystallization from ether yielded the pure diol V, m.p. 148–148.5°. The compound was in every respect identical with the sample obtained from the hydroboration–oxidation of the unsaturated methyl ester IV.

Reduction of the *trans* Lactone XII to the *trans* Diol VI.—The *trans* lactone XII (100 mg., 0.4 mmole) was dissolved in 16 ml. of anhydrous ethanol; 600 mg. (15.8 mmole) $NaBH_4$ was added in small portions to the stirred solution which was then allowed to stand at 20° for 72 hr. Ice–water was added to the solution, and it was acidified with cold 2 *N* HCl. Most of the ethanol was evaporated *in vacuo* and the crystalline precipitate was filtered off and dried *in vacuo* at 50° for 16 hr. Recrystallization from 80% ethanol gave 85 mg. (84%) of diol VI, m.p. 177–178°. The compound was in every respect identical with the sample obtained from the hydroboration–oxidation of the unsaturated methyl ester IV.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-7-methoxy-4-oxo-2α-phenanthrenecarboxylic Acid (XIV). A. By Oxidation of the *cis* Nonlactonizing Hydroxy Acid X.—CrO_3 (1.25 g.) was added in portions to 12.5 ml. of anhydrous pyridine while stirring at 15°. After the formation of the CrO_3–pyridine complex[17] was complete, a solution of 1.25 g. of hydroxy acid X in 12.5 ml. of anhydrous pyridine was added at once, and the slurry was stirred at 20° for 5 hr.

It was then poured into ice–water and acidified in the cold to pH 3.0 with 2 *N* HCl. The mixture was shaken with ethyl acetate and filtered through a pad of Celite. The precipitate was washed carefully with warm ethyl acetate. The ethyl acetate was separated from the aqueous layer which, in turn, was re-extracted with ethyl acetate and with ether. The combined extracts were dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 0.87 g. (70.2%) of the crude keto acid XIV, 163–165°. Recrystallization from acetone gave the analytical

(17) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

sample: m.p. 171.5–172°, λ_{max} 225 mμ (ε 7300) and 278 mμ (ε 1800), λ_{infl} 287 mμ (ε 1500), ν_{max} (in 10% piperidine–$CHCl_3$) 1705 (keto carbonyl) and 1610, and 1570 cm.$^{-1}$ ($-COO^-$ bands).

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.19; H, 6.87.

B. By Oxidation of the *cis* Lactonizing Acid (XXIV).—The hydroxy acid XXIV (800 mg.) in 10 ml. of anhydrous pyridine was added to a stirred suspension of the CrO_3–pyridine complex[17] prepared from 800 mg. of CrO_3 in 10 ml. of anhydrous pyridine. The mixture was stirred at 20° for 5 hr. and it was worked up as in A to give 795 mg. of crude keto acid XIV. Recrystallization from acetone gave pure XIV, m.p. 170–171°. The compound was in every respect identical with the sample obtained by the oxidation of the *cis* nonlactonizing acid (X).

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2β-phenanthrenecarboxylic Acid Lactone (XV).—The *cis* hydroxy methyl ester XIII (1.0 g.) was refluxed and stirred under nitrogen in 100 ml. of 2 *N* $NaOCH_3$ in methanol for 20 hr. Water (20 ml.) was added, and refluxing was continued for an additional 5 hr. to saponify the esters. The solution was then added to 30 ml. of water, and most of the methanol was removed *in vacuo*. The solution was extracted with ether to remove any unsaponified material. The water solution was cooled in an ice bath, and the stirred solution was acidified with ice-cold 2 *N* HCl to pH 3.0. After stirring for 30 min. in an ice bath, the precipitate was filtered off. It was dried *in vacuo* at 60° for 16 hr. to give 0.95 g. of a mixture of hydroxy acids.

