studies in the ether–chloroform eluates. Evaporation of the solvent yielded 1.00 g. of a fraction which was recrystallized from 1 ml. of ethyl acetate and 10 ml. of methylcyclohexane to give 423 mg. of II, m.p. 102–106°, $[\alpha]^{26}D$ +83° (*c* 1.213 in chloroform).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.99; H, 9.90.

These physical constants together with infrared studies showed II to be identical with authentic 11α-hydroxypregnane-3,20-dione.[1a]

11α-Acetoxypregnane-3,20-dione (III).—Compound II (70.5 mg.) in pyridine was acetylated at room temperature with acetic anhydride and gave III, m.p. 152–153° after several recrystallizations from ether–Skellysolve B, $[\alpha]^{23}D$ +63° (*c* 0.800 in chloroform).

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15; acetyl, 11.50. Found: C, 73.93; H, 9.32; acetyl, 11.60.

11α-Hydroxyallopregnane-3,20-dione (V).—To a 24-hour growth of *Rhizopus nigricans*, 0.5 g. of allopregnane-3,20-dione (IV) was added. Following a 24-hour conversion period, the steroids were extracted in the usual manner.[2] An aliquot, examined by papergram studies, indicated that approximately 40% of a compound was produced, whose mobility was identical to V and a small amount of a more highly polar compound. In addition about 60% of the substrate was unconverted.

The extract, 1.45 g. was dissolved in 50 ml. of benzene and chromatographed over 25 g. of alumina as previously described.[2] The components were located in the various eluates by means of papergram studies. The benzene–ether, ether, ether–chloroform, chloroform, chloroform–acetone and acetone fractions were combined and dissolved in 3 ml. of hot ethyl acetate. After refrigeration, 270 mg. of crystals obtained were decolorized with Magnesol[2] in methylene chloride solution. After solvent removal, crystallization from ethyl acetate was repeated to yield a product, m.p. 140–160°. Infrared analyses showed this material to be a mixture of 60% 11α-hydroxyallopregnane-3,20-dione (V) and 40% L-leucyl-L-proline anhydride[3] separable by fractional sublimation or chromatography over carbon.

A 99-mg. sample of crystals, as obtained from the above preceding chromatographic separation, was dissolved in 8 ml. of methanol and chromatographed over a mixture of 9 g. of carbon (Darco G-60) and 9 g. of diatomaceous earth (Celite #545). The column was developed with five 72-ml. portions of methanol and seven 72-ml. portions of methylene chloride. The first four eluates yielded 29 mg. of L-leucyl-L-proline anhydride analyzed by infrared. The methylene chloride eluates gave a fraction weighing 82.8 mg. which upon recrystallization from 1 ml. of ethyl acetate, resulted in 50.9 mg. of V, m.p. 197–200°, $[\alpha]^{23}D$ +82° (*c* 1.316 in chloroform).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 76.00; H, 9.48.

These physical constants together with infrared analyses demonstrated that II was identical to authentic 11α-hydroxyallopregnane-3,20-dione.[1a]

11α-Acetoxyallopregnane-3,20-dione (VI).—Compound V (24 mg.) in pyridine was acetylated at room temperature with acetic anhydride and yielded VI, m.p. 181–182° after several recrystallizations from ethyl acetate–Skellysolve B, $[\alpha]^{23}D$ +67° (*c* 0.480 in chloroform).

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 74.09; H, 9.34.

Acknowledgment.—We wish to thank Dr. A. H. Nathan of our laboratories for assistance in preparing the 11α-acetoxy derivatives of pregnane-3,20-dione and allopregnane-3,20-dione, and Mr. Byron A. Johnson for supplying the pregnane-3,20-dione. We are grateful to the following members of the Upjohn Research Division for their coöperation and assistance on various aspects of our problems: Dr. J. L. Johnson, Mr. L. Scholten and Mrs. G. S. Fonken for ultraviolet and infrared analyses; Mr. W. A. Struck and his associates for rotations and microanalyses; and the Misses Jennie I. Mejeur, Irene N. Pratt and Mr. Glenn Staffen for technical assistance. The helpful suggestions and stimulating interest of Drs. R. H Levin and D. I. Weisblat have been greatly appreciated.

KALAMAZOO, MICHIGAN

(3) J. L. Johnson, W. G. Jackson and T. E. Eble, THIS JOURNAL, **73**, 2947 (1951).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

Approaches to the Total Synthesis of Adrenal Steroids.[1] V. 4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one and Related Tricyclic Derivatives

BY G. I. POOS, G. E. ARTH, R. E. BEYLER AND L. H. SARETT

RECEIVED JULY 14, 1952

The addition of methyl vinyl ketone to 5-methylperhydro-(4aα,8aα)-naphthalene-1β,4β-diol-6-one (I) proceeds stereospecifically to give 4b-methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one (II). The steric relationship of C4a and C4b, which is established in this reaction, is shown to be *anti* from consideration of steric hindrance in the *cis*-decalin molecule. This tricyclic intermediate (II) and its 7-ethylenedioxy derivative (III) can be selectively oxidized to the corresponding 1-keto derivatives. Inversion at C10a with base affords the desired BC *trans*-keto alcohols IX and X. This reaction series provides a stereospecific and rational approach to the natural (*anti-trans*) series of tricyclic steroidal intermediates. The preparation and properties of some related tricyclic compounds are described. It is noted that, in contrast to the 11-keto function in the steroids, the corresponding 4-keto function in the *anti-trans*-polyhydrophenanthrenes is reduced to the 4α-hydroxy derivative by $LiAlH_4$. Also described is the use of chromium trioxide–pyridine, an oxidizer which smoothly converts hydroxyl to carbonyl groups without attack on double bonds, acid-sensitive groups and the like.

A single isomer,[2] 4b-methyl-1,2,3,4,4aα,4b,5,6,7,-9,10,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one (II) resulted from the Triton B-catalyzed addition of methyl vinyl ketone to 5-methylperhydro-(4aα,8aα)-naphthalene-1β,4β-diol-6-one (I).[3a,b] The phenanthrene skeleton present in this condensa-

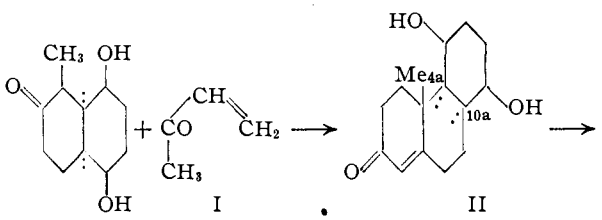
(1) The recent total syntheses of non-aromatic steroids by R. B. Woodward, F. Sondheimer and D. Taub (THIS JOURNAL, **73**, 3547, 4057 (1951)) and by H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann and R. Robinson (*Chemistry and Industry*, **20**, 389 (1951)) represent outstanding synthetic advances. There remains a distinct need, however, for direct synthetic routes to the adrenal hormones themselves.

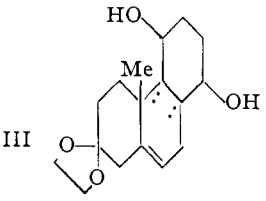
(2) The nomenclatural convention used herein has been described in part I of this series: THIS JOURNAL, **74**, 1393 (1952).

