floating colonies with a white aerial mycelium, almost forming a pellicle. A similar layer of growth covered the bottom of the flask. On the fifth day a heavy wrinkled white mat of mycelium had formed and on the eighth day there were some submerged areas containing spores.

Ten liters of culture medium, after eight days incubation, was freed of mycelium by decantation and filtered through several layers of cheese cloth. The resulting clear greenish-yellow solution was divided into three portions and extracted thoroughly by repeatedly shaking with benzene, using a total of about 5-l. of solvent. The benzene extracts were washed with water, combined, and concentrated on a steam-bath to a volume of about 300 ml. The last of the benzene was distilled off under reduced pressure in an all-glass apparatus. The slightly yellow crystalline residue was triturated with two 25-ml. portions of petroleum ether to wash out fatty material. The crystalline mixture of antibiotics, after washing, weighed 1.1 g.

The mixture was dissolved in 100 ml. of benzene, warmed with decolorizing carbon and filtered. The filtrate was concentrated to a volume of about 40 ml., diluted with petroleum ether (b.p. 30–60°) until a turbidity developed, and cooled in a refrigerator. This procedure effected precipitation of most of the gliotoxin, which was separated by filtration. The crystalline precipitate was taken up in 40 ml. of benzene and the gliotoxin fraction reprecipitated by dilution with petroleum ether and cooling, as before. The crude gliotoxin after the second precipitation melted at 180–190°; after several crystallizations from ethanol it was obtained in substantially pure condition, m.p. 190–192°.

The mother liquors from the isolation of gliotoxin were evaporated to dryness under reduced pressure and the residue was recrystallized twice from ethanol. This gave 300 mg. of a pure product, m.p. 162–163°, for which analytical data are shown in Table I. Acetyl determination gave the value 11.1%, *vs.* 11.7% calculated for one acetyl group. Methoxyl analysis showed 2.0 and 1.8%, which is much lower than the value 8.3% required for one methoxyl group.

The crystals of gliotoxin monoacetate are quite different from those of gliotoxin[10] and are readily identified under the microscope. Dr. John H. Andreen has kindly prepared for us a crystallographic description of gliotoxin monoacetate, crystallized from benzene (Fig. 1). The crystals are orthorhombic and in their most common habit possess the forms: basal pinacoid, 001; macrodome, 101; and brachydome, 011. In some crystals the basal pinacoid, 001, is very small or entirely absent. The interfacial angles $011:01\bar{1}$ and $101:10\bar{1}$ are 143 ± 1°. The optic axial plane is 100, with γ, the acute bisectrix, parallel to "c". The sign of double refraction is positive. In sodium light the optic axial angles are $2V = 9 \pm 1°$, and $2E = 14.5 \pm 1°$. For sodium light the refractive indices are: α, 1.6110; β, 1.6120; and γ (calcd.), 1.80 ± 0.05.

Methanolysis of Gliotoxin Monoacetate.—In a small flask 500 mg. of the new antibiotic, m.p. 162–163°, was placed with 100 mg. of *p*-toluenesulfonic acid and 30 ml. of methanol. The mixture was heated and methanol was distilled off slowly at the rate of about 15 ml. per hour. The distillate was collected in a receiver cooled in ice. More methanol was added from time to time to maintain a volume of 20–30 ml. of liquid in the flask.

After ten hours heating, the reaction mixture was reduced to a volume of 15 ml., 50 ml. of chloroform added, and the organic solvent washed with 100 ml. of water. The aqueous layer was extracted again with 50 ml. of chloroform. The combined chloroform extracts were washed with 50 ml. of water and then evaporated to dryness. Benzene (50 ml.) was added and evaporated to dryness to remove all of the chloroform. After two crystallizations from methanol the residue formed pale yellow crystals, m.p. 188–189°; weight 150 mg. A mixture with authentic gliotoxin showed no depression of the melting point.

The distillate (150 ml.) obtained during the ten hours heating with methanol was treated with 5 ml. of *N* sodium hydroxide solution and refluxed for two hours to saponify methyl acetate. Titration of an aliquot indicated that 76.4% of the theoretical amount of acetic acid had been formed. The neutralized solution was evaporated to dryness and the resulting sodium acetate was identified as the S-benzylthiouronium salt, according to the procedure of Shriner and Fuson.[11] The derivative melted at 130–132° and showed no depression when mixed with an authentic specimen of the acetate derivative.

(10) J. R. Johnson, W. F. Bruce and J. D. Dutcher, THIS JOURNAL, **65**, 2008 (1943).

(11) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y.

ITHACA, N. Y.

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

Approaches to the Total Synthesis of Adrenal Steroids. VII. A New Method for the Attachment of Ring D. Part A

BY L. H. SARETT, W. F. JOHNS, R. E. BEYLER, R. M. LUKES, G. I. POOS AND G. E. ARTH

RECEIVED DECEMBER 22, 1952

The first phase of a new method for attaching ring D to 1-ketopolyhydrophenanthrenes is described. A three-carbon system corresponding to C-17, C-20 and C-21 of the pregnane skeleton is added. Thus the condensation of methallyl iodide with 2α,4b-dimethyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (I) gives the 2β-methyl-2-methallyl derivative II. Application of the same reaction to the 2-methyl-1,4-diketone IV gives chiefly the epimeric 2α-methyl-2-methallyl compound V. In partial ozonolyses and partial hydroxylations with osmium tetroxide the side chain double bond is affected preferentially. The structures of dilactols related to these 1-keto-2-methallyl compounds are discussed.