This mixture was put into 40 ml. of benzene and refluxed and stirred in the presence of 20 mg. of *p*-toluenesulfonic acid monohydrate using the Dean–Stark apparatus. After 15 min. of reflux, the solution was cooled to 20°. The nonlactonizing hydroxy acid X was extracted from the benzene with a $NaHCO_3$ solution.

The benzene solution was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue weighed 450 mg. and had m.p. 154–155°. Recrystallization from acetone gave the analytical sample of XV: m.p. 156–157°, λ_{max} 280 mμ (ε 2200) and 288 mμ (ε 2110), $\nu_{max}^{CHCl_3}$ 1772 cm.$^{-1}$ (γ-lactone carbonyl).

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.43; H, 7.08.

The $NaHCO_3$ extract was cooled in an ice bath and acidified while stirring with cold 2 *N* HCl to pH 3.0. The hydroxy acid X was extracted with ethyl acetate and ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 480 mg. of hydroxy acid X, m.p. 191–193°, which was in every respect identical with the sample previously obtained by the hydroboration and oxidation of IX.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2β-phenanthrenecarboxylic Acid (XVI).—The lactone XV (7.4 g.) was stirred and refluxed under nitrogen with 200 ml. of 1 *N* NaOH for 15 min. The solution was cooled to 20° and extracted with ether to remove any unhydrolyzed material. The aqueous layer was cooled in an ice bath, stirred, and acidified with 2 *N* HCl. After stirring for 1 hr. at ice-bath temperature, the precipitated acid XVI was filtered off, washed with ice–water, and dried *in vacuo*. It was recrystallized from ethyl acetate and gave 5.7 g. (72%) of the lactonizing acid XVI: m.p. 215–216° dec.; λ_{max} 220 mμ (ε 9490), 278 (1950), and 285 (1800); ν_{max}^{KBr} 3320 (OH group), 2740–2650 (associated OH of acid), and 1700 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.45; H, 7.56.

Lactonization of Hydroxy Acid (XVI).—Hydroxy acid XVI (0.5 g.) was stirred and refluxed for 20 min. in 300 ml. of benzene with 0.2 g. of *p*-toluenesulfonic acid monohydrate in a Dean–Stark apparatus. The benzene solution was then cooled and extracted with 100 ml. of 2% $NaHCO_3$ solution. It was washed with water, dried over Na_2SO_4, and evaporated *in vacuo*, to yield 0.42 g. (90%) of lactone XV, m.p. 154–156°. Recrystallization from chloroform–hexane gave pure XV, m.p. 156–157°. The compound was in every respect identical with the sample obtained from the *cis* hydroxy ester XIII.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-7-methoxy-4-oxo-2β-phenanthrenecarboxylic Acid (XVII). A. By the Oxidation of the Lactonizing Acid (XVI).—The lactonizing acid XVI (20 g.) was dissolved in 600 ml. of hot, $KMnO_4$-treated acetone. The solution was cooled to 10–15° and 25 ml. of 8.0 *N* CrO_3–H_2SO_4 was added within 15 min. to the stirred solution. The mixture was then poured into 1 l. of ice–water and most of the acetone was removed *in vacuo* using a Dry Ice–acetone cooled trap. The aqueous solution was extracted with ethyl acetate which, in turn, was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residual solid yielded, upon recrystallization from methanol, 15.0 g. of keto acid XVII[18]: m.p. 196–198°, λ_{max} 278 mμ (ε 1800) and 284 mμ (ε 1600), ν_{max}^{KBr} 2450–2700 (associated OH of acid) and 1700–1710 cm.$^{-1}$ (carbonyl of acid and ketone).

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.90; H, 6.62.