(3) (a) R. E. Beyler and L. H. Sarett, *ibid.*, **74**, 1406 (1952); (b) this method of adding a six-membered ring to β-decalones and β-tetralones is based upon the classical investigations of R. Robinson and his associates: E. C. DuFeu, F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 53 (1937); F. J. McQuillin and R. Robinson, *ibid.* 1097 (1938); R. Robinson and F. Weygand; *ibid.*, 386 (1941); Martin and R. Robinson, *ibid.*, 491 (1943).

tion product was demonstrated by aromatization to phenanthrene.

In considering the stereochemistry of II, it is clear that configurations at C1, C4, C4a and C10a remain as in the original dihydroxyketone. The





introduction of fixed asymmetry at C4b by the addition of methyl vinyl ketone necessitates the assignment of configuration at this center relative to the configuration at the other asymmetric centers. It has been shown[3a] that reduction of a derivative of *cis*-1,4-diketodecalin with lithium aluminum hydride gives only that diol in which the hydroxyl groups are *trans* to the bridgehead hydrogen atoms. It may thus be inferred that the steric hindrance governing the approach of reagents to the C1 and C4 positions of this molecule affects primarily only one face of the molecule and that this hindered face is the opposite of that on which the bridgehead hydrogen atoms lie. Furthermore, C5 and C8, the other pair of carbon atoms adjacent to the bridge, are *a priori* subject to essentially identical steric influences. Hence the carbanion of I should be accessible on the same face of the molecule as that which affords entry to lithium aluminum hydride[4] (the "back" face as the formulas are drawn in the present series). The tricyclic product, II, must on this basis have the *anti-cis* relationship at C4b–C4a–C10a (C10–C9–C8 according to steroid numbering).

Research on the tricyclic dihydroxyketone, II, had two aims: first, conversion to the *anti-trans*-4β-hydroxy-1-ketopolyhydrophenanthrene, IX, or derivatives thereof (*e.g.*, X and XI); second, proof of the *trans* linkage of the potential BC ring juncture in IX and its derivatives.

Conversion of 1β,4β-Dihydroxypolyhydrophenanthrenes to 4β-Hydroxy-1-ketopolyhydrophenanthrenes.—Several methods were found useful for partial oxidations of this sort, either with or without preliminary protection of the unsaturated keto group as the ethylenedioxy derivative.[5]

The C4-hydroxyl group exhibited an inertness parallel to, but even more pronounced than, that in the precursory bicyclic series. Acetylation of II with pyridine–acetic anhydride led to a monoacetate (IV). Warm acetyl chloride yielded the triacetate (V) along with the 1,7-diacetate (VI).[6] Partial saponification of the triacetate (V) with potassium carbonate gave a monoacetate (VII) isomeric with the 1-monoacetate. Oxidation of this 4-monoacetate gave a non-crystalline material which was converted on alumina to a single crystalline acetoxydiketone (VIII), from which the free hydroxydiketone (IX) could be obtained by vigorous saponification.

Another approach to the 1-keto-4-hydroxy series consisted of the direct partial oxidation of II, or its 7-ethylenedioxy derivative (III). Each of these underwent preferential oxidation at C1 with N-bromoacetamide,[7] the former in satisfactory yield, the latter only in considerably lower yield, owing to extensive bromination.

A more efficient method for effecting the partial oxidation of the dihydroxyethylenedioxy derivative (III) consisted of the Oppenauer oxidation, which yielded 70% of X on direct crystallization. Several by-products were isolated from the reaction

(4) L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949), have shown that reduction with lithium aluminum hydride is attended by inversion. D. Noyce and D. B. Denny, *ibid.*, **72**, 5743 (1950), have provided strong evidence for the applicability of this concept to carbonyl reductions.

(5) The formulation of the 3-ethylenedioxy derivatives in the present series as β,γ-unsaturated instead of α,β arises from the following considerations. Fernholz (*cf.* E. Fernholz and H. E. Stavely, Abstracts of the 102nd Meeting of the American Chemical Society, Atlantic City, N. J., 1941, 39M; see also E. Fernholz, U. S. Patents 2,356,154 and 2,378,918) has proved the β,γ formulation for the ethylenedioxy derivative of 4-cholesten-3-one. Inasmuch as this work has until recently been overlooked, the α,β formulation has been in general use. Very recently, however, Antonucci and co-workers (R. Antonucci, S. Bernstein, D. Grancola, M. Heller, R. Lenhard, R. Littell, K. J. Sax and J. H. Williams, Abstracts of the 4th Meeting-in-miniature of the New York Section of the American Chemical Society, New York City, N. Y., 1952, p. 36) have noted the β,γ shift and have applied it to the synthesis of steroid $\Delta^{5,7}$-dienes.

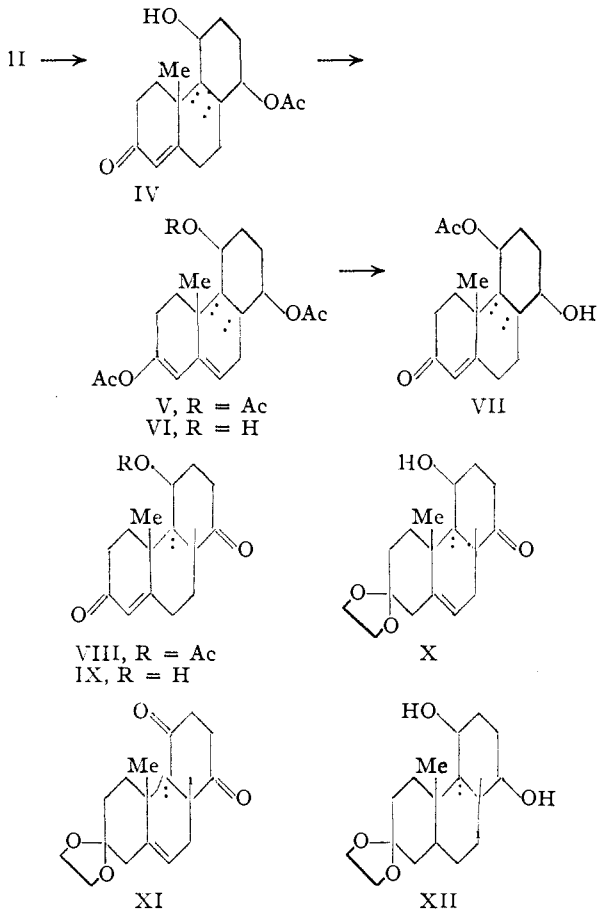
In order to test a method for locating the double bond in our tricyclic compound III, cholestenone was investigated as a model. The oxide of the 3-ethylenedioxy derivative of cholestenone (*cf.* Fernholz, ref. above) when treated first with aqueous perchloric acid followed by alkali yielded cholestane-3,6-dione, a product to be expected from the β,γ formulation. Application of this reaction series to the tricyclic dioxolane derivative III gave a dihydroxydiketone which had none of the properties of an α,β-diketone. Since the latter grouping would have arisen from an α,β-unsaturated dioxolane structure, III is formulated as the β,γ-isomer.