The gain of five carbon atoms is required to convert the tricyclic methyl hydroxyketone[1] I into a pregnane derivative. Three of these, which represent C-17, C-20 and C-21 of the pregnane skeleton, may be conveniently introduced by a condensation with an allylic halide. It is with this condensation and attendant stereochemistry that the present paper is concerned.

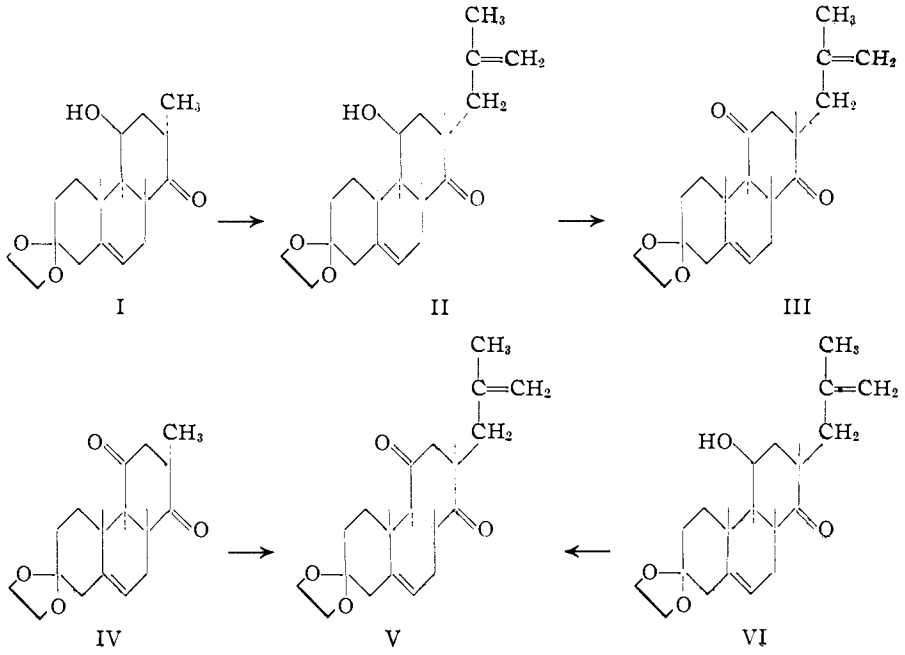
The reaction of 2α,4b-dimethyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (I) with methallyl iodide in the presence of potassium *t*-butoxide gave a good yield of a single crystalline 2-methyl-2-methallyl derivative II.[2] The corresponding diketone III resulted from oxidation of this alcohol with the chromium trioxide–pyridine complex.[3] When the methyl diketone IV was methallylated, the major product consisted of an isomeric methyl meth-

(1) R. M. Lukes, G. I. Poos, R. E. Beyler, W. F. Johns and L. H. Sarett, THIS JOURNAL, **75**, 1707 (1953).

(2) The results of structure assignments given below are anticipated here for the sake of clarity.

(3) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

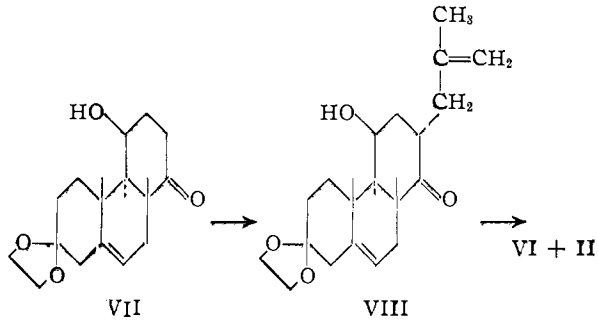
allyl diketone V together with a small amount of III.



The assignments of structure made above were dictated by a number of considerations. The placement of the methallyl substituent at the C-2 position of the hydroxyketone II follows by analogy with the course of methylation of the unsubstituted tricyclic ketone.[1] Moreover, Cornubert[4] has shown that alkylation of methylcyclohexanone occurs on the C-methyl carbon atom,[5] which argues that substitution of the methyl tricyclic ketone I should be at least as selective as that of the unmethylated precursor. Finally it has been shown[6] with α-decalone that in the competition of the bridgehead methinyl and the methylene group for methyl iodide, the latter is successful.

In the diketone series the same factors served to eliminate the two bridgehead carbon atoms as likely sites for the methallyl group. Of the two remaining possibilities C-2 was almost certainly the correct one both because of the activating effect of the methyl group in the precursor and also by analogy with the Claisen condensation of the unsubstituted 1,4-diketone.[1] The minor product III of the methallylation of the methyl diketone IV could by virtue of its formation *via* oxidation of II be assigned the C-2-methallyl structure. The major product, on the other hand, which on the basis of the above arguments should have had the structure V, could not be immediately correlated with a methallyl hydroxyketone, since only one pure isomer was obtainable by methallylation of the hydroxyketone I. In order to achieve this correlation and thereby eliminate the possibility of condensation having occurred at C-3, the synthesis of the missing 2-methyl-2-methallyl hydroxyketone VI was attempted. The unmethylated hydroxyketone VII gave the 2α-methallyl[7] derivative VIII in satisfactory yield. Treatment of this compound with methyl iodide resulted in a mixture from which a few per cent. of a new methyl methallyl hydroxyketone VI could be isolated. Its oxidation afforded a compound V identical with the major product of methallylation of the diketone IV. This result showed conclusively that this product was the expected 2-methyl-2-methallyl diketone V.[8]

With the establishment of the C-2 position for the methallyl group in both of the methyl methallyl diketones III and V, the isomerism of these two compounds must be attributed to a configurational difference at C-2. It follows that reaction of the methyl *diketone* IV with methallyl iodide gave access to one epimer at C-2 while methallylation of the methyl *hydroxyketone* I led to the other.