B. By Oxidation of the Nonlactonizing Hydroxy Acid (XIX).—The acid XIX (15.7 g.) was dissolved in 550 ml. of hot, $KMnO_4$-treated acetone. The solution was cooled to 10–15°, and it was oxidized with 20 ml. of 8.0 *N* CrO_3–H_2SO_4 as in A. The reaction mixture was worked up as previously and gave 11.4 g. of keto acid XVII, which was in every respect identical with the sample described in A.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4α-hydroxy-2β-phenanthrenecarboxylic Acid (XIX) and the *cis* Lactone XV.—The *cis* keto acid XVII was dispersed at 5–10° in 1690 ml. of 0.1 *N* NaOH·$NaBH_4$ (16.0 g.) was added in small portions to the cold stirred mixture. The acid gradually dissolved and was allowed to stand at 20° for 24 hr. The solution was then cooled in an ice bath and acidified, while stirring, with 2 *N* HCl. A mixture of the two isomeric acids XVI and XIX precipitated. The suspension was stirred for 1 hr. in the cold and was then filtered off. The precipitate was washed with ice–water and dried *in vacuo* at 40° for 16 hr. The mixture of the acids was suspended in 2.5 l. of benzene, 1.0 g. of *p*-toluenesulfonic acid monohydrate was added, and the mixture was stirred and refluxed in a Dean–Stark apparatus for 1 hr.

The benzene solution was then cooled in an ice bath and stirred for 45 min. with 1 l. of 7% $NaHCO_3$ solution to extract the nonlactonizing acid XIX. After separation, the benzene phase was extracted once again with 500 ml. of 7% $NaHCO_3$ solution. The bicarbonate extracts were combined and worked up to give the nonlactonizing acid XIX, whereas the benzene solution yielded the lactone XV, as shown below.

The combined bicarbonate extract was cooled in an ice bath, stirred, and acidified to pH 4.5 with 2 *N* HCl. The nonlactonizing acid XIX precipitated. The suspension was stirred for 1 hr. in the ice bath. It was then filtered off, washed with ice–water, and dried *in vacuo* at 40° for 16 hr. to give 33.9 g. (73%) of the nonlactonizing acid XIX, m.p. 174–176°. Recrystallization from acetonitrile gave an analytically pure sample of XIX: m.p. 180–182°; λ_{max} 220 mμ (ε 9000), 278 (2070), and 286 (1940); ν_{max}^{KBr} 3550 (OH group), 2560–2740 (associated OH of acid), and 1710 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.73; H, 7.39.

Evaporation of the bicarbonate-extracted benzene solution *in vacuo* gave 6.95 g. (16%) of the *cis* lactone XV, m.p. 156–157°. The compound was in every respect identical with the sample obtained from the *cis* hydroxy ester XIII.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-7-methoxy-4-oxo-2β-phenanthrenecarboxylic Acid, Oxime (XVIII).—The *cis* keto acid XVII (5.4 g.) was dissolved in 54 ml. of THF. NaOAc·$3H_2O$ (21.6 g.) was dissolved in 40 ml. of water and this was added to 10.8 g. of $NH_2OH \cdot HCl$ in 14 ml. of water. The resulting solution was added to the THF solution with stirring. Enough methanol was added to obtain a homogenous solution. After about 15 min., the oxime started to precipitate. Stirring was continued for 16 hr. Water (250 ml.) was then added and the solvents were removed *in vacuo*. The crystalline precipitate was filtered, dried, and recrystallized from ethanol to yield 5.3 g. (93%) of the oxime acid XVIII: m.p. 210° dec.; λ_{max} 278 mμ (ε 1780) and 286 mμ (ε 1640); ν_{max}^{KBr} 3330, 2500–2600 (OH bands), 1716 (carbonyl of acid), and 1660 cm.$^{-1}$ (C=N band).

Anal. Calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.51; H, 6.68; N, 4.89.

