[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Potential Steroid Substitutes. III.[1] The Preparation of Some 2,6-Dioxygenated Hydronaphthalenes and Hydroanthracenes

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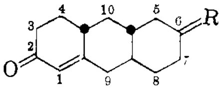
Catalytic hydrogenation of 2,6-naphthalenediol followed by oxidation of the product gave *cis*- and *trans*-decahydro-2,6-naphthalenedione (IV and V). Birch reduction of 6-methoxy-1,2,3,4-tetrahydro-2-naphthol produced 6β- and 6α-hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (VIII and IX). The preparation of the four possible 6-hydroxydecahydro-2-naphthalenones, X through XIII, and the six possible decahydro-2,6-naphthalenediols, XIV through XIX, is described. Positive relative configurational assignment has been made to each compound. The spectra of these compounds and of their acetates are reported and discussed. 6β- and 6α-hydroxy-2,3,4,4aβ,5,6,7,8,8aα,9,10,10aβ-dodecahydro-2-anthracenone (Ia and Ib) have been synthesized from 6β- and 6α-hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα-decahydro-2-naphthalenone (X and XIII). The stereochemistry of Ia and Ib was established. Neither of these anthracenones possessed androgenic activity.

Part I

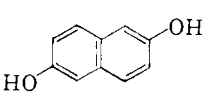
In the course of a search for non-steroidal androgenic substances it appeared desirable to prepare 6β- and 6α-hydroxy-2,3,4,4aβ,5,6,7,8,8aα,9,10,-10aβ-dodecahydro-2-anthracenone[2,3] (Ia and Ib). When earlier efforts to prepare these compounds



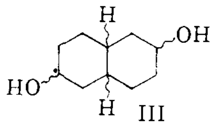
Ia, R = H, β-OH
Ib, R = H, α-OH

failed,[1,2] attention was turned to the synthesis of certain *trans* bicyclic ketones (X and XIII of Chart I) which might be transformed ultimately into Ia and Ib. This approach proved successful and compounds Ia and Ib are described here.

The perhydrogenation of 2,6-naphthalenediol (II) was studied first. Tetrahydrogenation of II has



II



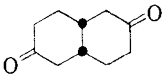
III

been accomplished with a variety of catalysts at 120–180° and 2000–3000 p.s.i. of hydrogen.[4] Robinson and Weygand[5] report perhydrogenation of II but only with cleavage of a hydroxyl group. After the present work was completed, Runge and Goldann[6] reported the perhydrogenation of II at 195° under 3300 p.s.i. of hydrogen with a nickel–alumina catalyst.

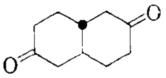
The II used in the present study was prepared from the sodium salt of Schaeffer's acid by a modification[7] of the method of Willstätter and Parnas.[8] The use of a nickel crucible and fusion with pure potassium hydroxide largely eliminated traces of iron from the reaction and led to crude yields of about 60%.

The most effective way found for purifying II for hydrogenation was to convert it to its diacetate,[9] recrystallize this ester, and then regenerate II. Thus purified, II could be tetrahydrogenated in the presence of fresh W-7 Raney nickel[10] and potassium hydroxide[4b] under 2000 p.s.i. of hydrogen at *room temperature*. Elevation of the temperature to 85° caused hydrogenation of the second ring to give a mixture of decahydro-2,6-naphthalenediols, III.

Chromic acid oxidation of crude III afforded *cis*-decahydro-2,6-naphthalenedione (IV, 15% yield) m.p. 73–75°, and *trans*-decahydro-2,6-naphthalenedione (V, 0.9% yield), m.p. 139.5–141.5°, along with a trace of *cis*-decahydro-2,6-naphthalenediol (XVI) m.p. 150–152° (see below). The



IV



V

compound melting at 73–75° was found to have a dipole moment of 2.84 D. which is in accord with the *cis* structure IV.[11] The assignments given to IV and V are confirmed below.

Reduction of the *cis*-diketone IV with lithium aluminum hydride afforded two *cis*-decahydro-2,6-naphthalenediols which melted at 136–137.5° (XV) (15% yield) and 150.5–152° (XVI) (40% yield). The latter compound was identical with that isolated from the chromic acid oxidation of a crude perhydronaphthalenediol mixture (see above).

Since the desired *trans* compound V was isolated in such low yield, attention was turned to the preparation of 6β- and 6α-hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (VIII and IX). The required intermediate, 6-methoxy-1,2,3,4-tetrahydro-2-naphthol[4b] was prepared originally from naphthalene-2,6-diol by tetrahydrogenation at room temperature (see above) followed by methylation of the phenolic group. This preparation proved less adaptable to large scale work than did its preparation from 2-bromo-6-methoxynaphthalene. Conversion of 2-bromo-6-methoxynaphthalene to 6-methoxy-2-naphthol was accomplished by the method of Britton[12]

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[1] Paper II, R. L. Clarke, W. T. Hunter and S. J. Marsala, THIS JOURNAL, **81**, 5710 (1959).

[2] R. L. Clarke and W. S. Johnson, *ibid.*, **81**, 5706 (1959).

[3] All of the compounds described here which contain centers of asymmetry are racemic mixtures with the exception of the *meso* compounds V, XVII and XIX. For convenience, the racemates are represented in both name and drawing by one enantiomorph.

[4] (a) C. Schuster and O. Stichnoth, German Patent 712,218, September 8, 1941; (b) H. E. Ungnade and F. V. Morriss, THIS JOURNAL, **72**, 2112 (1950).

[5] R. Robinson and F. Weygand, *J. Chem. Soc.*, 386 (1941).

[6] F. Runge and K. Goldann, *Chem. Ber.*, **86**, 377 (1953).

[7] M. Gates, private communication.

[8] R. Willstätter and J. Parnas, *Chem. Ber.*, **40**, 1406 (1907).

[9] A. Emmert, *Ann. Chem.*, **241**, 368 (1887).

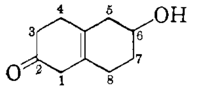
[10] H. Adkins and H. R. Billica, THIS JOURNAL, **70**, 695 (1948).

[11] The *trans*-dione V has a center of symmetry.

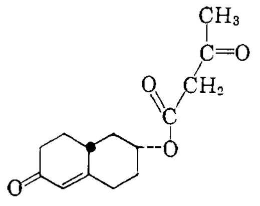
[12] E. C. Britton, U. S. Patents 1,959,283 (May 15, 1934) and 1,996,744 (April 9, 1935).

as modified by Gates and Webb.[13] Use of fresh W-7 Raney nickel[10] allowed tetrahydrogenation of 6-methoxy-2-naphthol at room temperature to give 6-methoxy-1,2,3,4-tetrahydro-2-naphthol.

Reduction of 6-methoxy-1,2,3,4-tetrahydro-2-naphthol with lithium and ammonia using the method of Wilds and Nelson,[14] followed by hydrolysis of the intermediate enol ether with oxalic acid[15] in order to avoid migration of the $\Delta^{4a,8a}$-bond furnished 6-hydroxy-1,2,3,4,5,6,7,8-octahydro-2-naphthalenone (VI, m.p. 64–67°) which was desired for physiological testing.