This formulation can also be derived from a consideration of the mechanism of such double bond shifts to the β,γ-position. It is likely that acid-catalyzed reaction of the Δ^4-3-ketosteroids with ethylene glycol proceeds *via* the $\Delta^{3,5}$-enolic form in a manner analogous to the formation of the $\Delta^{3,5}$-enol acetates. Since the predominant enolic form of the tricyclic α,β-unsaturated ketone II is the α,β,γ,δ-diene, as indicated by formation of the exocyclic enol acetates V and VI, the analogy between the dioxolanation of II and of 4-cholesten-3-one appears to be sound.

It seems probable that the hemithioketal derivatives of Δ^4-3-ketosteroids (*e.g.*, testosterone) (J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4961 (1951)) should be formulated as the Δ^5-structure by inference from reported rotational data (*cf.* D. H. R. Barton, *J. Chem. Soc.*, 512 (1946)). An interesting contrast is provided by the reaction of 4-cholestene-3-one with ethanedithiol (H. Hauptmann, THIS JOURNAL, **69**, 562 (1947). The cyclic mercaptal, as the author clearly shows, retains the double bond at the 4,5 position.

(6) Formulation of the enol acetates as the exocyclic dienes is based on the ultraviolet absorption spectra. *Cf.* U. Westphal, *Ber.*, **70**, 2128 (1937).

(7) It is worth noting that the hydroxyl group primarily attacked by N-bromoacetamide in a polyhydroxy compound is not necessarily the same one attacked by the chromium trioxide–pyridine complex (*vide infra*). Without exception the 11β-hydroxyl group in the steroids appears always to be the first to be attacked by chromic acid and its derivatives [*cf.* J. von Euw, A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **27**, 821 (1944)]. It is also sensitive to oxidizing agents not ordinarily considered to be effective in the oxidation of alcohols to ketones, such as ozone [J. von Euw, A. Lardon and T. Reichstein, ref. above] and to lead tetraacetate [*ibid.*, **27**, 1287 (1944)]. The preferential oxidation of the C1-hydroxyl group in the 1β,4β-dihydroxyketone (II) with N-bromoacetamide is therefore somewhat surprising.

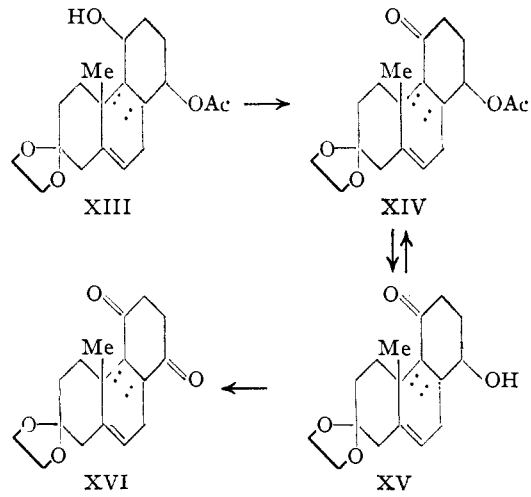


mixture, among them a diketone (XI) which could also be prepared by oxidation of the hydroxyketone (X).

The Configuration of 1-Ketopolyhydrophenanthrene Derivatives at C10a.—Oxidation of the C1 hydroxyl group to a ketone permitted inversion of the adjacent asymmetric center to the desired BC *trans* series. This inversion occurred smoothly and completely during the course of the selective Oppenauer oxidation and in part under the other conditions of selective oxidation mentioned above. Mixtures of such incompletely isomerized 1-ketones could be converted to the pure *trans* isomer by passage over alumina.

That the expected isomerization at C10a to the more stable[8] BC *trans* isomer had actually occurred during the Oppenauer oxidation[9] of III to X, could be substantiated by several pieces of evidence. The stability of the Oppenauer oxidation product to strong bases such as sodium methoxide was one indication of the *trans* character of the BC ring juncture. Another involved the reduction of this compound (X) with lithium aluminum hydride. The sole product was a 1β,4β-dihydroxy compound (XII)[10] isomeric with the *cis*-1β,4β-diol (III). Had the *cis* BC linkage persisted through the Oppenauer oxidation, the reduction should have regenerated the original *cis*-1β,4β-diol (III). (This point was confirmed by reduction of a BC *cis*-1-acetoxy-4-ketone (XIV) which did in fact regenerate the *cis*-1β,4β-diol (III); see below.)

A final proof of the *trans* character of the BC ring juncture in X involved the preparation of a pure *cis*-1,4-diketone. Attempts to oxidize the *cis*-dihydroxy compounds II and III directly to the pure *cis*-1,4-diketones did not succeed. In order to obtain the requisite *cis*-diketone (XVI), stepwise oxidations were employed. The 1β-acetoxy-4β-hydroxy compound (XIII) with the chromium trioxide–pyridine complex gave the *cis*-1β-acetoxy-4-ketone (XIV). Reduction of XIV with lithium aluminum hydride to the *cis*-dihydroxy precursor (III) showed that no inversion at C4a had occurred. Mild saponification of XIV gave the *cis*-1β-hydroxy-4-ketone (XV) which, since it yielded the starting acetate with acetic anhydride–pyridine, had not suffered inversion during the saponification step. (A second and more direct preparation of the *cis*-1β-hydroxy-4-ketone (XV) consisted of the partial oxidation of the *cis*-dihydroxy compound (III) with the chromium trioxide–pyridine complex.) Oxidation of the *cis*-1-hydroxy-4-ketone (XV) gave a new diketone



which was very easily isomerized on alumina to the stable diketone XI. The most reasonable interpretation of these data entails the conversion of the *cis*-hydroxyketone (XV) to the *cis*-diketone

(8) *Cf.* W. S. Johnson, *Experientia*, **8**, 315 (1951). An interesting exception to the general rule of greater stability of substituted *trans*-decalins over the *cis* isomers is pointed out by R. P. Linstead and R. R. Whetstone, *J. Chem. Soc.*, 1428 (1950). This exception (*trans-syn-cis*-polyhydrophenanthrene) has been rationalized by W. S. Johnson (ref. above) on the principle of maximization of equatorial bonds at ring junctures.

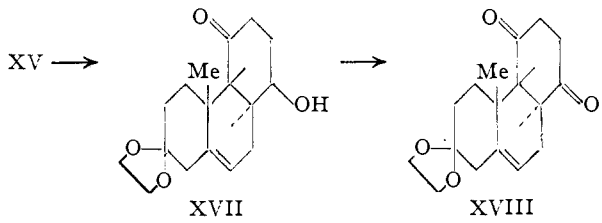
(9) The aluminum alkoxides in spite of their relatively non-polar character are quite able to generate carbanions in ketonic systems. Among other cases in point may be cited the well-known oxidation-rearrangement of the 3-hydroxy-5-stenols to the α,β-unsaturated stenones (R. Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937)) and the oxidation-rearrangement of *cis-syn-cis*-perhydrophenanthrene-9-ol to the *trans-syn-cis*-9-ketone (R. P. Linstead, R. R. Whetstone and P. Levine, THIS JOURNAL, **64**, 2014 (1942)).