1,2,3,4-Tetrahydro-7-methoxy-2-phenanthrenecarboxylic Acid (XXI).—The *cis* keto acid XVII (2.5 g.) was dissolved in 75 ml. of acetic acid, 2.5 ml. of 30% HBr in acetic acid was added, and the mixture was kept at 60° for 16 hr. Sodium acetate (5 g.) was then added and the mixture was stirred at 20° for 30 min. Most of the acetic acid was then evaporated *in vacuo* and water was added to the solid residue. It was extracted with ethyl

(18) This compound was first prepared by Dr. Karl J. Doebel in our laboratories.

acetate and the extract was washed with brine, dried over $MgSO_4$, evaporated *in vacuo*, and gave 2.4 g. of crude acid XXI. Recrystallization from methanol gave 1.1 g. of pure acid XXI: m.p. 202–203° (lit.[10] m.p. 201–203°); λ_{max} 228 mμ (ε 60,000), 255 (3920), 265 (4900), 275 (5110), 285 (3320), 321 (1900), 330 (1720), and 335 (2410).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.99; H, 6.34.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4α-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid Lactone (XXII) and 1,2,3,4,4aα,-9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid (XXIII). A. In 0.1 *N* NaOH.—The *cis* keto acid XIV (1.32 g.) was dissolved in 50 ml. of 0.1 *N* NaOH at 20°. It took 20 min. to dissolve the acid. The solution was then cooled in an ice bath, and 0.46 g. of $NaBH_4$ was added in small portions to the stirred solution. After stirring for 1 hr. at ice-bath temperature, the stirring was stopped and the solution was kept at 20° for 16 hr.

The pH adjusted to 3.0 by adding cold 0.5 *N* HCl to the cooled and stirred solution. The mixture was extracted with ethyl acetate and with ether, and the extracts were combined and washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 1.21 g. (91%) of a mixture of hydroxy acids, m.p. 170–176°.

The hydroxy acid mixture was suspended in 65 ml. of anhydrous benzene, 30 mg. of *p*-toluenesulfonic acid monohydrate was added, and the mixture was stirred and refluxed for 1.5 hr. using the Dean–Stark apparatus. The solution was cooled to 20° and was then extracted with a $NaHCO_3$ solution.

The benzene solution was dried over Na_2SO_4, filtered, and evaporated *in vacuo* to give 742 mg. (72%) of the *cis* lactone XXII, m.p. 185–187°. Recrystallization from acetone gave analytically pure lactone XXII: m.p. 187.5–188.5°; λ_{max} 223 mμ (ε 8120), 278 (1980), and 286 (1840); ν_{max}^{KBr} 1780 cm.$^{-1}$ (γ-lactone carbonyl).

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.40; H, 7.22.

The $NaHCO_3$ solution containing the nonlactonizing hydroxy acid sodium salt was cooled with an ice bath, stirred, and acidified to pH 3.5 with cold 1 *N* HCl. The mixture was extracted with ethyl acetate and with ether. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 314 mg. (28%) of *trans* nonlactonizing hydroxy acid XXIII, m.p. 192–194°. Recrystallization from acetone gave the analytical sample: m.p. 199–200°; λ_{max} 219 mμ (ε 9700), 278 (2060), and 286 (1910); ν_{max}^{KBr} 3200–3400 (OH bands), 2500–2700 (associated OH of acid), and 1700 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.69; H, 7.38.

B. In 1.0 *N* NaOH.—The *cis* keto acid XIV (4.7 g.) was dissolved in 185 ml. of 1.0 *N* NaOH. It was stirred under nitrogen at 20° for 45 min. $NaBH_4$ (1.65 g.) was then added at once. A solution resulted first, but after 5 min. of stirring, a heavy crystalline precipitate formed which was dissolved by the careful addition of 550 ml. of ice–water. The solution was then stored for 16 hr. at 20°. It was then acidified to pH 3.5, filtered, and dried *in vacuo* at 56° for 16 hr. The 4.46-g. mixture of hydroxy acids was separated by lactonization, as described under A, and gave 0.7 g. of the *cis* lactone XXII (19.9%), and 2.95 g. of the *trans* hydroxy acid XXIII, (66.0%). Both XXII and XXIII were in every respect identical with the samples described in A.