Although consideration of steric effects to be

(4) R. Cornubert, *Compt. rend.*, **186**, 441 (1928).

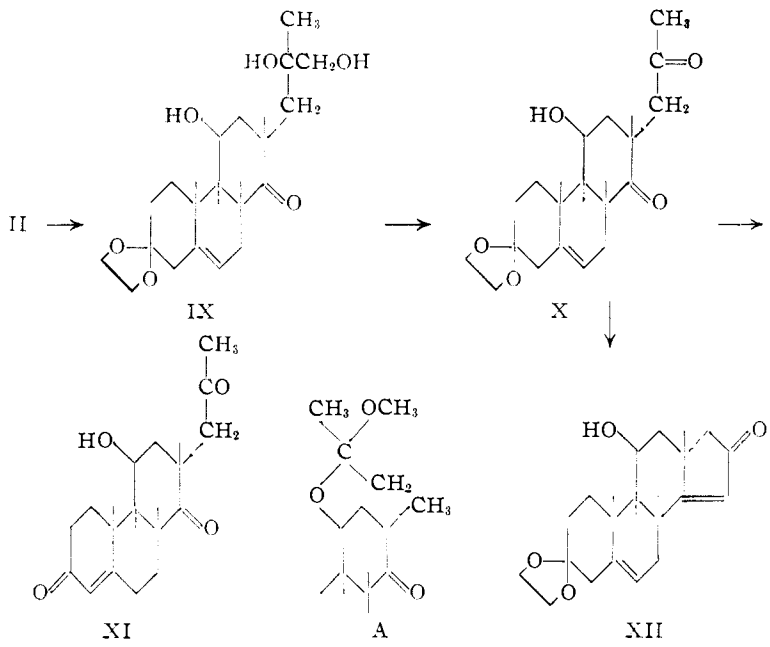
(5) The reactivity of monomethylated ketones of the acetoacetic ester series and other carbonyl compounds toward alkyl halides may be greater than that of the unsubstituted ketoester. See W. G. Brown and K. Eberly, THIS JOURNAL, **62**, 113 (1940), for a discussion and pertinent references.

(6) J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 817 (1937).

(7) The configuration at C-2 of 2-monoalkyl-1-ketopolyhydrophenanthrenes belonging to the present series of compounds has been touched upon in Part VI (ref. 1). In the case of the unmethylated 2-methallyl-1-ketone VIII, data were at hand which permitted provisional assignment of stereochemical configuration at C-2. This substance according to the criteria of chromatographic homogeneity and sharpness of melting point was a pure compound and, therefore, represented one of the two possible epimers at C-2. Moreover mixed melting point determinations of VIII with both of the 2-methyl 2-methallyl hydroxyketones (II and VI) showed clearly that the melting point of VIII was depressed by VI but not by II. This result implied a similarity in crystal structure between VIII and II and a difference between VIII and VI which could reasonably be accounted for only on the basis of similar orientation of the methallyl side chain in both VIII and II. Since the latter is known to belong to the 2α-methallyl series (see below), the former may be assigned the same configuration. On the basis of the stability of VIII toward hot alcoholic potash, the methallyl group in VIII resided in the more stable configuration at C-2. By analogy, the more stable configuration for the methyl substituent at C-2 in the 4β-hydroxy-1-ketone I is also α.

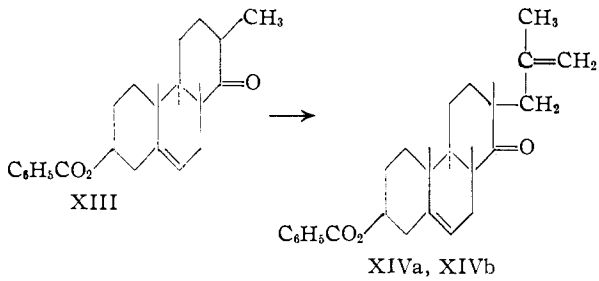
(8) The possibility of double inversion of the BC bridgehead during reactions of the diketones involving strong bases can be dismissed since the *anti-trans*-1,4-diketones were stable to sodium methoxide and to potassium *t*-butoxide.

expected from the presence of the 4β-hydroxyl group would lead to the prediction that the major product of methallylation of I should be the α-methallyl isomer II, additional information on configuration at C-2 seemed desirable. A projected scheme for obtaining this evidence involved oxidation of the 2-methallyl side chain of VI and II to an acetonyl group, giving a pair of epimers one of which should form a strain-free lactol ether (A) with the 4β-hydroxyl and should, therefore, be the 2β-methallyl derivative; the other epimer, having a *trans* relationship between C-2 and C-4, could not.