VI

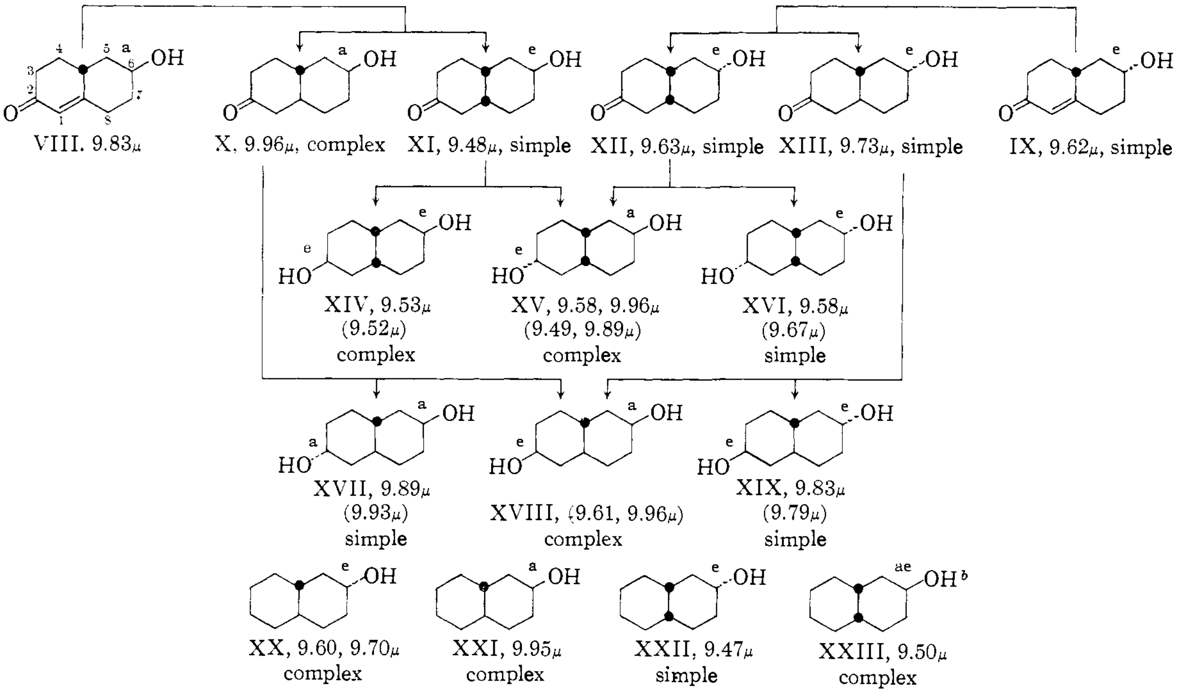


VII

Migration of the double bond into conjugation with the 2-keto group was accomplished with alcoholic hydrogen chloride. Of the two isomers produced (VIII and IX), the one possessing an *equatorial* hydroxyl group (IX) was expected to be formed in somewhat greater quantity than that having an *axial* hydroxyl group (VIII). The two isomers were isolated in yields of 42% (m.p. 98.5–101°) and 21% (m.p. 83–85.5°) and were tentatively assigned the structures 6α-(IX) and 6β-(VIII) hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone, respectively. These structures are confirmed below.

The acetoacetate ester of IX,[16] as drawn in VII, bears a distant resemblance to 11-oxo-progesterone. It, along with compounds VI, VIII and IX, failed to show any hormonal activity.

CHART I[a]



[a] The *a* or *e* by each hydroxyl group denotes the axial or equatorial nature of this group. The wave lengths given immediately underneath the formulas are those (in CS_2) believed related to the axial and/or equatorial character of the hydroxyl groups present. The corresponding values in KBr are given in parentheses. Following these values is a description of the 8 μ band of the acetate ester of the compound shown. [b] *Cf.* W. G. Dauben, R. C. Tweit and C. Mannerskanz, THIS JOURNAL, **76**, 4420 (1954).

Part II

The next phase in the synthesis of the desired anthracenones Ia and Ib involved reduction of the double bonds of VIII and IX in a manner which would furnish the *trans*-hydroxyketones. This reduction has given all four possible hydroxyketones, X through XIII. Reduction of these hydroxyketones has furnished the six decahydro-2,6-naphthalenediols. Positive relative configurational assignment has been made to each compound.

Catalytic hydrogenation of VIII evidently involved preferential adsorption of the relatively flat molecule (*cf.* formula XXIV) on the side away from the axial hydroxyl group for the *trans* compound X, m.p. 85.5–88°, was produced in 66% yield. The *trans* nature of this compound was indicated by its oxidation to *trans*-decahydro-2,6-naphthalenedione (V) (also see below). The lesser product, m.p. 65–68°, (8% yield) was assigned the *cis* structure XI.

At this point it was possible to confirm all of the structural assignments tentatively made above. The hydroxyketone X was converted to its tri-

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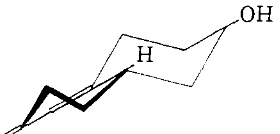
(13) M. Gates and W. G. Webb, THIS JOURNAL, **80**, 1186 (1958).

(14) A. L. Wilds and N. A. Nelson, *ibid.*, **75**, 5360 (1953).

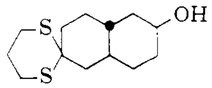
(15) A. L. Wilds and N. A. Nelson, *ibid.*, **75**, 5366 (1953).

(16) Prepared by the method of A. R. Bader, L. D. Cummings and H. A. Vogel, THIS JOURNAL, **73**, 4195 (1951).

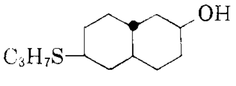


XXIV

methylene-dithio derivative XXV, m.p. 91.5–94°, and this thioketal desulfurized with Raney nickel. Along with unchanged starting thioketal



XXV



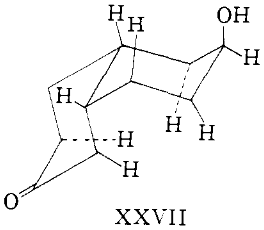
XXVI

XXV (24% yield), some partially desulfurized material (XXVI), m.p. 66–68.5° (17.5% yield), and some hydroxyketone X (5.5% yield), was obtained 1,2,3,4,4aα,5,6,7,8,8aβ-decahydro-2β-naphthol (XXI) which corresponded in melting point, the mixture melting point and infrared spectrum with an authentic sample kindly furnished by Dr. W. G. Dauben. The structure of this compound (XXI) has been determined unequivocally.[17] Thus the configurations of compounds IV, V, VIII, IX, X and XI are firmly established.

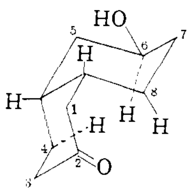
As mentioned above, there are four possible racemic forms of 6-hydroxydecahydro-2-naphthalenone (X, XI, XII and XIII), two *cis* and two *trans*. Theoretically, reduction of the carbonyl groups in these four compounds would produce eight diols. Only six diols result, however, because common products are formed in certain pairs of reductions. For example, reduction of the *trans*-hydroxyketone X (axial OH) gives rise to a *trans*-diaxial diol (XVII) and a *trans*-axial-equatorial diol (XVIII). Likewise, reduction of the *trans*-hydroxyketone XIII (equatorial OH) gives rise to a *trans*-diequatorial diol XIX and a *trans*-axial-equatorial diol, the latter being the same compound (XVIII) produced by reduction of X. It is evident, therefore, that the diols possessing one axial and one equatorial hydroxyl group in both the *cis* and the *trans* series (compounds XV and XVIII) can be recognized positively by their production in a dual manner.

Reduction of the *trans*-hydroxyketone X (axial OH) with sodium borohydride furnished two *trans*-diols. The product formed in greater yield (35%), m.p. 158–160.5°, was tentatively assigned the *trans*-axial-equatorial diol structure XVIII.[18] The lesser product (20% yield), m.p. 197.5–201°, was in like manner assigned the *trans*-diaxial diol structure XVII.

The hydrogenation of compound VIII produced such a low yield (8%) of *cis*-hydroxyketone XI that efforts were directed toward improving it. Hydrogenation of VIII in the presence of potassium hydroxide[19] failed to affect the ratio of isomers. Chemical reduction of VIII should produce X and XI in a ratio related to their thermodynamic stabilities. There are two possible chair–chair conformations for the *cis* compound XI, these being represented by structures XXVII and XXVIII.



XXVII



XXVIII

Conformation XXVIII, with its equatorial hydroxyl group and its carbonyl group in a position to eliminate some of the H–H interactions found in XXVII, is significantly more stable than XXVII. However, in the transition state for formation of the *cis* compound, the hydroxyl group must be axial; hence, the stabilities to be compared are those of X and of XXVII. Compound X is the favored structure. In actuality, reduction with lithium in ammonia gave a 59% yield of the *trans* compound X. None of the *cis* form XI was isolated. Thus, attempts to improve the yield of XI failed.

The *cis* - hydroxyketone XI (equatorial OH) was reduced with sodium borohydride to yield the *cis*-axial-equatorial diol XV, m.p. 133–134.5°, as the only product isolated (65% yield) . The reason for formation of an axial hydroxyl group in this reduction is evident from examination of the conformation of this hydroxyketone as shown by XXVIII. Axial approach of the borohydride ion to the carbonyl group with formation of an equatorial hydroxyl group is very effectively blocked by hydrogen on C_8. Here is a clear case where "steric approach control" dominates "product development control."[20] When this *cis*-hydroxyketone was reduced with lithium in ammonia, the thermodynamically more stable diequatorial diol XIV, m.p. 174–177°, was the only product isolated (35% yield).