(10) The C1 hydroxyl group in the diols obtained by lithium aluminum hydride reduction of X and XI was assigned the β configuration on the basis of the following evidence. Reduction of the hydroxy ketone X and the diketone XI with sodium in *n*-butyl alcohol gave in each case the *same* diol as that obtained with lithium aluminum hydride. From X the 1β,4β-diol was obtained in 74% yield; the diketone XI gave the 1β,4α-diol as the sole crystalline product in 57% yield. Since sodium–alcohol reduction of a substituted cyclohexanone gives the alcohol with the equatorial (more stable) configuration (*cf.* D. H. R. Barton, *Experientia*, **6**, 316 (1950)), the C1 hydroxyl group in these reduction products is assigned the β (equatorial) configuration.

(XVI) followed by isomerization to a *trans*-diketone. That this *trans*-diketone must be the *anti-trans* isomer XI is shown by its preparation from the Oppenauer oxidation product, the 4β-hydroxy-1-ketone (X), since the latter could have been inverted only at C10a. Conversely the 4β-hydroxy-1-ketone (X), being directly convertible into the *trans*-diketone under conditions known to be insufficient to epimerize the *cis*-diketone XVI, must itself belong to the *trans* series.

A similar isomerization of the *cis*-1,4-diketone to the *anti-trans*-diketone was also demonstrated in the 7-keto series.

The reactions described in this series of papers thus provide a rational and stereospecific route to tricyclic intermediates of the natural (*anti trans*) series. In addition, because of the presence of the C4 oxygen function, compounds of the isomeric *syn-trans* series[11] were accessible. Two of these were prepared for purposes of comparison. Vigorous treatment of the *anti-cis*-4-ketone XV with potassium carbonate gave the isomeric (*syn-trans*)-hydroxyketone XVII and thence the *syn-trans*-diketone XVIII.



XVII XVIII

An interesting contrast in the rate of isomerization at C10a and C4a became apparent from the present investigation: the *anti-cis*-4-ketones were much less readily isomerized than the *anti-cis*-1-ketones. In accordance with these observations, the *anti-cis*-1,4-diketones when permitted to isomerize did so entirely to the *anti-trans* rather than the *syn-trans* isomer.

Another point of interest lay in the stereochemical course of reductions of C4-ketones with lithium aluminum hydride. In contrast to the formation of 4β-hydroxy derivatives by reduction of both the *anti-cis*-4-ketone and 11-ketosteroids,[12] the *anti-trans*-4-ketones gave only the 4α-epimer. The α configuration of the C4 hydroxyl group was shown by its ready acetylation.

The Chromium Trioxide–Pyridine Complex, a Useful Oxidizing Agent.—The oxidation of hydroxyl groups to ketones or aldehydes has long been accomplished by the use of chromic acid. The salts of chromic acid have also been used but only in an acidic medium.[13] The usefulness of N-bromoacetamide as an oxidizing agent for secondary alcohols was first noted by Reich and Reichstein.[14] In dealing with polyfunctional molecules containing an acid-sensitive group, the necessity for an oxidizing agent which would operate under neutral or alkaline conditions arose. A modification of the N-bromoacetamide procedure consisting of the use of pyridine–*t*-butyl alcohol as solvent was therefore devised.[15] In oxidations of alcohols containing not only an acid-sensitive group but also a double bond or a thioether group, this oxidizing agent is not satisfactory, the latter functions also being attacked.[16] It seemed reasonable to us that the complex derived from chromic anhydride and a stable tertiary amine might well be capable of adding to a hydroxyl group to form a chromate ester which should then decompose in the usual manner to yield the corresponding ketone or aldehyde.[17] A series of heterocyclic amine–chromic anhydride complexes has been described by Sisler, Bush and Accountius,[18] among them the pyridine complex, $CrO_3 \cdot 2C_5H_5N$. Upon testing this substance, we found that it indeed smoothly converted primary and secondary alcohols to the corresponding carbonyl compounds, the yields of ketones from monohydric secondary alcohols approaching the theoretical. Furthermore, the complex showed the desired inertness toward double bonds and thioethers. It is apparent that these groups, which have only a modest electron-donating power, cannot compete with trivalent nitrogen for the chromic anhydride.

NOTE: As pointed out by Sisler, Bush and Accountius, the chromium trioxide–pyridine complex can inflame during its preparation. We have found in a very great number of runs, however, that the reagent could be safely prepared provided a few simple precautions were taken. Without these precautions, a fire resulted with regularity (see Experimental).

Acknowledgment.—The authors are indebted to Dr. Jacob van de Kamp, Mr. William Paleveda, Mr. Robert Gasser and their associates for the preparation of intermediates.

Experimental[19]

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one (II).—To a solution of 5.0 g. (0.0252 mole) of 5-methyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydronaphthalene-1β,4β-diol-6-one[3a] (I) in 50 cc. of ethanol was added 10.3 cc. of 40% aqueous benzyltrimethylammonium hydroxide, "Triton B" (4.30 g., 0.0257 mole), followed by 6.5 cc. of 85% aqueous methyl vinyl ketone (4.9 g., 0.070 mole). The solution was heated at reflux for two hours after which it was cooled and acidified with 20 cc. of 3 *N* hydrochloric acid. The acidic reaction mixture was boiled for 30 minutes. Ethanol was distilled from the mixture *in vacuo* and the resulting aqueous suspension

(11) This is the third possible arrangement of the C4b-C4a-C10a centers. P. A. Robins and J. Walker, *J. Chem. Soc.*, 642 (1952), have shown in their model studies that the fourth possible arrangement, the *syn-cis*, is accessible *via* condensation of 1-vinylcyclohexene and *p*-benzoquinone. However, these authors (*ibid.*, 1610 (1952)) have demonstrated that the method is unsuccessful when applied to intermediates which would provide the required angular methyl group.

(12) See, for example, N. Wendler, R. Graber, R. Jones and M. Tishler, THIS JOURNAL, **72**, 5792 (1950); L. H. Sarett, M. Feurer and K. Folkers, *ibid.*, **73**, 1777 (1951); P. L. Julian, E. W. Meyer, W. J. Karpel and W. Cole, *ibid.*, **73**, 1982 (1951).

(13) For recent examples of the use of chromic salts under various conditions in the oxidation of steroidal alcohols, see Fieser and Rajagopalan, *ibid.*, **73**, 118 (1951), and preceding papers.

(14) H. Reich and T. Reichstein, *Helv. Chim. Acta*, **26**, 562 (1943).

(15) L. H. Sarett, THIS JOURNAL, **71**, 1165 (1949).

(16) It appears from the work of S. Ball, T. W. Goodwin and R. A. Morton, *Biochem. J.*, **42**, 516 (1948), (see also J. Attenburrow, *et al.*, *J. Chem. Soc.*, 1094 (1952) for leading references) that manganese dioxide in petroleum ether has general applicability in the oxidation of allylic alcohols.

(17) F. Holloway, M. Cohen and F. H. Westheimer, THIS JOURNAL, **73**, 62 (1951).

(18) H. H. Sisler, J. D. Bush and O. E. Accountius, *ibid.*, **70**, 3827 (1948).

(19) Melting points were determined on the Kofler micro hot-stage. Ultraviolet absorption spectra were determined in methanol.

was continuously extracted with chloroform. The chloroform solution was concentrated, the last traces of solvent being removed from the residue by warming *in vacuo*. Trituration of the residue with 25 cc. of warm acetone caused the product to crystallize. After cooling, the product was collected on a filter and washed once with cold acetone: 2.46 g. (39.0%), m.p. 235–243°. One recrystallization from methanol, after Darco G-60 treatment, produced colorless prisms, m.p. 244–246°; λ_{max} 245 mμ, E_{mol} 16,200.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.19; H, 8.73.