Experimentally, the epimer II obtained by methallylation of the methyl hydroxyketone reacted smoothly with one equivalent of osmium tetroxide. The resulting osmate ester yielded on hydrolysis the glycol IX[9] together with a derived substance (see discussion of dilactols below). When the glycol was treated with periodic acid in a mixture of water, methanol and pyridine, the desired acetonyl compound X was obtained. It could also be prepared by careful ozonolysis of the methallyl compound II. In agreement with this formulation the acetonyl compound gave an α,β-unsaturated ketone XII under the conditions found by Wilds to effect cyclization of related 1,4-diketones.[10] Acid hydrolysis of the acetonyl compound X yielded the corresponding α,β-unsaturated ketone XI. The latter with methanolic hydrogen chloride failed to give any trace of a lactol ether and could, therefore, be tentatively assigned a 2α-acetonyl structure. It was unfortunately not possible to amass enough of the other methallyl hydroxyketone VI to conduct a comparable series of reactions in the epimeric series. Nonetheless, the failure of one of the 2-acetonyl-4β-hydroxy 1-ketones to form a lactol was felt to be significant, especially so since there was no apparent cause for this lack of reactivity other than that created by stereoisomerism at C-2.[11] Ultimate confirmation of this diagnosis was obtained by conversion to known steroids.[12]

In order to test the scope of the methallylation procedure it was applied to the Köster–Logemann ketone,[13] a tricyclic degradation product of cholesterol. Reaction of the benzoate of this compound (XIII) (systematic name: 2,4b-dimethyl-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ - dodecahydrophenanthrene-7β-ol-1-one benzoate)[14] with methallyl iodide–potassium *t*-butoxide gave a satisfactory yield of the expected 2-methyl-2-methallyl product XIV. In this instance the two C-2 epimers could be separated chromatographically and were found to be present in a ratio of approximately three to one. Since, as indicated above no general *a priori* basis for the prediction of configuration at C-2 was available, no assignment of configuration to these epimers was made.



As described above, the hydroxylation of the various 2-methallyl-1-ketopolyhydrophenanthrenes led in part to glycols such as IX. However, by-products of a rather novel structure were also obtained. For example in the case of the 4β-hydroxy-1-ketone II, reaction with osmium tetroxide and subsequent reductive hydrolysis of the osmate ester yielded a considerable amount of a compound, $C_{22}H_{32}O_5$, in addition to the glycol IX. This empirical formula is that of the expected glycol less the elements of water. An infrared spectrum showed the presence of a hydroxyl group but carbonyl bands were lacking. Oxidation with the chromium trioxide–pyridine complex proceeded without loss of carbon to give a derivative $C_{22}H_{30}O_5$, possessing a ketone but no hydroxyl function. These data required the formulation of the hy-

(9) A. Butenandt, J. Schmidt-Thomé and H. Paul, *Ber.*, **72**, 1112 (1939), quote unpublished results of U. Westphal and Y. L. Wang to the effect that a 3-acyl substituent protects a steroidal double bond at the 5,6-position against attack by osmium tetroxide.

(10) A. L. Wilds, THIS JOURNAL, **64**, 1421 (1942).

(11) The "steric hindrance" associated with the 11β-hydroxyl group in the steroids is measured in terms of intermolecular reactions. Intramolecular addition reactions such as the formation of lactones and lactols, are, of course, not subject to this kind of "steric hindrance." *Cf.* R. C. Fuson and W. C. Hamman, *ibid.*, **74**, 1626 (1952).

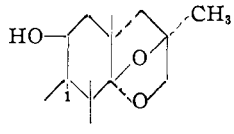
(12) L. H. Sarett, G. E. Arth, R. M. Lukes, R. E. Beyler, G. I. Poos, W. F. Johns and J. M. Constantin, *ibid.*, **74**, 4975 (1952).

(13) H. Köster and W. Logemann, *Ber.*, **73**, 293 (1940).

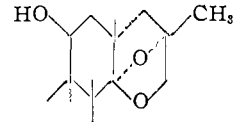
(14) The configurational indices agree with the convention of Fieser and Fieser, "Natural Products Related to Phenanthrene," Second Edition, Reinhold Publishing Corp., New York, N. Y., 1937.

droxylation product as a cyclic ketal (dilactol) such as B or C. The basic structural features of such dilactols have been observed before in the tricyclic trimethyl 1,4;1,5-dianhydroglucose of Hess and Neumann.[15]

An examination of the factors involved in dilactol formation with the aid of molecular models showed that each of the two possible glycols derived from either a 2α- or 2β-methallyl derivative (four possible glycols in all) should be capable of forming a dilactol provided that no restriction on conformation of ring C be made. The experimental fact that one of the two glycols derived from the methallyl ketone II did not form a dilactol thus implied the intervention of secondary effects. There are three such effects which could conceivably prevent dilactol formation from a given glycol: (1) the strain attending the boat conformation of a non-terminal ring in a polycyclic system[16]; (2) the increased strain to be expected in the fusion of a *trans* five-membered ring and a *cis* six-membered ring to a cyclohexane ring (structure B) as compared with *cis* five-, *trans* six- fusion to the cyclohexane ring (structure C); (3) a factor associated with the nature of the substituent at C-4. Since a quantitative evaluation of these factors was not possible, an examination of the hydroxylation products of the five available 2-methyl-2-methallyl tricyclic ketones (II, III, V, XIVa and XIVb) was undertaken with the hope that an *empirical* relationship between configuration at C-2 and formation of dilactols could be established.



B



C

In each case the crude hydroxylation mixture was chromatographed on acid-washed alumina. This step served to separate those glycols which were capable of forming dilactols under these conditions from those which were not. Table I summarizes these results.

TABLE I

Source of glycol	Configuration of methallyl	Number of dilactols	Free glycol[a]	Conformation of ring C required by dilactol
II	α	1	Present	Chair
III	α	1	Present	Chair
V	β	0	Present	Boat
XIVa	?	2	Absent	...
XIVb	?	0	Present	...

[a] The possibility of monolactol forms is not excluded.

These data make it clear that dilactol formation by the glycols derived from a given 2-methallyl substituent is not a simple function of configuration at C-2. A precise evaluation of the role of each of the structural factors involved must attend investigation of simpler systems.

(15) K. Hess and F. Neumann, *Ber.*, **68**, 1360 (1935).