Catalytic hydrogenation of the other α,β-unsaturated ketone IX produced the *cis*- and *trans*-hydroxyketones XII, m.p. 78.5–80°, and XIII, m.p. 84.5–86°, in 30 and 8% yields, respectively. Reduction of the double bond of IX with lithium in ammonia was successful when the hydroxyl group was protected as a tetrahydropyranyl ether[21] and the *trans*-hydroxyketone XIII (30% yield) was the only product isolated. The assignment of the *cis* and *trans* configurations was based upon oxidation of the two hydroxyketones to the corresponding *cis*- and *trans*-diketones of known configuration (see above).

Reduction of the *cis*-hydroxyketone XII (equatorial OH) with sodium borohydride gave the *cis*-diequatorial diol XVI, m.p. 148–150.5°, in 44% yield and the *cis*-axial-equatorial diol XV, m.p. 132–134°, in 12% yield. The latter compound was identical (mixture m.p. and infrared spectrum)

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(17) W. Hückel, *Ann. Chem.*, **441**, 1 (1925); **451**, 109 (1927); D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(18) Sterically, the keto group present resembles that in cyclohexanone and would be expected to give predominantly an equatorial hydroxyl group. The structural assignment proved correct (see below), but the amounts isolated are no reflection of the real ratio produced.

(19) P. L. Julian, "Recent Advances in Hormone Research," Vol. VI, Academic Press, Inc., New York, N. Y., 1951; R. Yashin, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4654 (1951).

(20) *Cf.* W. G. Dauben, G. J. Fonken and D. S. Noyce, *ibid.*, **78**, 2579 (1956).

(21) Otherwise an insoluble lithiumoxy derivative formed.

with the product XV formed by reduction of the *cis*-hydroxyketone XI (axial OH) as described above. The axial-equatorial nature of this product was thus established unequivocally.

Reduction of the *trans*-hydroxyketone XIII (equatorial OH) with sodium borohydride produced only the *trans*-diequatorial diol XIX, m.p. 195.5–200.5°. It was assigned the diequatorial configuration since it was different from the other two *trans*-diols (XVII and XVIII) already described.

Catalytic reduction of XIII (platinum in acetic acid) produced a mixture of isomers which we were not able to separate by chromatography on silica gel or alumina or by fractional crystallization. The infrared spectrum of this mixture was a perfect summation of the infrared spectral curves of the *trans*-diequatorial diol XIX, and the major product isolated from reduction of the hydroxyketone X (tentatively assigned the *trans*-axial-equatorial structure XVIII). The axial-equatorial nature of compound XVIII is thus conclusively demonstrated.

The acetates of the four hydroxyketones, X through XIII, are described in Table I. The diacetates of the six diols discussed above are described in Table II.

Discussion of Spectra.—There is general agreement in the literature that in cyclic systems the C–OH vibration for an axial hydroxyl group will occur at a wave length higher than that for the corresponding equatorial hydroxyl group.[22–24] With the 3-acetoxy steroids, Jones and associates[25] made some generalizations about the stereo relationship of the C$_3$-acetoxyl group with C$_5$-hydrogen and the character of the C–O–C band in the 8 μ region. Cole[26] later modified this correlation to state that *complexity* or *simplicity* of the 8μ band was indicative of an axial or equatorial (respectively) conformation of the acetoxyl group and was independent of the C$_5$-hydrogen.

Dauben, Hoerger and Freeman[27] reported how these correlations apply to the four possible decahydro-2-naphthols. These data are included in Chart I (compounds XX through XXIII).

The present series of compounds, wherein the conformations of the hydroxyl and acetoxyl groups are firmly established, furnished an excellent opportunity for further study of the relationship between spectra and axial and equatorial conformations. Spectral data for this series are presented in Chart I, Fig. 1, and Fig. 2.

Adjacent to each hydroxyl group in Chart I is a notation on the axial (a) or equatorial (e) conformation of this group. With each *cis* compound, two chair-chair configurations are possible (*e.g.*, XXVII and XXVIII above) with accompanying change in axial *versus* equatorial character of the substituent groups. Generally, one form is more stable than the other and the predominant extant conformation is designated.

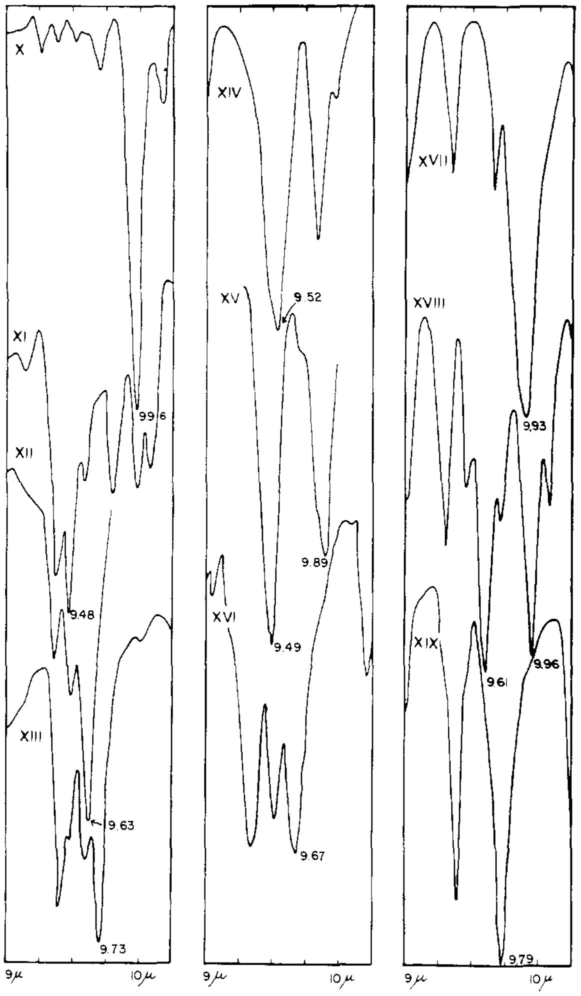

Fig. 1.—Infrared absorption spectra of compounds X–XIX.

Figure 1 presents the pertinent portions of the spectral curves for compounds X–XIX. Figure 2 shows the 8 μ region of spectral curves for the acetate esters of compounds X–XIX.

The data show that both the *cis* and the *trans* compounds containing axial hydroxyl groups (X, XV, XVII, XVIII and XXI) absorb between 9.89 and 9.96 μ.[28] The possible *cis* axial compound XI, as discussed above, exists predominantly in the inverted equatorial form exhibiting its strongest band at 9.48 μ. This situation is also true for compounds XIV and XXIII which show bands at 9.53 and 9.50 μ, respectively.

The *cis* compounds with equatorial hydroxyl groups absorb between 9.47 and 9.63 μ (XII, XV, XVI and XXII together with XI, XIV and XXIII discussed immediately above) whereas the *trans* compounds with equatorial hydroxyl groups absorb between 9.60 and 9.83 μ (XIII, XVIII, XIX

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(22) A. R. H. Cole, R. N. Jones and K. Dobriner, THIS JOURNAL, **74**, 5571 (1952).

(23) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

(24) S. Archer and T. R. Lewis, *Chemistry & Industry*, 853 (1954).

(25) R. N. Jones, R. Humphries, F. Herling and K. Dobriner, THIS JOURNAL, **73**, 3215 (1951).

(26) A. R. H. Cole, *J. Chem. Soc.*, 4969 (1952).

(27) W. E. Dauben, E. Hoerger and N. K. Freeman, THIS JOURNAL, **74**, 5206 (1952).

(28) R. A. Pickering and C. C. Price, *ibid.*, **80**, 4931 (1958), have empirically assigned the strong absorption at 10.47 μ found in the infrared spectrum of *cis*-4-*t*-butylcyclohexanol to an axial C–OH stretching frequency. It should be noted that the spectrum of this compound contains a strong 9.91 μ band which is in the region previously related to axial hydroxyl groups and supported by the present work.