1,2,3,4,4aβ,9,10,10aβ-Octahydro-4α-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid (XXIV).—The *cis* lactone XXII (1.0 g.) was refluxed with stirring in 50 ml. of 1 *N* NaOH for 1 hr. The basic solution was cooled to 20° and then extracted with ether to remove any unsaponified material. The solution was cooled in an ice bath and acidified while stirring with 1 *N* HCl to pH 3.0. It was extracted with ethyl acetate and with ether, and the combined extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 1.05 g. of crude hydroxy acid XXIV, m.p. 196° dec. Recrystallization from acetone gave the analytical sample: m.p. 202° dec.; λ_{max} 220 mμ (ε 8200) and 278 mμ (ε 1860); λ_{infl} 286 mμ (ε 1550); ν_{max}^{KBr} 3450 (OH band), 2480–2700 (associated OH of acid), and 1710 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.16; H, 7.24.

1,2,3,4,4aα,9,10,10aβ-Octahydro-7-methoxy-4-oxo-2α-phenanthrenecarboxylic Acid (XXV). A. By Oxidation of the *trans* Nonlactonizing Hydroxy Acid (XXIII).—The *trans* hydroxy acid XXIII (750 mg.) was dissolved in 7.5 ml. of anhydrous pyridine and added to a stirred suspension of the CrO_3–pyridine complex,[17] prepared from 750 mg. of CrO_3 and 10 ml. of anhydrous pyridine. The mixture was stirred at 20° for 2.5 hr. and was worked up as in the preparation of XIV (method A) to give, after recrystallization from methanol, 288 mg. (38.6%) of *trans* keto acid XXV: m.p. 195–199°; λ_{max} 220 mμ (ε 8290), 277 (1720), and 284 (1680); ν_{max}^{KBr} 2570–2680 (associated OH of acid), 1715 (carbonyl of ketone), and 1700 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.80; H, 6.77.

B. By Oxidation of the *trans* Lactonizing Acid XI.—The *trans* lactonizing acid XI (500 mg.) was dissolved in 5 ml. of anhydrous pyridine and added to a stirred suspension of 500 mg. of CrO_3 in 6 ml. of anhydrous pyridine. The mixture was stirred at 20° for 5 hr. and was worked up as in the preparation of XIV (method A) to give 500 mg. of crude keto acid XXV, m.p. 175–181°. Recrystallization from methanol gave 200 mg. of pure keto acid XXV, m.p. 195–199°, which was in every respect identical with the sample described under method A.

1,2,3,4,4aα,9,10,10aβ-Octahydro-7-methoxy-4-oxo-2α-phenanthrenecarboxylic Acid, Oxime (XXVI).—The oxime XXVI of the *trans* keto acid XXV was prepared according to the method described for the preparation of the isomeric oxime–acid XVIII. The *trans* keto acid XXV (100 mg.) gave 94.5 mg. of pure oxime acid XXVI: m.p. 210° dec., after recrystallization from methanol; λ_{max} 225 mμ (ε 8150), 278 (1710), and 285 (1590); ν_{max}^{KBr} 3250, 3150, 2500–2600 (OH bands), 1695 (carbonyl of acid), and 1660 cm.$^{-1}$ (C=N band).

Anal. Calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.72; H, 6.72.

1,2,3,4,4aα,9,10,10aβ-Octahydro-4α-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid (XI).—The *trans* boat lactone XII (450 mg.) was saponified in refluxing 1 *N* NaOH. After 15 min. of reflux, the mixture was worked up as described for the preparation of XXIV to give 205 mg. of analytically pure *trans* lactonizing hydroxy acid XI: m.p. 225–227° dec.; λ_{max} 220 mμ (ε 8510) and 277 mμ (ε 1750); λ_{infl} 285 mμ (ε 1550); ν_{max}^{KBr} 3580 (OH band), 2600–2740 (associated OH of acid), and 1698 cm.$^{-1}$ (carbonyl of acid).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.79; H, 7.22.