(16) This strain is by no means prohibitive, at least in the case of some simpler tricyclic systems, as has been noted by W. S. Johnson, *Experientia*, **8**, 315 (1951).

Experimental[17]

2β,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (II).—A suspension of 65.0 g. of 2α,4b-dimethyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one in 900 ml. of benzene was concentrated to 800 ml. in order to remove traces of moisture. A solution of 290 ml. of anhydrous *t*-butyl alcohol containing 11.6 g. (1.4 molecular equivalents) of dissolved potassium was then added followed by 65 ml. of methallyl iodide.[18] The initially homogeneous solution rapidly deposited potassium iodide. At the end of one hour the solution was washed with water, dried over sodium sulfate and evaporated to dryness *in vacuo*. The residue was crystallized from ethyl acetate giving 48.1 g. of crystals, m.p. 163–168°. Chromatography of the mother liquors gave an additional 3.5 g. (total, 68%). In addition, 6 g. of a crystalline mixture m.p. *ca.* 140° was obtained, which could not be separated into its components chromatographically. Recrystallization of a sample of the 2β-methyl-2-methallyl ketone from ethyl acetate gave a pure product, m.p. 166–168°; λ_{max} 2.84, 5.97[19] and 6.09 μ.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 73.15, 73.10; H, 8.96, 8.65.

2β,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione (III).—A suspension of the chromium trioxide–pyridine complex[3] prepared from 20.0 g. of chromium trioxide and 200 ml. of pyridine was treated with a solution of 20.0 g. of the hydroxyketone II, m.p. 166–168°, in 200 ml. of pyridine. The mixture was allowed to stand overnight, then diluted with water, extracted with three portions of ether and the ethereal extract evaporated, finally *in vacuo* to remove most of the pyridine. The residual solution, *ca.* 50 ml., was diluted with 20 ml. of methanol, and the crystalline product precipitated by careful addition of water. The crystals were filtered, washed with water, and dried, giving 19.4 g. (98%), m.p. 139°. Recrystallization did not change the melting point; λ_{max} 5.84, 6.08 μ.

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.97; H, 8.42.

2α,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione (V).—A solution of 16.0 g. of a crystalline mixture of 2α- and 2β,4b-dimethyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,-8,10,10aβ-dodecahydrophenanthrene-1,4-dione (IV), m.p. 115–142°, in 190 ml. of benzene was concentrated to 160 ml. to remove traces of water. The solution was stirred under a nitrogen atmosphere and treated first with 16.0 ml. of methallyl iodide and then with 70 ml. of anhydrous *t*-butyl alcohol containing 2.31 g. of dissolved potassium. The mixture was stirred at room temperature overnight, then diluted with water, extracted with ether and the ethereal extract evaporated to dryness, finally *in vacuo*. The residue was chromatographed over 800 g. of alumina using mixtures of ether and petroleum ether. From the eluates rich in petroleum ether, there was obtained 7.7 g. of crude crystalline methallyl ketone V, m.p. 95–102°. Recrystallization of a sample from ether gave a constant-melting product, m.p. 107°; λ_{max} 5.85, 6.08 μ.

Anal. Found: C, 73.69; H, 8.28.

Careful chromatography of the mother liquors of V permitted isolation of small amounts of the pure epimer III, m.p. and mixed m.p. 139°.

4b-Methyl-2α-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (VIII).—Ten grams of the hydroxyketone VII was dissolved in 100 ml. of tetrahydrofuran, and to this was added 50 ml. of 0.85 *M* potassium *t*-butoxide in *t*-butyl alcohol. With rapid stirring, 10 ml. of methallyl iodide was added to the solution; the mixture became warm and potassium

(17) Ultraviolet absorption spectra were determined in methanol. Melting points were determined on the Kofler micro hotstage. Infrared spectra were determined in Nujol mull unless otherwise specified.

(18) The methallyl iodide was prepared by treatment of the chloride with sodium iodide in acetone. It boiled at 116–118° with decomposition and at 37–40° (29 mm.).

(19) The carbonyl stretching frequency of all of the 2-methallyl 1-monoketones was found at the unusually long wave length of 5.95–5.97 μ.

iodide separated. After one hour the reaction mixture was diluted with 200 ml. of benzene and then filtered. Evaporation of the filtrate yielded 11 g. of a crystalline residue which was dissolved in 50 ml. of benzene and adsorbed on 350 g. of alkaline alumina. Stepwise elution with mixtures of petroleum ether and ether yielded in the 1:1 fraction 5 g. of VIII, m.p. 161–162° after recrystallization from methanol; λ_{max} 2.86, 5.97, 6.08 μ.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.94; H, 8.49.

In another experiment, 2.25 g. of crude product, m.p. 145–151°, was boiled for 30 minutes in a solution of 20 ml. of 6 *N* aqueous potassium hydroxide in 60 cc. of methanol. Dilution with water and cooling precipitated 1.95 g. of VIII, m.p. 161–162° after recrystallization from ethyl acetate and from acetone.

Mixtures of VIII with the 2β-methyl-2-methallyl hydroxyketone II, m.p. 166–168°, melted sharply at temperatures between 162 and 168°. A mixture of VIII with the epimer VI (see below) melted at 142–148°.