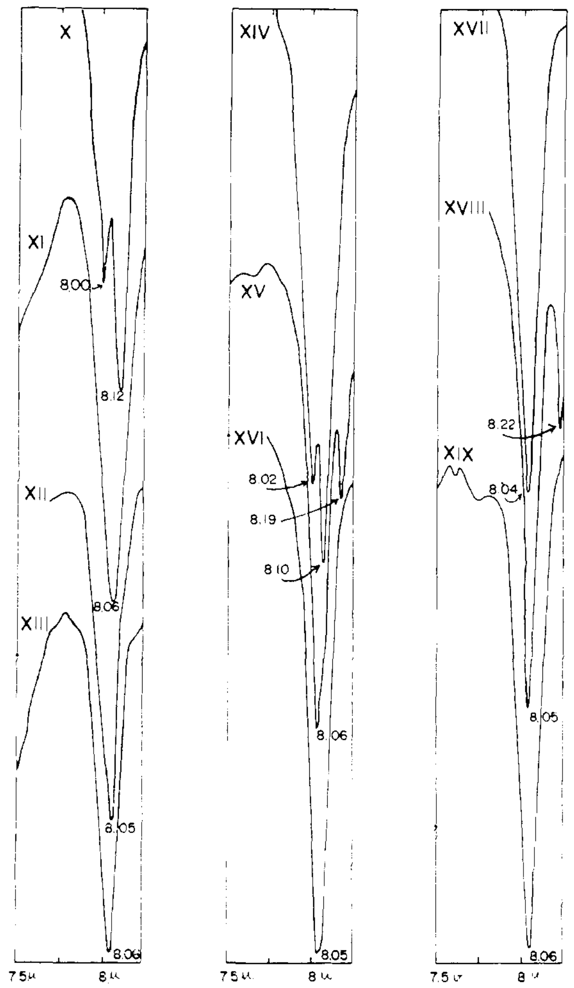


Fig. 2.—Infrared absorption spectra of the acetate esters of compounds X-XIX.

and XX).[29] The structures of compounds VIII and IX place these compounds in a slightly different series, but their spectra are in general agreement with the principles under discussion.

Where both axial and equatorial hydroxyl groups are present in the same molecule, *i.e.*, XV and XVIII, two strong bands are observed in their appropriate regions.

Attempted extension of the 8 μ acetate band correlation (simple *vs.* complex) reveals, as can be seen in Fig. 2 and by the notations in Chart I, anomalous results for the acetates of compounds XIV, XVII and XX. The acetate of XIV, which is far more likely to exist in the diequatorial form than in the diaxial form, has a complex band. The acetate of XVII, a *trans* diaxial compound which cannot undergo inversion, has a simple band. The rigid equatorial structure XX shows a complex band. These results suggest that the above acetate band correlation, found applicable to a large group of steroids, is not applicable to this simpler, less rigid ring system.

TABLE I

Acetate of	M.p., °C.	Crystal form	Found,^{a} % Carbon	Hydrogen
X	68–71	Prisms^{b}	68.7	8.7
XI^{c}	....	....	..	..
XII	148–150^{d}	1.4873^{e}	68.0	8.5
XIII	46.5–51	Dendrites^{f}	68.6	8.6

^{a} *Anal.* Calcd. for $C_{12}H_{18}O_3$: C, 68.53; H, 8.63. ^{b} From hexane. ^{c} The acetate of XI was an oil in such small quantity that it was characterized by spectrum alone. ^{d} Boiling point at 0.9 mm. ^{e} n^{25}D. ^{f} From pentane.

TABLE II

Diacetate of	M.p., °C.	Crystal form^{a}	Found,^{b} % Carbon	Hydrogen
XIV	84.5–88	Prisms	66.0	8.8
XV	95–96.5	Needles	66.0	8.7
XVI	110–111.5	Needles	65.9	8.8
XVII	136.5–138	Blades	66.5	8.8
XVIII	79–80.5	....	66.3	8.4
XIX	112.5–115.5	Blades	66.4	8.6

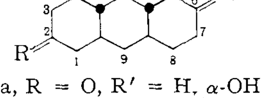
^{a} The diacetate of XIV was recrystallized from methanol-water, the others from hexane. ^{b} *Anal.* Calcd. for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72.

Part III

The final phase of this problem concerned the conversion of the *trans*-hydroxy-ketones VIII and IX to the desired anthracenones Ia and Ib. This conversion was first attempted on IX using the method of du Feu, McQuillin and Robinson[30] for the conversion of *trans*-β-decalone to 2,3,4,4aβ,5,6,7,8,8aα,9,10,10aβ-dodecahydro-2-anthracenone (6-desoxy compound I). This method, employing 4-dimethylaminobutanone-2 and sodamide, failed in the present case.

The elegant procedure of Stork, Terrell and Szmuskovicz,[31] involving the reaction of methyl vinyl ketone with the pyrrolidine enamine derivative of a ketone, was successful with compound IX and gave the anthracenone Ib. A strong 9.70 μ band in the infrared spectrum of Ib is apparently related to the *equatorial* configuration of the hydroxyl group (see above). Similarly, compound VIII was converted to the epimeric anthracenone Ia. A strong 10.04 μ band in the infrared spectrum of Ia is apparently related to the *axial* configuration of the hydroxyl group (see above).

Reduction of the tetrahydropyranyl ether derivative of compound Ib with lithium in liquid ammonia gave 6α-hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ-tetradecahydro-2-anthracenone (XXIXa), together with a trace of 1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ-tetradecahydro-2β,6α-anthracenediol (XXIXb). The 2-hydroxyl group in XXIXb was assigned the β-configuration (equatorial) since that configuration was favored by the extant reduction conditions.



XXIXa, R = O, R′ = H, α-OH
XXIXb, R = H, β-OH, R′ = H, α-OH
XXIXc, R = R′ = O
XXIXd, R = R′ = H_2

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(29) An unsuccessful attempt was made to add the curves for XX and XXI and then subtract the curve of decalin to obtain the curve of the corresponding decalin diol XVIII. The failure of this procedure was probably due to considerable interaction of the hydroxyl groups, and might explain the rather wide range of C–OH wave lengths.

(30) E. C. du Feu, F. J. McQuillin and Robert Robinson, *J. Chem. Soc.*, 53 (1937).

(31) G. Stork, R. Terrell and J. Szmuskovicz, THIS JOURNAL, **76**, 2029 (1954).

Chromic acid oxidation of the hydroxyketone XXIXa produced 1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ - tetradecahydro - 2,6 - anthracenedione (XXIXc) which, upon reduction with zinc amalgam and hydrochloric acid, gave 1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ - tetradecahydroanthracene (XXIXd). The stereochemistry of this *trans-trans* hydrocarbon has been determined by chemical methods[32] and X-ray analysis.[33] The hydrocarbon XXIXd proved identical with an authentic sample prepared by hydrogenation of anthracene.[32]

The series of transformations just described firmly established the stereochemistry of the ring junctions in Ib. The relationship between the angular hydrogens and the hydroxyl group in this molecule was determined above. The stereochemistry at C_{4a} in the epimer was not proved, but may be assigned as shown in formula Ia by analogy with the configuration of Ib.

Compounds Ia and Ib failed to show androgenic activity.

Experimental[34]

Purification of 2,6-Naphthalenediol (II).—2,6-Naphthalenediol[7,8] was converted to its diacetate ester by heating it with acetic anhydride for 2 hr. at 95°. This diacetate was recrystallized from absolute ethanol to give a product melting at 175–178° (reported[9] 175°). The diacetate was then hydrolyzed by dissolving 143 g. (0.59 mole) of it in 2.2 l. of hot acetic acid, adding 1.1 l. of water, and then 700 ml. of concentrated hydrochloric acid. The solution was refluxed for 1 hr., a second 700-ml. portion of concentrated hydrochloric acid added, and the refluxing continued for 2 hr. The solution was cooled and 35% sodium hydroxide added to just before the neutral point whereupon a very faint fluorescence appeared. The precipitated product was filtered at 30°[35] and the filtrate extracted twice with ether. The ether extracts were washed once with saturated sodium bicarbonate solution, dried (Na_2SO_4), and the ether was removed to furnish a solid residue. The combined solids, recrystallized in two portions from 3 l. of water with Darco G-60 added, melted at 220.5–223° (70.5 g., 75% yield).