A similar result was obtained using 1-diethylaminobutanone-3-methiodide (with an added equivalent of base for its decomposition) in place of methyl vinyl ketone. The reaction was also successfully carried out in either water or tetrahydrofuran.

Conversion of 4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one (II) to Phenanthrene.—A solution of 700 mg. of II in 90 cc. of dry tetrahydrofuran was added to 500 mg. of lithium aluminum hydride in 60 cc. of dry tetrahydrofuran. The resulting heavy suspension was stirred for one hour at room temperature and then treated cautiously with enough water to decompose the excess lithium aluminum hydride and to hydrolyze the salt complexes. Granular inorganic material was separated by filtration and the filtrate was concentrated. The oily residue gave 510 mg. of a crystalline mixture of triols on trituration with ether. This mixture was combined with 50 mg. of 10% palladium–carbon catalyst and heated under reflux at 310–320° for one hour and then at 320–345° for another hour. Thorough extraction of the cooled reaction mixture with ether followed by evaporation of the solvents left an oil which was distilled *in vacuo*. The product (200 mg.) was crude phenanthrene, m.p. 87–99°, leaflets from methanol. One recrystallization from methanol gave material melting at 96–98° alone or when mixed with an authentic sample.

The picrate from ethanol melted at 138–144° and did not depress the melting point of an authentic sample of phenanthrene picrate (m.p. 143–144°).

Essentially identical ultraviolet absorption spectra were obtained from the phenanthrene prepared in this experiment and an authentic sample.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1β,4β-diol (III).—A flask arranged for the addition of solvent, stirring and distillation was charged with 1.80 g. of II, 1.8 cc. of redistilled ethylene glycol, 50 cc. of dry ethylene dichloride and 20 mg. of *p*-toluenesulfonic acid hydrate. The mixture was heated with stirring while 200 cc. of ethylene dichloride–water slowly distilled over a two-hour period, the original volume being maintained by the continuous addition of ethylene dichloride. After cooling, the reaction mixture was washed with 20 cc. of 1% potassium carbonate, and this aqueous layer then thrice extracted with ethylene dichloride. The combined dried ethylene dichloride solutions left a crystalline residue after concentration. Trituration with a small volume of cold acetone gave 1.84 g. (87%) of product, m.p. 186–188°. Two recrystallizations from acetone raised the melting point to 188–189.5°.

Anal. Calcd. for $C_{17}H_{26}O_4$: C, 69.35; H, 8.90. Found: C, 69.30; H, 8.70.

4b-Methylperhydrophenanthrene-1β,4β-diol-7,9-dione.—A solution of 1.00 g. (0.00342 mole) of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aα-dodecahydrophenanthrene-1β,4β-diol (III) in 9 cc. of ethylene dichloride was treated with 10.5 cc. of benzene containing 0.535 g. (0.00387 mole) of perbenzoic acid. After one hour at room temperature, an aliquot gave only a faintly positive peroxide test. The reaction mixture was poured into 20 cc. of 1 *N* potassium hydroxide, the organic layer was separated and the aqueous phase was extracted twice with chloroform. The combined organic solution was washed with water, dried and concentrated. Trituration of the residue with ether gave 905 mg. (86%) of 4b-methyl-8a,9-oxido-7-ethylenedioxyperhydrophenanthrene-1β,4β-diol, m.p. 167–171°.

To a solution of 850 mg. of this oxide in 8 cc. of tetrahydrofuran was added 4 cc. of 3 *N* perchloric acid. The reaction mixture was allowed to stand at room temperature for three hours. Tetrahydrofuran was evaporated and to the resulting aqueous solution was added 4 cc. of 4 *N* sodium hydroxide. After a brief period of warming, the solution was extracted continuously with chloroform. The chloroform extract was concentrated to dryness and the residue was triturated with acetone giving 0.545 g. (61%) of 4b-methylperhydrophenanthrene-1β,4β,8a,9-tetrol-7-one melting at 224–230°. A sample recrystallized from acetone for analysis melted at 233–234°.

Anal. Calcd. for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.12; H, 8.46.

A solution of 160 mg. of the glycol above in 5 cc. of 1 *N* potassium hydroxide was kept at 100° for 1.5 hours. The reaction mixture was saturated with sodium sulfate and was extracted continuously with chloroform. Evaporation of the chloroform gave 60 mg. (40%) of residue which crystallized from methanol. The product, 4b-methylperhydrophenanthrene-1β,4β-diol-7,9-dione, separated as colorless prisms from methanol, m.p. 223–225°; transparent to ultraviolet light.

Anal. Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.94; H, 8.11.

Cholestane-3,6-dione from 3-Ethylenedioxy-5-cholestene.—To a solution of 750 mg. of the ethylenedioxy derivative of 4-cholestene-3-one, m.p. 134–135°,[20,21] in 4 cc. of benzene was added a solution of 275 mg. of perbenzoic acid in 5.5 cc. of benzene. After standing at room temperature for 30 minutes, the solution gave only a faint positive test with acidified potassium iodide solution. It was then diluted with ether, washed with aqueous potassium hydroxide, then with water and concentrated to dryness. The crude oxide tended to gel. It was dissolved without purification in 4 cc. of tetrahydrofuran and treated with 2 cc. of 3 *N* aqueous perchloric acid. The resulting oily suspension after standing at room temperature for five minutes became homogeneous. After three hours the solution was diluted with water, extracted with ether, the ethereal solution was washed with aqueous potassium hydroxide and with water and concentrated to dryness. The crude keto glycol was sparingly soluble in ethyl acetate and separated from ethanol as a gel. It was dissolved in 10 cc. of ethanol and treated with 3.5 cc. of 1.0 *N* aqueous potassium hydroxide. After brief boiling, crystals separated and were filtered and washed with water. The product 469 mg. melted at 165–170°. Recrystallization from ethanol gave crystals, m.p. 173–174°, not depressed on admixture with a sample of cholestane-3,6-dione.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one 1-Acetate (IV).—To 16 cc. of dry pyridine containing 698 mg. of II was added 8 cc. of acetic anhydride. The mixture was heated on the steam-bath for ten minutes and, after cooling, was treated with three volumes of cold water. The product was extracted into chloroform which was washed with dilute hydrochloric acid, dried and concentrated. Crystallization of the residue from ether gave 775 mg. (95%) of monoacetate (IV) melting at 160–168°. Three recrystallizations from ether raised the melting point to 169.5–170.5°.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.86; H, 8.38.

4b-Methyl-1,2,3,4,4aα,4b,5,6,10,10aα-decahydrophenanthrene-1β,4β,7-triol Triacetate (V).—In a system protected from moisture, a mixture of 480 mg. of II and 7 cc. of acetyl chloride was heated under reflux for four hours. Dissolution of the crystalline starting material during the first hour was accompanied by evolution of hydrogen chloride, which could no longer be detected after four hours. Excess acetyl chloride was removed *in vacuo*. Chromatographic purification of the residue over acid-washed alumina afforded 618 mg. (86.5%) of the triacetate V, m.p. 132–136°. After three recrystallizations from methanol, the product melted at 137.5–139°; $\lambda_{max.}$ 235 mμ, $E_{mol.}$ 16,500.