2α,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,-4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (VI).—To a solution of 1.70 g. of the methallyl hydroxyketone VIII in 10 ml. of tetrahydrofuran was added with rapid stirring 11 ml. of 0.85 *M* potassium *t*-butoxide in *t*-butyl alcohol and then 4 ml. of methyl iodide. The mixture gave an immediate precipitate and became warm. After a half-hour the reaction mixture was evaporated *in vacuo* to a paste, diluted with 100 ml. of benzene, and filtered. Evaporation of the filtrate gave 1.74 g. of crystalline residue which was very carefully chromatographed over 75 g. of alkaline alumina, developing with mixtures of petroleum ether and ether. At 7:3 petroleum ether–ether there was eluted 20 mg. of a substance of m.p. 222° (not identified), followed immediately by 171 mg. of VI. The latter, after recrystallizations from ether, methanol and ethyl acetate, had m.p. 161–162°; λ_{max} 2.86, 5.95, 6.08 μ.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 73.51; H, 8.71.

Further development of the chromatogram yielded only inseparable crystalline mixtures.

Attempts to obtain more VI by repeating the above methylation were unsuccessful. The reaction seemed to be very erratic, and the products unpredictable. One such experiment yielded, as the only identifiable product, a small amount of the normal methyl methallyl compound II.

Oxidation of the 2α-Methyl-2-methallyl-4β-hydroxy-1-ketone (VI) to the 2α-Methyl-2-methallyl-1,4-diketone (V).—A sample (16 mg.) of the hydroxyketone VI, m.p. 161–162°, was oxidized with the chromium trioxide–pyridine complex prepared from 19 mg. of chromium trioxide in the usual manner. Dilution of the reaction mixture with water and extraction with ether gave crystals of the 1,4-diketone V, m.p. and mixed m.p. 107°.

Hydroxylation of 2β,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (II).—To a solution of 3.00 g. of the hydroxyketone II in 25 ml. of benzene and 8 ml. of tetrahydrofuran was added 2.45 g. of osmium tetroxide. The solution was then allowed to stand at room temperature for 1.5 hours. At the end of this time, the resulting osmate ester was dissolved in 200 ml. of ethanol, treated with a solution of 6.1 g. of sodium sulfite in 120 ml. of water, and boiled for one hour. The cooled solution was filtered and concentrated to a small volume *in vacuo*. The residue was extracted with 2:1 ether–ethyl acetate and the resulting solution washed, dried and concentrated *in vacuo* to dryness. The oil obtained, on crystallization from methanol, yielded a total of 1.05 g. of crystals, m.p. 199–201°. Several recrystallizations from ethanol produced an analytically pure compound, m.p. 207–208°, 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,-5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one 1,1-dilactol; λ_{max} 2.82 μ.

Anal. Calcd. for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57. Found: C, 70.35; H, 8.49.

The remaining 1.85 g. of material, crude 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,-4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (IX), failed to crystallize.

The dilactol was unaffected by treatment with 2.5% aqueous potassium hydroxide at 100° for six hours. It was also stable to aqueous periodic acid in methanol–pyridine solution at room temperature for one hour. Further, in order to investigate the stability of this dilactol to mineral acids, the dioxolane was removed by hydrochloric acid–acetone hydrolysis (see below) and the resulting α,β-unsaturated ketone treated with a 0.3% solution of anhydrous hydrogen chloride in absolute methanol at room temperature for 60 hours. The starting material was recovered essentially unchanged.

Removal of the dioxolane from the dilactol was accomplished by treating a solution of 90 mg. of the compound in 3 ml. of acetone with 0.5 ml. of 2.5 *N* hydrochloric acid and refluxing the solution for eight hours. The solution was then extracted with chloroform and this extract washed, dried and concentrated to dryness *in vacuo*. Recrystallization of the residue yielded 70 mg. of 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-1,2,3,4,4aα,4b,5,6,7,9,10,-10aβ-dodecahydrophenanthrene-4β-ol-1,7-dione 1,1-dilactol, m.p. 182–183°. The analytical sample melted at 185–186°; λ_{max} 2.80, 5.98, 6.15 μ.

Anal. Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.52; H, 8.19.

2β,4b-Dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,-4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X).—To a solution of the above 1.85 g. of crude 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (IX) in 12 ml. of methanol and 3.5 ml. of pyridine was added 1.8 g. of paraperiodic acid dissolved in 10 ml. of water. The solution was allowed to stand at room temperature for 40 minutes, at which time the reaction mixture was diluted with 75 ml. of water, concentrated to *ca.* 25 ml. *in vacuo*, and extracted with chloroform. The chloroform extract, on evaporation, gave an oil, which crystallized in part to give a material melting at 173–175°. Recrystallization from ethanol gave a molecular compound, melting sharply at 176°, shown by chromatographic analysis to be a mixture of the dilactol of m.p. 207–208° and 2β,4b-dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,-10,10aβ-dodecahydrophenanthrene-4β-ol-1-one, (X), m.p. 196–198°; λ_{max} 2.87, 5.91 μ. Chromatography of the entire product yielded 0.57 g. of this acetonyl derivative (X).

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.77; H, 8.10.

2β,4b-Dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,-4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione.—To a solution of 68 mg. of the hydroxydiketone X in 0.7 ml. of pyridine was added 65 mg. of chromic anhydride in 0.7 ml. of pyridine. The mixture was allowed to stand at room temperature for 16 hours, at which time it was diluted with water and extracted with ether. After drying, the organic solvent was removed *in vacuo* leaving 60 mg. of an amorphous residue. Chromatography of this material yielded 41 mg. of the triketone which, after several recrystallizations, melted at 175–176°; λ_{max} 5.83 μ.

Anal. Calcd. for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83. Found: C, 69.69; H, 7.65.