Decahydro-2,6-naphthalenediol (III).—To a solution of 0.5 g. of sodium in 800 ml. of absolute alcohol was added 70.5 g. (0.44 mole) of purified 2,6-naphthalenediol, m.p. 220.5–223°, and 1.5 teaspoonfuls of fresh W-7 Raney nickel catalyst.[10] Hydrogenation at 2000 p.s.i. and room temperature resulted in the smooth absorption of 2 moles of hydrogen in 3 hr. At 85° further absorption began and 3 moles more was absorbed in 4 hr. The catalyst was filtered off, the solvent removed, and the residual, very viscous oil distilled at unrecorded temperature (0.8 mm.) to give 54.8 g. (73% yield) of crude product. This distillate, a hard glass, was warmed to 125° and poured in a fine stream into cold pentane. The brittle fiber produced was pulverized and stored at 0–5° to keep it from sintering.

***cis-* and *trans*-Decahydro-2,6-naphthalenedione**.—To a vigorously stirred suspension of 54.8 g. (0.322 mole) of powdered decahydro-2,6-naphthalenediol in 1500 ml. of benzene containing 50 ml. of pentane[36] at 5° was added 507 ml. of chromic acid solution[37] (0.52 mole of CrO_3 [20% excess]) in 30 min. at 5–14°. Vigorous stirring was continued at 5–10° for 75 min., the mixture was filtered, and the layers were separated. The aqueous layer was saturated with sodium chloride, extracted twice with ether, and discarded. The extracts and the benzene layer were washed twice with saturated sodium chloride solution, twice with saturated potassium carbonate solution, and four times with saturated sodium chloride solution. The solution was dried (Na_2SO_4), the solvent removed, and the residue chromatographed on 500 g. of silica gel in 1:4 ether–pentane. Six liters of the 1:4 mixture was followed by 10 l. of 3:7 mixture and 18 l. of 2:3 mixture before ***trans*-decahydro-2,6-naphthalenedione** (**V**) was eluted. The next 8 l. contained this compound contaminated with some *cis* isomer. Rechromatography of the eluate to this point, followed by recrystallization from ether–pentane, furnished 0.458 g. (0.9% yield) of the pure *trans* isomer, m.p. 139.5–141.5°.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.1; H, 8.3.

The following 10 l. of 2:3 eluate, 6 l. of 1:1 eluate and 6 l. of 3:2 eluate removed ***cis*-decahydro-2,6-naphthalenedione** (**IV**). Recrystallization of this solid once from ether–pentane and once from ether gave 7.85 g. (15% yield) of m.p. 73–75°.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.1; H, 8.6.

The solubility of these diones in water (>20%) was not appreciated in the course of this work; hence higher yields may be expected.

Further elution of this column with ether and finally ether–acetone mixtures resulted in the isolation of a trace of ***cis*-decahydro-2,6-naphthalenediol** (**XVI**) (identical with the product obtained below by reduction of IV).

***cis*-Decahydro-2,6-naphthalenediols XV and XVI**.—A 4.7-g. (0.028 mole) sample of *cis*-decahydro-2,6-naphthalenedione (IV) in 200 ml. of dry ether was added to a solution of 1.0 g. of lithium aluminum hydride in 200 ml. of dry ether and the mixture shaken frequently during 15 min. This mixture was poured into 15 ml. of 3 *N* hydrochloric acid with vigorous stirring and the ether layer decanted. The water layer was extracted twice with ether and the combined ether solutions dried (Na_2SO_4). The ether solution was adjusted to a 500-ml. volume, 500 ml. of pentane was added, and this solution was chromatographed on 200 g. of silica gel.

Gradual increase in the ether content of the eluting solvent to 70% removed ***cis*-decahydro-2,6-naphthalenediol** (**XV**) which, when recrystallized from ether, melted at 136–137.5 (715 mg., 15% yield).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.0; H, 10.5.

The following 8 l. of eluate contained oily mixtures and then ***cis*-decahydro-2,6-naphthalenediol** (**XVI**) was recovered. Recrystallized from 35 ml. of ethyl acetate, it weighed 1.92 g. (40% yield), m.p. 150.5–152°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.9; H, 10.9.

1,2,3,4-Tetrahydro-2,6-naphthalenediol.—This compound was prepared from 2,6-naphthalenediol by hydrogenation as described above for decahydro-2,6-naphthalenediol except that the reaction was worked up after the 2 moles of hydrogen had been absorbed at room temperature. The catalyst and solvent were removed and the residue recrystallized once from water–ethanol and once from xylene to give a 60% yield of tetrahydro derivative, m.p. 140–144° (reported[6] m.p. 136–138°).

6-Methoxy-1,2,3,4-tetrahydro-2-naphthol.—To a solution of 38.5 g. (0.24 mole) of 1,2,3,4-tetrahydro-2,6-naphthalenediol, m.p. 140–144°, and 10.3 g. (0.25 mole) of 97% sodium hydroxide in 150 ml. of water was added 34.6 g. (0.25 mole + 10%) of dimethyl sulfate at 7–10° in 10 min. with stirring and cooling. The mixture was warmed to 25° for 30 min. and heated on the steam-bath for 30 min. The mixture was

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[32] J. W. Cook, N. A. McGinnis and S. Mitchell, *J. Chem. Soc.*, 286 (1944), and references therein.

[33] S. Bog, O. Hassel and E. H. Vihovde, *Acta Chem. Scand.*, **7**, 1308 (1953).

[34] All melting points are corrected. The silica gel used (100–200 mesh) was obtained from the Davison Chemical Co., Baltimore, Md. The *dry* liquid ammonia referred to in this section was refluxed with and distilled from metallic lithium. All infrared spectra were determined with a model 21 Perkin–Elmer spectrophotometer equipped with NaCl optics. The CS_2 solutions were determined in concentrations varying from 1% w./v. to 0.04% w./v., depending upon the solubility, in cells of 1 mm., 1 cm. or 2 cm. path. The KBr pellets were prepared using Harshaw infrared quality powdered KBr in concentrations of 1% w./w. Appreciation is extended to Mr. Kenneth D. Fleischer and his associates for the analytical data reported, to Mrs. Madelyn W. Becker for her assistance in recording the spectra, and to Dr. Arthur L. Beyler for the biological tests. Many helpful discussions with Dr. William S. Johnson are gratefully acknowledged.

[35] A lower temperature greatly increases the chances of heavy precipitation of sodium acetate.

[36] This serves to prevent freezing of the benzene.

[37] Prepared from 84 g. of sodium dichromate dihydrate, 63 ml. of acetic acid, 114 ml. of concentrated sulfuric acid and 372 ml. of water.

cooled, stirred for 15 min. with an additional 20 g. of sodium hydroxide in 50 ml. of water, and extracted twice with ether. The extracts were washed twice with 10% potassium carbonate, once with water, and dried (Na_2SO_4). The ether was removed and the residue distilled to give 25.5 g. of the desired product, b.p. 125–132° (0.6 mm.), which solidified, m.p. 53–55° (reported[3b] 52.8–53.5°). A forerun, b.p. 118–125° (0.6 mm.), 6.8 g., solidified and was recrystallized from benzene to furnish 6.35 g., m.p. 53.5–56°. The total yield was 31.9 g. (75%).

6-Hydroxy-1,2,3,4,5,6,7,8-octahydro-2-naphthalenone (VI).—A solution of 82.5 g. (0.463 mole) of 6-methoxy-1,2,3,4-tetrahydro-2-naphthol in 500 ml. of ether was added to 2.5 l. of liquid ammonia with stirring in 10 min. Lithium wire (32.5 g., 4.68 moles) was then added in 25 min. and the mixture stirred for 1.5 hr. Absolute ethanol (360 ml.) was added in 1.25 hr. and the ammonia then evaporated from the mixture by warming. The residue was treated with 1.2 l. of ether and 350 ml. of water with stirring, the mixture was filtered, and the cake washed well with ether. (The amount of water added is such as to produce a damp solid and no water layer.) The filtrate and washings were freed from ether and alcohol by warming at <40° *in vacuo*. The residue, in two layers, was extracted twice with ether and the extracts freed from solvent at <40° *in vacuo*.