Anal. Calcd. for $C_{21}H_{28}O_6$: C, 67.00; H, 7.47. Found: C, 67.01; H, 7.67.

A second compound, 4b-methyl-1,2 3,4,4aα,4b,5,6,10,-10aα-decahydrophenanthrene-1β,4β,7-triol 1,7-diacetate (VI), 47 mg. (7.5%), m.p. 150–151°, from ether, was

(20) C. S. Grob, W. Jundt and H. Wicki, *Helv. Chim. Acta*, **32**, 2427 (1949), give m.p. 134–135°.

(21) The rotation of this substance was determined as $[\alpha]^{25}D$ −25.5° (chloroform). E. Fernholz, ref. 5, gives $[\alpha]D$ −28° (solvent unspecified).

recovered by further elution of the alumina, λ_{max} 240 mμ, E_{mol} 16,400.

Anal. Calcd. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 67.97; H, 7.80.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β,4β-diol-7-one 4-Acetate (VII).—A solution of 455 mg. of V in 25 cc. of 4% potassium carbonate in 75% methanol–water was heated at reflux for ten minutes. Methanol was distilled *in vacuo* from the reaction mixture maintained at room temperature. The product was extracted from the aqueous suspension with five portions of ether. Evaporation of the dried ethereal extracts and crystallization from ether gave 210 mg. (59%) of crude product, m.p. 156–165°. A sample twice recrystallized from ether melted at 168–170°, λ_{max} 237 mμ, E_{mol} 16,500.

Anal. Found: C, 70.01; H, 8.43.

A mixture with the isomeric acetate IV melted at 135–155°.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aβ-dodecahydrophenanthrene-4β-ol-1,7-dione 4-Acetate (VIII).—An ice-cold solution of 180 mg. of the hydroxyacetoxyketone, VII, in 5 cc. of 90% acetic acid was treated portionwise with a solution of 180 mg. of chromium trioxide dissolved in 1.8 cc. of 90% acetic acid. The reaction was allowed to proceed for an hour after attaining room temperature. The solution was diluted with 20 cc. of water and exhaustively extracted with chloroform. After washing with saturated aqueous sodium bicarbonate, the dried solution upon evaporation gave 123 mg. of a gummy residue which could not be crystallized. When chromatographed on basic alumina, this non-crystalline residue was converted into 72 mg. (40%) of product, VIII, m.p. 103–105°. Two recrystallizations from ether raised the melting point to 106.5–107°; λ_{max} 237 mμ, E_{mol} 15,600.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.62; H, 7.43.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aβ-dodecahydrophenanthrene-4β-ol-1,7-dione (IX).—A solution of 40 mg. of VIII in 1 cc. of benzene and 1 cc. of 1 *N* methanolic potassium hydroxide was heated under reflux for one hour. Benzene (20 cc.) was added and the solution was acidified with 1 cc. of 1 *N* hydrochloric acid. The benzene extract was dried and distilled leaving 33 mg. of product which crystallized from acetone, m.p. 194–197°. The pure product, IX, m.p. 201–202°; λ_{max} 237 mμ, E_{mol} 19,400, was obtained by a second crystallization from acetone.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.28. Found: C, 72.80; H, 7.91.

N-Bromoacetamide Oxidation of II.—A supersaturated solution of 877 mg. (0.0035 mole) of the diolone, II, in 9 cc. of pyridine was attained by warming followed by careful cooling to room temperature. After the addition of 570 mg. (0.00413 mole) of N-bromoacetamide, the oxidation in the resulting solution was allowed to proceed at room temperature for three hours, when titration of an aliquot in the usual manner indicated that 90% of the active bromine had been consumed. The reaction mixture was then cooled and added to excess cold 5 *N* hydrochloric acid. Five chloroform extractions followed by drying and concentration of the combined extracts left a gummy residue which on trituration with acetone provided 171 mg. of crystals melting at 190–225°. This was shown to be the starting diolone, II, m.p. 241–244°, by recrystallization from methanol. The acetone-soluble material (539 mg., 62%) melted at 155–185°. Four recrystallizations of this crude product from acetone gave a small amount of 4b-methyl-1,2,3,4aα,4b,5,6,7,9,10,10aβ-dodecahydrophenanthrene-4β-ol-1,7-dione (IX). After the crude product (m.p. 155–185°) had been chromatographed on basic alumina, it melted at 195–200°. One recrystallization of this product from acetone provided IX, m.p. and mixed m.p. 201–202°.

N-Bromoacetamide Oxidation of III.—Repetition of the above oxidation using 147 mg. of the 7-ethylenedioxy derivative (III) of the dihydroxy ketone gave 5 mg. of crude 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X), m.p. 210–217° after chromatography. A mixed melting point with a sample of X, m.p. 219–220°, prepared by the Oppenauer oxidation of III (see below) melted at 215–220°. A bromine-containing by-product, m.p. 155–156°, was also isolated.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X).—Two grams (0.0069 mole) of the 7-ethylenedioxydiol (III) was dissolved in 50 cc. (0.48 mole) of cyclohexanone and 45 cc. of dry benzene. A solution of 2.0 g. (0.0097 mole) of freshly distilled aluminum isopropoxide in 5.0 cc. of dry benzene was added and the mixture heated under reflux (bath temperature 120–125°) for 16 hours. The reaction mixture was cooled and treated with 4.0 cc. of water. The precipitated aluminum salts were collected by filtration and thoroughly washed with benzene. Concentration of the filtrate, finally by heating to 135–140° at 0.1 mm., left a crystalline residue. The crystals were triturated with 1:1 ether–petroleum ether, collected by filtration and washed with the same solvent. One recrystallization from acetone afforded 1.35 g. (68%) of X, m.p. 218–219.5°. After recrystallization from acetone the melting point was 219–220°.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 70.13; H, 8.51.

Hydrolysis of X in methanol containing a trace of hydrochloric acid gave the free hydroxydiketone IX as shown by melting point and mixed melting point.

Chromatography of the residue obtained from the fraction soluble in 1:1 ether–petroleum ether (see above) on basic alumina provided 400 mg. (20%) of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione (XI), m.p. 117–120.5°, raised to 120–120.5° after recrystallization from ether.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.53; H, 7.60.

Chromic Acid Oxidation of X.—A solution of 410 mg. of X in 10 cc. of 90% acetic acid was treated portionwise with a solution of 400 mg. of chromium trioxide in 4.0 cc. of 90% acetic acid with external cooling. After two hours at room temperature, the reaction mixture was poured into 40 cc. of water and extracted with chloroform. The chloroform extract was washed with aqueous sodium bicarbonate, dried and concentrated leaving 250 mg. of gummy residue. This material was adsorbed on acid-washed alumina. With 1:1 ether–petroleum ether there were eluted crystals of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,9,10,10aβ-dodecahydrophenanthrene-1,4-dione (XI), m.p. 117–119°. After one recrystallization from ether, this product melted at 119–120.5° alone or when mixed with XI as obtained above. Further elution with 1:1 ether–chloroform gave 4b-methyl-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4,7-trione, m.p. 114–116°. Recrystallization from benzene raised the melting point to 117–117.5°; λ_{max} 237 mμ, E_{mol} 16,400.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 73.16; H, 7.37. Found: C, 73.14; H, 7.26.