Ozonolysis of 2β,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (II).—A solution of 1.00 g. (2.78 mmoles) of the hydroxyketone II in 75 ml. of methanol and 75 ml. of ethyl acetate was cooled to *ca.* −80° and a stream of oxygen containing approximately one molecular equivalent of ozone was bubbled through. To the reaction mixture was then added 100 ml. of water, 3 g. of zinc dust and 80 ml. of 7% aqueous acetic acid. The mixture was stirred and allowed to warm to 0° over a period of 30 minutes. The zinc dust was filtered and the filtrate concentrated *in vacuo* to one-half the original volume. The remaining solution was extracted with ether, and the extract washed with aqueous potassium carbonate and with water. Evaporation of the organic solvent *in vacuo* gave 1.02 g. of a crystalline product, which on chromatography yielded 0.53 g. of starting material (II) and 0.47 g. of the desired product, 2β,4b-dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,-8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X), m.p. and mixed m.p. 196–198°.

***dl*-$\Delta^{5,14}$-3-Ethylenedioxyandrostadiene-11β-ol-16-one (XII).**—To 50 ml. of an aqueous 2.5% solution of potassium hydroxide was added 500 mg. of 2β,4b-dimethyl-2-acetonyl-

7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X). A few milliliters of water was distilled *in vacuo*. A slow stream of nitrogen was then passed over the surface of the mixture as it was heated to 100° and maintained at this temperature for 2.5 hours. The reaction mixture was then cooled and filtered. Chromatography and several recrystallizations of the crystalline mixture yielded 150 mg. of the α,β-unsaturated ketone (XII), m.p. 235–239°; λ_{max} 235 mμ, E_{mol} 12,200; λ_{max} 3.0, 5.98, 6.21 μ.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.28; H, 7.95.

2β,4b-Dimethyl-2-acetonyl-1,2,3,4,4aα,4b,5,6,7,9,10,-10aβ-dodecahydrophenanthrene-4β-ol-1,7-dione (XI).—A solution of 530 mg. of 2β,4b-dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (X) in 10 ml. of acetone containing 0.5 ml. of 2.5 *N* hydrochloric acid was refluxed for 1.5 hours. The reaction mixture was diluted with 10 ml. of water and the acetone distilled *in vacuo*. The remaining aqueous solution was cooled and filtered yielding 430 mg. of crystals, m.p. 180–182°. Recrystallization yielded an analytically pure sample, m.p. 185.0–185.5°; λ_{max} 239 mμ; E_{mol} 14,900; λ_{max} 3.0, 5.85, 6.01 μ.

Anal. Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.41; H, 8.02.

Stability of the Hydroxytriketone XI to Methanolic Hydrogen Chloride.—To 430 mg. of XI was added 13 ml. of methanol containing 0.3% of dry hydrogen chloride. This was allowed to stand at room temperature for 18 hours at which time the reaction mixture was made alkaline with 2 *N* methanolic sodium methoxide solution and extracted with chloroform. The washed and dried extract was concentrated *in vacuo* giving 377 mg. of a crystalline residue. Chromatography showed that it was essentially pure starting material (XI). Several repetitions of this experiment under more drastic conditions led to partial decomposition of the molecule but chromatographic analysis revealed no methyl lactol ether in any case.

Hydroxylation of 2β,4b-Dimethyl-2-methallyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione (III).—To 2.5 g. of the methallyl diketone III in 25 ml. of ether–benzene (4 to 1) was added 1.96 g. of osmium tetroxide. After 35 minutes 115 ml. of ethanol was added followed by a solution of 5 g. of sodium sulfite in 75 ml. of water. The resultant mixture was shaken for 15 minutes and then allowed to stand for an hour with occasional shaking. The solvent was decanted from the gummy inorganic osmium compounds and the latter were thoroughly washed with ethanol, which was added to the solvent mixture. Concentration of this combined extract to *ca.* 35 ml., thorough extraction with ether, drying, and distillation of ether yielded 2.92 g. of residue. Trituration with ether and decantation of ether-soluble material left 2.21 g. (81%) of product, m.p. 160–190°. Fractional recrystallization of this material yielded only a mixture of dilactol and glycol (as indicated by elemental analysis). Chromatography of a sample of this material on acid-washed alumina gave a 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione 1,1-dilactol in the early petroleum ether–ether eluates. One recrystallization from methanol gave the pure compound, m.p. 181–182°, λ_{max} 5.83 μ.

Anal. Calcd. for $C_{22}H_{30}O_5$: C, 70.56; H, 8.08. Found: C, 70.80, 70.50; H, 8.16, 8.00.

The later petroleum ether–ether eluates and also the chloroform–ether and acetone eluates gave crystalline mixtures of glycol and (or) monolactols from which no single sharp melting compound could be obtained by fractional crystallization.

2β,4b-Dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione 1,1-Dilactol.—A solution of 95 mg. of pure 2β,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one 1,1-dilactol, m.p. 207–208°, in 1 ml. of pyridine was added to 90 mg. of chromic anhydride in 1 ml. of pyridine and the mixture allowed to stand at room temperature for 16 hours. The reaction mixture was diluted with water and extracted with chloroform. This extract, upon concentrating *in vacuo* yielded 70 mg. of an oil, which after chromatography gave 60 mg. of the keto dilactol, m.p. and mixed m.p. with the sample prepared in the preceding experiment, 177–179°.

2α,4b-Dimethyl-7-ethylenedioxy-2-(2-methyl-2,3-dihydroxypropyl)-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione.—A solution of 2.0 g. of the 2α-methyl-2-methallyl diketone V, m.p. 107°, in 20.0 ml. of absolute ether was treated with 1.6 g. of osmium tetroxide. When the osmium tetroxide had dissolved, the mixture was allowed to stand for 24 hours, then diluted with 90 ml. of alcohol and 10 ml. of benzene. To this solution was added 4.0 g. of sodium sulfite dissolved in 60 ml. of water. The mixture was boiled for one hour, filtered, concentrated *in vacuo* to a small volume and extracted thrice with ether. Concentration of the extracts gave 2.12 g. of crystalline residue from which a sample of m.p. 179–181° was obtained after several recrystallizations from acetone–ether.