The residual oil, dissolved in 475 ml. of methanol, was mixed with a solution of 4.67 g. (0.052 mole) of oxalic acid in 54 ml. of water (this gives a solution 0.1 molar in oxalic acid discounting the volume of the oil) and the resulting solution was allowed to stand for 1 hr. Solid sodium bicarbonate (16.8 g., 0.2 mole) was added, the mixture stirred thoroughly, and filtered. All solvent was removed at <40° *in vacuo* and the residual oil was chromatographed on 700 g. of silica gel. Elution of the column with 8 l. of 1:1 ether–pentane washed the first of the desired product off the column and the ensuing 24 l. of this same solvent eluted a total of 56.5 g. (73% yield) of crude product, m.p. 47–62°. Two recrystallizations of approximately 8 g. of this solid by melting it, diluting it with ether, and allowing crystallization, furnished 5.6 g. of VI, m.p. 64–67°.

Anal. Cacld. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.2; H, 8.5.

6β- and 6α-Hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (VIII and IX).—A solution of 49.9 g. (0.3 mole) of crude 6-hydroxy-1,2,3,4,5,6,7,8-octahydro-2-naphthalenone (VI), m.p. 47–62°, in 100 ml. of 95% ethanol was treated with 20 ml. of 8*N* alcoholic hydrogen chloride and the resulting solution held at 28–30° for 1 hr. The solution was then stirred well with 42 g. of sodium bicarbonate, filtered, and freed from the solvent *in vacuo* at <40°. The residual oil was dissolved in 1 l. of ether and the solution diluted with 1 l. of pentane, whereupon some of IX separated. Recrystallized from 35 ml. of acetone, it afforded 11.55 g. of IX, m.p. 96–99°. The residues from the original and recrystallization mother liquors were chromatographed on 700 g. of silica gel in 1:1 ether–pentane; VIII was eluted first and, after one recrystallization from ether, amounted to 10.4 g. (21% yield), m.p. 83–85.5°, $\lambda_{\max}^{\mathrm{EtOH}}$ 240 mμ (log *E* 4.2). Further recrystallization failed to sharpen this melting point.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.0; H, 8.7.

Continued elution with the same solvent gave a further 9.6 g. (after one recrystallization from acetone) of IX, m.p. 98.5–101°; total yield, 21.15 g., 42%. The analytical sample, recrystallized again from acetone, melted at 99–101°, $\lambda_{\max}^{\mathrm{EtOH}}$ 238 mμ (log *E* 4.1).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.2; H, 8.8.

The acetate of IX was prepared by reaction of IX with acetic anhydride in pyridine at room temperature over a weekend. The dimorphic product crystallized from hexane–ether as heavy needles, m.p. 80–82°, or as massive prisms, m.p. 83–85° (83% yield). The massive prisms are the stable form at 25°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.19; H, 7.74. Found: C, 69.3; H, 7.6.

The 2,4-dinitrophenylhydrazone of IX formed deep red dendrites from absolute ethanol, m.p. 193–196.5°.

Anal. Calcd. for $C_{16}H_{18}N_4O_5$: N, 16.2. Found: N, 15.9.

6α-Acetoacetoxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (VII).—A solution of 1.0 g. of the unsaturated hydroxyketone IX, m.p. 96–99°, in 7 ml. of ethyl acetoacetate was heated at 100° under reduced pressure (200 mm.) for 17 hours.[16] The excess acetoacetic ester was removed by distillation at 0.3 mm. (100° maximum bath temperature) and the residue chromatographed on 25 g. of silica gel in 3:7 ether–pentane. The solid VII was recrystallized twice from ether to give 0.94 g. (63% yield), m.p. 51.5–54°.

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.0; H, 7.1.

Reduction of 6β-Hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (VIII). (A) Catalytically.—A solution of 8.6 g. (0.052 mole) of 6β-hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone, m.p. 83–85.5°, in 300 ml. of 95% grain alcohol was treated with hydrogen under 60 p.s.i. at room temperature in the presence of 2 g. of 2% palladium-on-calcium carbonate. Absorption of hydrogen was complete in 1 hr.

The catalyst and solvent were removed and the residue put on 150 g. of silica gel in 3:7 ether–pentane. Elution with 4:6 ether–pentane afforded 6.04 g. of **6β-hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα-decahydro-2-naphthalenone (X)**, m.p. 70–86°. One recrystallization of this crude product from ether gave 5.0 g., m.p. 85.5–88°. Reworking the mother liquors and adjacent fractions gave a further 0.8 g., m.p. 85.5–88°, total yield 5.8 g. (66%). Further recrystallization raised this melting point to 86–89°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.40; H, 9.59. Found: C, 71.6; H, 9.3. Continued elution with the same solvent mixture finally washed off **6β-hydroxy-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2-naphthalenone (XI)**, which, after two recrystallizations from ether, amounted to 0.40 g., m.p. 65–68°. This sample gave the analytical results shown below. Reworking of the mother liquors and adjacent fractions afforded an additional 0.28 g., m.p. 63–66.5°, total 0.68 g. (8% yield).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.40; H, 9.59. Found: C, 71.2; H, 9.4.

(B) **With Lithium in Ammonia.**—A mixture of 1.5 g. of VIII, 60 ml. of ether, 5 ml. of dihydropyran and 30 mg. of *p*-toluenesulfonic acid was allowed to stand for 1 hr. to form the tetrahydropyranyl derivative. This ether solution was added to a solution of 0.35 g. of lithium wire in 250 ml. of dry liquid ammonia. After 6 min., 2 g. of solid ammonium chloride was added and the mixture stirred until the blue color disappeared. Then all solvent was removed at <40° *in vacuo*. The residue was treated with 50 ml. of 2 *N* HCl and 50 ml. of methanol for 1 hr. at room temperature. The excess acid was neutralized with saturated aqueous potassium carbonate, all solvent removed at <40° *in vacuo*, and the residue extracted thoroughly with ether. Solvent was removed from the dried (Na_2SO_4) extract and the residue chromatographed in 3:7 ether–pentane on 25 g. of silica gel. The *trans* compound X, m.p. 81–86° (0.9 g., 59% yield), was eluted. There was no evidence of the presence of any *cis* compound XI.

Oxidation of Compound X.—Compound X (100 mg.) in 30 ml. of benzene was shaken with 1 ml. of chromic acid solution[37] for 5 min. The benzene layer was then washed with two 2-ml. portions of saturated salt solution, once with 2 ml. of saturated potassium carbonate solution, and dried (Na_2SO_4). The benzene was removed and the residue recrystallized from ether–pentane. **The *trans*-decahydro-2,6-naphthalenedione (V)** so obtained melted at 139–141° and showed no depression in melting point upon admixture with a sample described above. The infrared spectra of the samples were identical.

1,2,3,4,4aα,5,6,7,8,8aβ-Decahydro-2β-naphthol (XXI).—A mixture of 1.7 g. (0.01 mole) of X, 5 ml. of acetic acid, 5 g. (0.046 mole) of propane-1,3-dithiol and 5 drops of boron trifluoride–ether complex (47%) was allowed to stand at room temperature for 3 days. This mixture was poured into 30 ml. of 20% aqueous sodium hydroxide with cooling and the thioketal extracted with ether. The ether extract was diluted with pentane to a 1:9 ether–pentane composition and poured onto a column of 25 g. of silica gel. Elution with the same solvent mixture gave a small amount of oil followed by 1.5 g. of crystalline thioketal. This solid was dissolved in 5 ml. of benzene, 5 ml. of pentane added, and the mixture cooled to give 1.0 g. of **6-trimethylenedithio-1,2,3,4,4aα,5,6,7,8,8aβ-decahydro-2β-naphthol (XXV)**, m.p. 91.5–94°.

Dilution of the filtrate afforded a further 0.25 g., m.p. 91–93°, total 1.25 g. (45% yield).

Anal. Calcd. for $C_{13}H_{22}OS_2$: S, 24.81. Found: S, 24.9.

A solution of 1.23 g. of thioketal XXV in 50 ml. of 95% ethanol was stirred with 20 g. of Raney nickel for 26 hr. at room temperature. The catalyst and solvent were removed and the residual oil was chromatographed on 30 g. of silica gel in 1:9 ether–pentane.

Solid came off the column very quickly and, due to its unexpectedly high volatility, most of the sample was lost. The 16 mg. of XXI obtained, purified by sublimation, melted at 50.2–50.6°. Upon admixture with an authentic sample obtained from Dr. Dauben (m.p. 53.4–54.7°), it melted at 50.5–53.9°. The infrared spectra of the two materials were identical.