This product was also obtained from XI by hydrolysis in methanolic hydrochloric acid.

Preparation and Use of the Chromium Trioxide–Pyridine Complex.—The general procedure which was found to be safe and reproducible involved addition of chromic anhydride to pyridine. (*If the pyridine was added to the chromic anhydride, the mixture usually inflamed.*) To ten parts of reagent grade pyridine at 15–20° was added one part of chromic anhydride in portions with swirling or stirring. The first phase of the reaction, particularly if the pyridine solution was colder than 15°, appeared to consist of slow dissolution of the anhydride without formation of the complex. After a few minutes—in some cases almost immediately—the red anhydride was transformed exothermally into a yellow solid which dissolved quite rapidly; the temperature was kept below 30° during the addition of subsequent portions. After about one-third of the chromic anhydride had been added and mostly dissolved, the yellow complex began to precipitate. At the end of the addition a slurry of the complex in pyridine remained. On a 100-g. scale the preparation required about an hour.

The chromium trioxide–pyridine complex was moderately soluble in pyridine and sparingly soluble in other organic solvents such as dioxane, benzene and acetone. It was ordinarily used, therefore, as the suspension in pyridine, to which was added a 10–12% pyridine solution of the alcohol to be oxidized.

Chromium Trioxide–Pyridine Oxidation of X.—A solution of 3.12 g. of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X)

in 30 cc. of pyridine was combined with 3.1 g. of chromium trioxide in 30 cc. of pyridine. The reaction flask was stoppered, the contents were mixed thoroughly and allowed to stand at room temperature overnight. The reaction mixture was poured into water and extracted with three portions of benzene–ether (1:1) using filtration through Super Cel to break the emulsions. The combined organic solution was washed with water, dried over anhydrous magnesium sulfate and concentrated, finally under high vacuum. Crystallization from ether gave 2.76 g. (89%) of XI. m.p. 117–120°.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-1β,4β-diol (XII).—To 1 g. of lithium aluminum hydride in 25 cc. of dry tetrahydrofuran was slowly added with stirring a solution of 884 mg. of X in 25 cc. of dry tetrahydrofuran. After stirring one hour at room temperature, 4.0 cc. of water was added dropwise and the precipitated inorganic salts separated by filtration. The tetrahydrofuran was distilled leaving a crystalline residue. Recrystallization from acetone gave a first crop yield of 538 mg., m.p. 175–176°. A second crop of 268 mg., m.p. 160–173°, brought the total yield to 90%. Recrystallization of the first crop from acetone did not change the melting point. A mixture of this product (XII), with III (m.p. 188–189.5°) melted at 153–175°.

Anal. Found: C, 69.36; H, 9.05.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-1β,4β-diol 1-Acetate.—The diol XII (1.40 g.) was acetylated with acetic anhydride in pyridine by the previously described procedure. The product after washing with ether weighed 1.32 g. (82%) and melted at 185–190°. A portion recrystallized from methanol melted at 191–192°.

Anal. Calcd. for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 68.26, 67.67, 68.24; H, 8.01, 7.38, 7.94.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-1β-ol-4-one 1-Acetate.—A solution of 836 mg. of 4b-methyl-7-ethylenedioxy-1,2,3,-4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1β,4β-diol 1-acetate in 8 cc. of pyridine was oxidized with 830 mg. of chromium trioxide in 8 cc. of pyridine by the usual procedure. Crystallization of the product from ether–petroleum ether gave 656 mg. (78%) melting at 110–111°. A sample for analysis was recrystallized from ether–petroleum ether, m.p. 111–112°.

Anal. Calcd. for $C_{19}H_{26}H_5$: C, 68.24; H, 7.84. Found: C, 68.15; H, 7.54.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-1β,4α-diol. A. From 4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1β-ol-4-one 1-Acetate.—A solution of 206 mg. of the *anti-trans*-acetoxy-4-ketone in tetrahydrofuran was reduced with excess lithium aluminum hydride by the procedure described above. There was obtained 155 mg. (86%) of diol, m.p. 195–198°. A portion recrystallized from acetone melted at 198–199.5°.

Anal. Found: C, 69 34; H, 8.85.

B. **From 4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,-6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione (XI).**—One hundred eighty milligrams of XI was reduced with lithium aluminum hydride as in the preceding section. The product (160 mg., 88%) melted at 198–199.5° alone or when mixed with the 4b-methyl-7-ethylenedioxy-1,2,3,-4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1β,4α-diol described above.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-1β,4α-diol Diacetate.—Thirty milligrams of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,β,4α-diol in a mixture of 1 cc. of pyridine and 0.5 cc. of acetic anhydride was kept at 100° for ten minutes. After the usual work-up, there was obtained 33 mg. (86%) of product, m.p. 160–165°, raised to 163–165° after recrystallization from ether–petroleum ether.

Anal. Calcd. for $C_{21}H_{30}O_6$: C, 66.64; H, 7.99. Found: C, 66.66; H, 8.19.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1β,4β-diol 1-Acetate (XIII).—A solution of 2.00 g. of III in 20 cc. of dry pyridine and 10 cc. of acetic anhydride was kept at 100° for ten minutes. Excess acetic anhydride was hydrolyzed with ice-water. The crystalline product was collected on a filter, washed thoroughly with water and dried; yield 2.04 g. (89%). A sample recrystallized from acetone melted at 183.5–184°.

Anal. Calcd. for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.58; H, 8.25.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1β-ol-4-one 1-Acetate (XIV).—Two grams of XIII in 20 cc. of pyridine was oxidized with 2.0 g. of chromium trioxide in 20 cc. of pyridine by the usual procedure. There was obtained 1.71 g. (86%) of product in two crops from ether. Recrystallization gave a sample of XIV melting at 143–144.5°.

Anal. Calcd. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.45; H, 7.78.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1β-ol-4-one (XV).—A solution of 726 mg. of XIV in 10 cc. of 0.25 *N* potassium carbonate in 75% methanol was heated under reflux for 12 minutes. Water was added and the methanol was removed *in vacuo*. Organic material was collected in chloroform and the chloroform solution was dried and evaporated to yield 552 mg. (87%) of crystalline product, m.p. 137–140°. Recrystallization from ether raised the melting point to 142–143°.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.75; H, 8.10.

A mixture with the starting acetate (XIV) melted below 130°. Upon passage over alkaline alumina, XV was recovered unchanged. Acetylation of XV with acetic anhydride–pyridine by the standard procedure gave the acetate precursor, XIV.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1,4-dione (XVI).—A solution of 182 mg. of XV in 2 cc. of pyridine was oxidized with 200 mg. of chromium trioxide in 2 cc. of pyridine at room temperature overnight. After dilution with water and extraction with benzene there was obtained 170 mg. of noncrystalline product. On standing, an ethereal solution of this material deposited 80 mg. of crystals, m.p. 135–145°. Several recrystallizations from ether raised the melting point to 146–148°.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.30; H, 7.87.

The first ether mother liquor was passed over alkaline alumina. There was obtained 75 mg. of XI, m.p. 118–119.5°, mixed m.p. 118.5–120°.