Lactonization of the *trans* Hydroxy Acid (XI).—The *trans* hydroxy acid XI (1.1 g.) was suspended in 550 ml. of benzene; *p*-toluenesulfonic acid monohydrate (350 mg.) was added and the mixture was stirred and refluxed for 3 hr. The preparation was worked up as described for the isomeric lactone XV. Upon acidification of the $NaHCO_3$ extract, 200 mg. of starting material XI was recovered, m.p. 220–222° dec.

Evaporation of the benzene solution *in vacuo* gave 800 mg. of the *trans* boat lactone XII, which was in every respect identical with the sample obtained by hydroboration and oxidation of the unsaturated isopropyl ester IX.

$NaBH_4$ Reduction of the *trans* Keto Acid XXV.—The *trans* keto acid XXV (274 mg.) was suspended in 9 ml. of distilled water. The suspension was stirred rapidly at 5° and 1.0 ml. of 1.0 *N* NaOH was added slowly to dissolve the compound. $NaBH_4$ (100 mg.) was added at once and the stirring was continued. After 3 min. a precipitate formed which was dissolved by the careful addition of 14 ml. of ice water. The solution was allowed to stand at 20° for 16 hr. The reaction mixture was worked up as in the preparation of the *trans* hydroxy acid XXIII and gave 237 mg. (86%) of XXIII, in every respect identical with the previously described sample.

1,2,3,4,4aα,9,10,10aβ-Octahydro-4β-hydroxy-7-methoxy-2β-phenanthrenecarboxylic Acid Lactone (XXVII) and the *trans* Hydroxy Acid (XXIII).—A solution of sodium isopropoxide in isopropyl alcohol was prepared by adding 13.0 g. of sodium in small pieces to 200 ml. of isopropyl alcohol. It was refluxed and stirred until all the sodium dissolved. The *cis* keto acid XVII (6.5 g.) was added and stirring and refluxing were continued for 20 hr. The solution was cooled to 20°, 200 ml. of ice–water was added, and it was acidified with cold 2 *N* HCl to pH 3.0. Most of the isopropyl alcohol was evaporated *in vacuo* and the aqueous solution was extracted with ethyl acetate and with ether. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated *in vacuo* to give 6.5 g. of an oil which

partially crystallized upon the addition of ether. The ether-insoluble portion was recrystallized from acetonitrile to give 2.0 g. of a mixture of hydroxy acids, m.p. 139–158°.

This mixture was suspended in 300 ml. of benzene, 200 mg. of *p*-toluenesulfonic acid monohydrate was added, and it was stirred and refluxed for 1 hr. using the Dean–Stark apparatus. The benzene solution was extracted with a $NaHCO_3$ solution which, in turn, was cooled in an ice bath, stirred, and acidified with cold 2 *N* HCl to pH 5.0. The crystalline precipitate was filtered off and dried *in vacuo* at 60° for 16 hr. to give 1.1 g. (16.0%) of *trans* nonlactonizing hydroxy acid XXIII, m.p. 196–197°. Recrystallization from methanol gave analytically pure XXIII, m.p. 199–200°, which was in every respect identical with the previously described sample obtained in the $NaBH_4$ reduction of the keto acid XXV.

The benzene solution was washed with brine, dried over Na_2SO_4, filtered, and evaporated *in vacuo* to give 0.5 g. (8%) of the *trans* chair lactone XXVII, m.p. 163–164°, after recrystallization from benzene–hexane. The melting point of the *trans* boat lactone XII was 165–166°. Mixture melting point determination of XII and XXVII gave a strong melting point depression with a m.m.p. of 138–150°: λ_{max} 221 mμ (ε 8650), 278 (2060), and 287 (1850); $\nu_{max}^{CHCl_3}$ 1780 cm.$^{-1}$ (γ-lactone carbonyl). The infrared spectrum of the *trans* chair lactone XXVII was obviously different from that of the *trans* boat lactone XII.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.34; H, 6.72.