Compound XXI was followed closely by **6-*n*-propylthio-1,2,3,4,4aα,5,6,7,8,8aβ-decahydro-2β-naphthol (XXVI)** which, once recrystallized from pentane, amounted to 180 mg. (17.5% yield) m.p. 66–68.5°.

Anal. Calcd. for $C_{13}H_{24}OS$: S, 14.04. Found: S, 13.4.

Elution of the column with 1:4 ether–pentane removed some unchanged thioketal XXV, which, after recrystallization from ether–pentane, amounted to 226 mg. (24% yield) and melted at 92–94°.

Elution with 7:3 ether–pentane afforded 42 mg. (5.5%) of the hydroxyketone X as indicated by its infrared spectrum.

Reduction of 6β-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα-decahydro-2-naphthalenone(X) with Sodium Borohydride.—To a solution of 2.0 g. (0.019 mole) of X, m.p. 86–89°, in 15 ml. of methanol was added 0.4 g. of sodium borohydride. After standing for 15 min., the mixture was acidified with dilute hydrochloric acid and freed from solvent by warming *in vacuo*. The residue was extracted with four 25-ml. portions of boiling acetone, and the acetone was removed from the combined extracts. The residual solid, dissolved in 4:1 ether–pentane, was chromatographed on 75 g. of silica gel. **1,2,3,4,4aβ,5,6,7,8,8aα-Decahydro-2α,6β-naphthalenediol (XVII)** came from the column first and, after recrystallization from acetone, amounted to 0.4 g. (20% yield) and melted at 197.5–201°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.8; H, 10.8.

The same solvent mixture then eluted **1,2,3,4,4aβ,5,6,7,8,-8aα-decahydro-2β,6β-naphthalenediol (XVIII)** which was recrystallized from acetone to give 0.7 g. (35% yield) of m.p. 158–160.5°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.5; H, 10.8.

Reduction of 6β-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2-naphthalenone(XI). (A) With Sodium Borohydride.—A solution of 0.30 g. of XI, m.p. 65–68°, in 3 ml. of methanol was treated with 0.1 g. of sodium borohydride. This solution was allowed to stand for 15 min. at room temperature, acidified with hydrochloric acid, and freed from solvent at <40° *in vacuo*. The residue was extracted with acetone, the extract freed from solvent, and the residual oil chromatographed on 20 g. of silica gel in 1:1 ether–pentane. Only **1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2α,6β-naphthalenediol (XV)** was found, which when recrystallized from ether–pentane, melted at 133–134.5°; 125 mg., 65% yield. This compound showed no depression in melting point upon admixture with the lower-melting *cis*-decahydro-2,6-naphthalenediol obtained by reduction of IV as described above and the infrared spectra of the samples were identical.

(B) **With Lithium in Ammonia.**—A mixture of 0.67 g. of XI, m.p. 63–66.5°, 75 ml. of ether, 2 ml. of dihydropyran and 15 mg. of *p*-toluenesulfonic acid was allowed to stand for 30 min. and was then added to a solution of 0.42 g. of lithium in 250 ml. of dry liquid ammonia. This mixture was stirred for 5 min. Absolute ethanol (5 ml.) was added in 3 min. and the mixture stirred until the blue color disappeared (15 min.). The ammonia was evaporated by warming *in vacuo*, the residue acidified with dilute hydrochloric acid, and 10 ml. of methanol added. This mixture was warmed to 40° for 15 min. and the solvent then removed at <40° *in vacuo*. The residue was extracted thoroughly with ether and the content of the extracts chromatographed on 25 g. of silica gel in 1:1 ether–pentane. Gradual change of the eluting solvent to 7:3 ether–pentane gave 430 mg. of very crude product which was recrystallized twice from acetonitrile. This gave 235 mg. (35% yield) of **1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2β,6β-naphthalenediol (XIV)**, m.p. 170–173°. Two additional recrystallizations from acetonitrile furnished 201 mg. of m.p. 174–177°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56: H, 10.66. Found: C, 70.4; H, 10.8.

Reduction of 6α-Hydroxy-2,3,4,4aβ,5,6,7,8-octahydro-2-naphthalenone (IX). (A) Catalytically.—A solution of 4.17 g. (0.025 mole) of compound IX, m.p. 99–102°, in 30 ml. of absolute alcohol was treated with hydrogen under 60 p.s.i. at 25° for 3.5 hr. in the presence of 0.6 g. of 2% palladium-on-charcoal. The catalyst and solvent were removed and the residue chromatographed on 100 g. of silica gel in 2:3 ether–pentane. **6α-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα-decahydro-2-naphthalenone (XIII)** was eluted first. Recrystallized from ether–pentane, it melted at 83.5–85° (0.34 g., 8% yield); again recrystallized, m.p. 84.5–86°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.40; H, 9.59. Found: C, 71.3; H, 10.0.

6α-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2-naphthalenone (XII) then followed from the column. Recrystallized twice from ether, it melted at 76–79° (1.25 g., 30% yield); twice further recrystallized, m.p. 78.5–80°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.40; H, 9.59. Found: C, 71.4; H, 9.3.

(B) **With Lithium in Ammonia.**—A mixture of 20.85 g. (0.125 mole) of IX, m.p. 97–100°, 500 ml. of ether, 60 ml. of dihydropyran and 0.3 g. of *p*-toluenesulfonic acid was allowed to stir overnight. This solution was added to 2.4 l. of dry ammonia containing 3.5 g. (0.5 mole) of dissolved lithium and the mixture was stirred for 5 min. Solid ammonium chloride (20 g.) was added portionwise to discharge the blue color. The ammonia was evaporated by slight warming; *in vacuo* toward the end. The residue was acidified with dilute hydrochloric acid, 125 ml. of methanol was added to achieve homogeneity, and the solution was allowed to stand for one hr. The solution was made neutral by addition of solid sodium bicarbonate and all possible solvent then removed at <40° *in vacuo*. The residue was extracted three times with acetone and the acetone removed from the combined extracts. The residual oil was extracted thoroughly with ether and the content of the ether extracts put on 400 g. of silica gel in 1:4 ether–pentane. Elution with 3:7 ether–pentane removed compound XIII as the only product isolated. Recrystallization from ether afforded 6.3 g. (30% yield) of XIII, m.p. 82–84.5°.

Oxidation of Compound XII.—The oxidation of XII was performed exactly as done on compound X described above. The ***cis*-decahydro-2,6-naphthalenedione** so obtained, after recrystallization from ether–pentane, melted at 73–74.5°. It showed no depression in melting point upon admixture with a sample of IV reported above and the infrared spectra of the samples were identical.

Oxidation of Compound XIII.—The oxidation of XIII was performed exactly as done on compound X described above. The *trans*-diketone V so obtained melted at 138–142° after recrystallization from hexane. It showed no depression in melting point upon admixture with a sample of V reported above and the infrared spectra of the samples were identical.

Reduction of 6α-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2-naphthalenone (XII).—A solution of 1.19 g. of XII, m.p. 73–77°, in 15 ml. of methanol was treated with 0.25 g. of sodium borohydride and the resulting solution allowed to stand for 15 min. This solution was poured into 10 ml. of 6*N* hydrochloric acid, the solvent was removed by warming *in vacuo*, and the residue extracted with acetone. The acetone was removed from the extracts and the residue extracted thoroughly with ether. The content of the ether extract was chromatographed on 75 g. of silica gel in 4:1 ether–pentane. The *cis*-axial-equatorial diol XV was eluted first and, after recrystallization from ethyl acetate, melted at 129–134° (140 mg., 12% yield). Recrystallized again, the sample melted at 132–134°. This melting point was not depressed upon admixture with the compound melting at 133–134.5° which was isolated from the sodium borohydride reduction of XI. The infrared spectra of the two compounds were identical.

Elution of the column with pure ether removed **1,2,3,4,-4aβ,5,6,7,8,8aβ-decahydro-2α,6α-naphthalenediol (XVI)**. Once recrystallized from ethyl acetate, it melted at 148–150.5° (0.53 g., 44% yield). Further recrystallization raised the melting point to 150–152°. This compound was identical with the higher-melting *cis*-decahydro-2,6-naphthalenediol obtained by reduction of IV (described above) as indicated by mixture melting point and spectral comparison.