Lithium Aluminum Hydride Reduction of XIV.—Two hundred milligrams of XIV in 10 cc. of anhydrous tetrahydrofuran was added dropwise to a stirred solution of 300 mg. of lithium aluminum hydride in 10 cc. of tetrahydrofuran. After stirring at room temperature for 1.5 hours, 1 cc. of water was added dropwise and the granular inorganic salts were separated by filtration. After the removal of tetrahydrofuran and crystallization from acetone there was obtained 167 mg. (95%) of III melting at 186–188°.

Oxidation of III with the Chromium Trioxide–Pyridine Complex.—Three grams of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aα-dodecahydrophenanthrene-1β,4β-diol (III) in 30 cc. of pyridine was combined with 3.0 g. of chromium trioxide in 30 cc. of pyridine, and allowed to stand at room temperature overnight. Dilution with water followed by extraction with benzene–ether, washing, drying and concentration gave 2.90 g. of crude, non-crystalline product.

When this material was chromatographed over 90 g. of alkaline alumina, the benzene eluate gave 480 mg. (16%) of XI, m.p. 113–118°. With ether and ether–chloroform (1:1) there were eluted first 200 mg. (7%) of X, m.p. 216–219° and finally 2.18 g. (73%) of XV, m.p. 130–138°.

It was possible to obtain XVI from III in about 30% yield by reoxidation of the crude product above with chromium trioxide–pyridine. Chromatography of this second-stage oxidation product over alkaline alumina gave XI in an over-all yield of 58%.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aβ,4b,5,6,7,8,10,-10aα-dodecahydrophenanthrene-1β-ol-4-one (XVII).—A solution of 98 mg. of XV in 5 cc. of 0.5 *N* potassium carbonate in 75% methanol was heated under reflux for three hours. Methanol was distilled and the product was collected in chloroform. Evaporation of the solvent gave 95 mg. of crystalline product, m.p. 113–116°. Recrystallization from ether raised the melting point to 117.5–118.5°.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.80; H, 8.26.

Hydrolysis and isomerization of XIV under similar conditions was used for the more direct preparation of XVII.

4b-Methyl-7-ethylenedioxy-1,2,3,4,4aβ,4b,5,6,7,8.10,-10aα-dodecahydrophenanthrene-1,4-dione (XVIII).—To the chromium trioxide–pyridine complex from 300 mg. of chromium trioxide and 3 cc. of pyridine was added a solution of 270 mg. of XVII in 3 cc. of pyridine. The mixture was left at room temperature for two hours and then was diluted with water and extracted with benzene. After removal of the solvent and vacuum-drying of the residue, crystallization from ether gave 190 mg. of product melting at 160–170° along with a small amount of unchanged starting material. The analytical sample was recrystallized three times from ether, m.p. 171–172°.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.51; H, 7.53.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β-ol-4,7-dione.—To a solution of 227 mg. of XV in 5 cc. of acetone was added one drop of 10% hydrochloric acid. The solution was boiled for 15 minutes and then diluted with water and the acetone distilled *in vacuo*. The aqueous suspension was extracted with chloroform and the chloroform solution was dried and evaporated to give 190 mg. (99%) of crystals, m.p. 118–123°. Recrystallization from ether gave a sample melting at 126–127°; λ_{max} 240 mμ, E_{mol} 14,300.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.28. Found: C, 72.67; H, 8.33.

4b-Methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1,4,7-trione.—A solution of 140 mg. of 4b-methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aα-dodecahydrophenanthrene-1β-ol-4,7-dione in 5 cc. of 90% acetic acid was cooled and treated portionwise with 1.4 cc. of 10% chromic acid in 90% acetic acid. After standing at room temperature for 1.5 hours, the product was recovered by the usual procedure; yield 121 mg., m.p. 160–164°. Crystallization from benzene–ether afforded a sample melting at 164–166°; λ_{max} 238 mμ. E_{mol}-15.100.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.27; H. 7.37.

Isomerization of 4b-Methyl-1,2,3,4,4aα.4b,5.6,7,9,10,-10aα-dodecahydrophenanthrene-1,4,7-trione to the *anti-trans*-Triketone.—Twenty-three milligrams of the *anti-cis*-triketone, m.p. 164–166° (preceding section), in benzene solution was adsorbed on 2 g. of alkaline alumina. After one hour (less time gave incomplete isomerization) the material was eluted with ether–chloroform (1:1) giving 20 mg. of crystals melting at 98–110°. Recrystallization from ether gave 4b-methyl-1,2,3,4,4aα,4b,5,6,7,9,10,10aβ-dodecahydrophenanthrene-1.4,7-trione, m.p. 117–117.5° alone or on admixture with the triketone obtained from XI by acid hydrolysis.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE RICE INSTITUTE]

The Effect of Structure of the Alkyl Group on the Rates of Decomposition of Alkyl Substituted Benzenediazonium Salts[1]

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The rates of decomposition of *m*- and *p*-alkylbenzenediazonium ions in water solution were measured. For the reaction of *p*-alkylbenzenediazonium fluoborates, the substituents, in order of increasing rate constants, are methyl, isopropyl, *s*-butyl and *t*-butyl, although these rate constants vary at most by a factor of only 1.8. With *m*-substituents the order of increasing rate constants is methyl, ethyl and *t*-butyl, with about a fourfold extreme variation. When compared to the unsubstituted compound, all *m*-alkyl substituents accelerate the decomposition and all *p*-alkyl groups retard it. The rate differences are not ascribable entirely to differences in heat of activation, and therefore cannot be explained by inductive and hyperconjugative effects alone.

The effect of alkyl substituents on the rates of various reactions of aromatic systems has been the subject of considerable interest. The concept of hyperconjugation is useful in predicting general effects of alkyl groups, and many more refined ideas have been proposed to explain the differences between the various alkyl groups.[2,3,4] A reaction which lends itself to facile kinetic measurements and has not been investigated from this point of view is the decomposition of dilute solutions of alkyl-substituted benzenediazonium salts in water. The product of this reaction is principally the phenol,[5] which is believed to result from a two-step process[5,6,7]; first, a rate-determining loss of nitrogen to give the aryl cation (eq. 1)

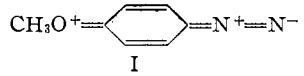
$$ArN_2^+ \longrightarrow Ar^+ + N_2 \qquad (1)$$

followed by the rapid reaction to give the phenol (eq. 2).

$$Ar^+ + H_2O \longrightarrow ArOH + H^+ \qquad (2)$$

The effect of substituents on the rate of diazonium salt decompositions is complicated. Two effects may be considered, an inductive effect and a resonance effect. In reaction (1), the center of positive charge moves from the nitrogen to the aromatic ring. It would therefore be expected from electrostatic considerations alone (the inductive effect) that electron-withdrawing substituents, which also make the ring positive, would retard the reaction. Correspondingly, from the same considerations, electron supplying substituents, like alkyl groups, should facilitate the reaction.

The resonance effect is important with *o*- and *p*-substituents capable of supplying electrons; for instance, the *p*-methoxyl group can interact with the diazonium group, because of the contribution of the structure I.



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Similarly, *p*-alkyldiazonium ions must have contributions from the analogous no-bond structures. Stabilization resulting from this resonance and the concurrent strengthening of the carbon–nitrogen

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