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Rearrangement Reactions of 2-Halo-1-methyl-1-tetralols[1]

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The *cis* isomer of 2-chloro-1-methyl-1-tetralol undergoes rearrangement when treated with methylmagnesium bromide or with silver tosylate to give 2-methyl-1-tetralone. The *trans* isomer of 2-bromo-1-methyl-1-tetralol, however, gives 1-methyl-2-tetralone in a reaction with phenylmagnesium bromide and 1-methylnaphthalene with silver tosylate. An α,β-unsaturated alcohol, 1-methyl-1-hydroxy-1,4-dihydronaphthalene, was also isolated from the latter reaction in a trace amount. The *trans* isomer of 2-bromo-1-methyl-1-tetralol forms an epoxide in alcoholic potassium hydroxide. This epoxide rearranges to 1-methyl-2-tetralone in the presence of sulfuric acid. Mechanisms for the rearrangements are discussed.

The semipinacol rearrangement of β-halohydrin by silver salts[2–4] and by Grignard reagents[4–8] have been the subject of many investigations. When the β-halohydrin is incorporated into an alicyclic ring where freedom of rotation is restricted, the stereochemistry about the C-α–C-β bond plays an important role in the determination of migration by competing groups and thus the rearrangement path.

The rearrangement of 2-iodo-1-hydroxy-1,2,3,4-tetrahydronaphthalene with silver nitrate, in which 1-indancarboxaldehyde is the product, has been reported by Tiffeneau[2,3] where ring contraction is the result of benzo migration. The necessity for the migrating group to be *trans* to the leaving group in this type of rearrangement has been demonstrated in the rearrangement reaction of 1-methyl-2-halo-1-cyclohexanol with Grignard reagents.[5,6] The *cis* isomer containing the methyl group *trans* to the leaving halogen rearranges to yield 2-methylcyclohexanone with the migration of the methyl group. The *trans* isomer, however, does not contain the methyl group in a position favorable for migration. Instead, it rearranges to yield 1-acetylcyclopentanone by ring contraction.

The thermal rearrangements of the halomagnesium derivatives of *cis*-2-chloro-1-indanol and *cis*-2-chloro-1-methyl-1-indanol have been shown to yield 1-indanone and 2-methyl-1-indanone, respectively.[8] The corresponding *trans* compounds afford large amounts of tarry materials.

The 2-halo-1-phenyl-1-tetralol series has also been studied.[4,7] The *cis* isomer of 2-chloro-1-phenyl-1-tetralol, under treatment of either silver tosylate[4] or a Grignard reagent,[4,7] yields 2-phenyl-1-tetralone as the rearranged product. This is a case of migratory competition between the benzo and phenyl groups, which are both in positions favorable to migration. The *trans* isomer undergoes rearrangement to give 1-benzoylindane when treated with a Grignard reagent, but produces 1-phenyl-2-tetralone in its reaction with silver tosylate. As the *trans* isomer does not have a phenyl group in a position favorable to migration, it has been suggested that benzo migration occurs to cause ring contraction in one case while rearrangement through an epoxide intermediate prevails in the other.

The present work describes the rearrangement reactions of 2-halo-1-methyl-1-tetralols in an effort to determine the relative tendency of methyl *vs.* benzo migrations and the stereochemical requirements for rearrangement in this special semipinacol system.

Results

The *trans* isomer of 2-bromo-1-methyl-1-tetralol (I) and the *cis* isomer of 2-chloro-1-methyl-1-tetralol (VIII) were synthesized by employing reactions of known stereochemistry which had been found successful in the production of their phenyl analogs.[4] The *trans*-bromohydrin formed an epoxide IV in alcoholic potassium hydroxide, thus establishing the *trans* configuration of the bromohydrin. This epoxide rearranged to 1-methyl-2-tetralone (II) in the presence of

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