Reduction of 6α-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα-decahydro-2-naphthalenone (XIII). (A) With Sodium Borohydride.—A solution of 0.66 g. of XIII, m.p. 82–84.5°, in 15 ml. of methanol was treated with 0.2 g. of sodium borohydride and the resulting solution allowed to stand for 20 min. This reaction was worked up in the manner described immediately above for the reduction of XII. **1,2,3,4,4aβ,5,6,7,8,8aα-Decahydro-2β,6α-naphthalenediol (XIX)** was the only product obtained. After one recrystallization from acetone, it melted at 195.5–200.5° (457 mg., 68% yield). Recrystallization from acetonitrile failed to sharpen this melting point.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.9; H, 10.8.

(B) **Catalytically.**—Compound XIII (0.8 g.) was added to a prereduced suspension of platinum oxide (0.2 g.) in 10 ml. of acetic acid and the mixture treated with hydrogen under 60 p.s.i. for 1 hr. at 25°. The catalyst and solvent were removed, the residue dissolved in ether, and the ether solution shaken with solid potassium carbonate. The content of the ether solution was then chromatographed in 3:2 ether–pentane on 25 g. of silica gel. The *trans*-diequatorial diol XIX and the *trans*-axial-equatorial diol XVIII were eluted together. Recrystallized from acetone, the mixture melted at 145–167° (0.51 g., 63% yield). It could not be separated into its components by fractional crystallization or by chromatography on neutral alumina or silica gel. The infrared spectrum of this mixture showed all the bands of XVIII (as prepared by reduction of X) and of XIX (as prepared by borohydride reduction of XIII) but no other bands.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.66. Found: C, 70.9; H, 10.7.

6α-Hydroxy-2,3,4,4aβ,5,6,7,8,8aα,9,10,10aβ-dodecahydro-2-anthracenone (Ib).—A mixture of 1.0 g. (0.006 mole) of IX, 1.7 g. (0.024 mole) of pyrrolidine and 50 ml. of pure benzene was refluxed for 1.5 hr. with a water separator attached. The benzene and excess pyrrolidine were removed by warming *in vacuo* and the residue was treated with 0.45 g. (0.0065 mole) of methyl vinyl ketone in 20 ml. of pure dioxane. After the resulting solution had stood for 22 hr., the solvent was removed at <40° *in vacuo*. The residue was refluxed for 4 hr. with a mixture of 4.5 g. of sodium acetate, 4.5 ml. of water, 30 ml. of methanol and 3 ml. of acetic acid. The *p*H of the mixture was adjusted to 7 with 0.5 *N* sodium hydroxide, solvent was removed at <40° *in vacuo*, water was added, and the product was extracted with ether. The solvent was removed from the dried (Na_2SO_4) ether extract and the residue in 1:4 ether–pentane, was chromatographed on 35 g. of silica gel.

Gradual increase in the ether concentration of the eluting solvent to 3:2 ether–pentane washed off 180 mg. (18% recovery) of starting material followed by 256 mg. of the desired anthracenone (Ib). A single recrystallization of the product from ether afforded 190 mg. (15% yield) of tight needle clusters which softened at 134° and melted at 140–142°. Repeated recrystallization gave a sample which still softened at 134° and then melted at 141–142.5°; λ_{max}^{EtOH} 239 mμ [*E* 18,600]; $\lambda_{max}^{CS_2}$ 2.78, 5.96 and 9.70 μ.

Anal. Calcd. for $C_{14}H_{20}O_2$: C. 76.32; H, 9.15. Found: C, 76.1; H, 9.2.

6β-Hydroxy-2,3,4,4aβ,5,6,7,8,8aα,9,10,10aβ-dodecahydro-2-anthracenone (Ia).—A mixture of 5.0 g. (0.03 mole) of VIII, m.p. 85–88°, 10 ml. of pyrrolidine and 200 ml. of pure benzene was refluxed for 2 hr. with a water separator attached. The benzene and excess pyrrolidine were removed by warming *in vacuo*, the residual solid was dissolved in 60 ml. of pure dioxane and this solution treated with 2.4 g. (0.034 mole) of methyl vinyl ketone dissolved in 15 ml. of dioxane. After 19 hr. at 25°, the solvent was removed at <40° *in vacuo*. The residue was refluxed for 4 hr. with a mixture of 21 g. of sodium acetate, 21 ml. of water, 14 ml. of acetic acid and 80 ml. of methanol. After addition of 90 ml. of 2 *N* sodium hydroxide solution, the volume of the solution was reduced to 75 ml. by warming *in vacuo* and the product was extracted from it with ether.

The content of the ether extract was chromatographed on 100 g. of silica gel in 1:4 ether–pentane. Gradual increase in the ether concentration of the eluting solvent to 1:1 ether–pentane washed off 1.85 g. (37% recovery) of starting material followed by compound Ia. Recrystallization of this compound from ether gave 1.6 g. (24% yield) of material which softened at 137° and melted at 146–149°. Further recrystallization from methanol gave white plates, m.p. 149–151°, λ_{max}^{EtOH} 240 mμ [*E* 17,400]; $\lambda_{max}^{CS_2}$ 2.79, 5.98 and 10.04 μ.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.3; H, 9.4.

6α-Hydroxy-1,2,3,4,4aβ,5,6,7,8,8aα,9aα,10,10aβ-tetradecahydro-2-anthracenone (XXIXa).—A mixture of 1.51 g. (6.85 millimoles) of Ib, m.p. 134–140°, 100 ml. of ether, 3.5 ml. of dihydropyran and 30 mg. of toluenesulfonic acid monohydrate was stirred for 1.5 hr. to effect homogeneity and for 0.5 hr. longer. This solution was dried with Drierite for 5 min. and then added dropwise with stirring in 5 min. to a solution of 0.2 g. (29 millimoles) of lithium dissolved in 250 ml. of dry liquid ammonia. The dark blue solution was stirred for 7 min. and 1.5 g. of ammonium chloride added. Solvent was removed from the resulting colorless mixture and the residue treated with 15 ml. of methanol and 30 ml. of 2 *N* hydrochloric acid for 15 min. This mixture was made neutral with saturated aqueous potassium carbonate and the methanol removed at <40° *in vacuo*. The residue was extracted three times with 1:1 ether–benzene and the dried (Na_2SO_4) extracts freed from solvent.

The solid residue was chromatographed on 70 g. of silica gel in 1:1 ether–pentane to give 854 mg. of white needles. Recrystallization from 8 ml. of benzene gave 768 mg. (50% yield) of compound XXIXa, m.p. 158–160°, λ_{max}^{KBr} 2.95 and 5.91 μ.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.64; H, 9.98. Found: C, 75.6; H, 9.9.

Further elution of the chromatogram with the same solvent mixture removed **1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ-tetradecahydro-2β,6α-anthracenediol (XXIXb)** which, after recrystallization from methanol (3 ml.), gave white plates (17 mg.), m.p. 259–261°.

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.0; H, 11.2.

1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ-Tetradecahydro-2,6-anthracenedione (XXIXc).—A solution of 292 mg. of compound XXIXa, m.p. 158–160°, in 25 ml. of benzene was shaken for 15 min. with 2.5 ml. of chromic acid solution.[37] The benzene layer was washed with water and saturated potassium carbonate solution and dried (Na_2SO_4). The benzene was removed and the residue recrystallized from ethyl acetate to furnish 243 mg. of heavy needles which softened at 204° and melted at 209–212°. This material was not purified further.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.0; H, 9.4.

1,2,3,4,4aβ,5,6,7,8,8aα,9,9aα,10,10aβ-Tetradecahydroanthracene (XXIXd).—A mixture of 11 g. of zinc amalgam,[38] 240 mg. of XXIXc, m.p. 209–212°, 15 ml. of 95% ethanol, and 7.5 ml. of concentrated hydrochloric acid was refluxed for 1.5 hr. More acid (7.5 ml.) was added and reflux continued for 16 hr. The mixture was extracted twice with pentane, the pentane removed from the extracts, and the residual solid subjected to steam distillation. The distillate (100 ml.) was extracted twice with pentane and the solid from the extracts was recrystallized twice from methanol. This hydrocarbon (65 mg.) melted at 88–90° and showed no depression in melting point upon admixture with an authentic sample prepared by hydrogenation of anthracene.[32] The infrared spectra of the two samples were identical.

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(38) "Organic Reactions," Vol. I, Roger Adams, *et al.*, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 163.