Anal. Calcd. for $C_{22}H_{32}O_6$: C, 67.31; H, 8.22. Found: C, 67.19; H, 7.84.

Chromatography of the crude glycol mixture over acid-washed alumina gave traces of starting material but no dilactol. (The dilactols, lacking the free hydroxyl groups, were easily eluted with ether–petroleum ether mixtures, while the free glycols or monolactols were not eluted until ether–chloroform mixtures were used.)

2α,4b-Dimethyl-2-acetonyl-7-ethylenedioxy-1,2,3,4,4aα,-4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-1,4-dione.—To a solution of 2.05 g. of the crude hydroxylation product of the 2α-methyl-2-methallyl diketone V in a mixture of 10 ml. of methanol and 2 ml. of pyridine was added a solution of 2.0 g. of periodic acid dihydrate in 8 ml. of water. The mixture became warm and crystals of the acetonyl product began to separate after 5 minutes. After standing at room temperature for an hour, the mixture was diluted with an additional quantity of water and the crystals filtered and dried. The product, 1.3 g., m.p. 154–165°, was recrystallized from acetone and then melted at 166°.

Anal. Calcd. for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83. Found: C, 70.28; H, 7.88.

(−)-2,4b-Dimethyl-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-7β-ol-1-one Benzoate (XIII).[20]—Two grams of (−)-2,4b-dimethyl-1,2,3,4,4aα,4b,5,6,7,8,-10,10aβ-dodecahydrophenanthrene-7β-ol-1-one (Köster-Logemann ketone) was dissolved in 9 ml. of pyridine and 9 ml. of benzoyl chloride added. After the initial exothermic reaction had subsided the heterogeneous mixture was heated 15 minutes on the steam-bath; 8 ml. of water and 5 ml. of pyridine were added and heating continued for another 30 minutes in order to decompose the benzoic anhydride. The cooled reaction mixture was poured into water, which was extracted with ether. From the ether extract, after dilute hydrochloric acid and aqueous sodium bicarbonate washes, there was obtained 2.96 g. of crude crystalline product. Recrystallization from ether yielded a first crop of 1.85 g. of the benzoate ester (XIII), m.p. 155–158°; the second crop obtained from methanol amounted to 0.80 g., m.p. 151–156° (93%). The analytical sample was prepared by recrystallization from methanol and ether, m.p. 158.5–160°, $[\alpha]^{25}D$ −30 ± 4° (*c* 0.5, chloroform); λ_{max} 5.86 μ.

Anal. Calcd. for $C_{23}H_{28}O_3$: C, 78.37; H, 8.01. Found: C, 78.17; H, 7.73.

The Epimeric 2,4b-Dimethyl-2-methallyl-1,2,3,4,4aα,-4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-7β-ol-1-one Benzoates (XIVa and b).—The dry Köster–Logemann ketone benzoate, 1.85 g., was dissolved in 25 ml. of dry benzene. To it was added 1.6 ml. of methallyl iodide and 6.65 ml. of a 1.0 *M* solution of potassium *t*-butoxide in *t*-butyl alcohol. The mixture warmed up to 40–45° and finely divided potassium iodide slowly precipitated. After the reaction mixture had stood for an hour at room temperature, it was poured into water–benzene. The benzene layer was combined with a second benzene extract and washed with dilute hydrochloric acid, sodium bicarbonate solution and water. Concentration of the dried extract gave 2.02 g. of yellow oil which crystallized when triturated with ether. The entire product was carefully chromatographed on a column of 100 g. of acid-washed alumina. Prolonged

(20) H. M. E. Cardwell, J. W. Cornforth, J. W. Duff, H. Holtermann and R. Robinson, *Chemistry and Industry*, **20**, 389 (1951), have reported the preparation of this compound without giving its physical constants.

elution with petroleum ether–ether (39:1) afforded first the crude high melting epimer (XIVb), then a mixture, and finally the crude low melting epimer (XIVa). These fractions amounted to 1.80 g. (84%) of crystalline material, but because of the difficult separation there was obtained after recrystallization 585 mg. (27.5%) of XIVa, m.p. 116–120°, and 299 mg. (10.8%) of XIVb, m.p. 140–146°. In an earlier run the yields were 21.0 and 8.7%, respectively, so that the ratio was fairly constant.

The more abundant epimer (XIVa) was recrystallized from methanol for analysis, m.p. 120–121°; $[\alpha]^{28}D$ −67.0 ± 2° (*c* 1.0, chloroform); λ_{max} 5.83–5.95, 6.10 μ.

Anal. Calcd. for $C_{27}H_{34}O_3$: C, 79.76; H, 8.43. Found: C, 79.57; H, 8.21.

The other epimer (XIVb) was recrystallized from methanol and from ether–petroleum ether, m.p. 146–148°; $[\alpha]^{28}D$ −60.0 ± 2° (*c* 1.0, chloroform); λ_{max} 5.88, 6.10 μ.

Anal. Found: C, 79.94; H, 8.45.

Hydroxylation of XIVa.—To 200 mg. of epimer XIVa in 2 ml. of dry ether was added 138 mg. of osmium tetroxide. The mixture was kept at room temperature for 30 minutes during which time a dark brown granular deposit of osmate ester formed. This was dissolved by adding 9 ml. of ethanol and swirling; then a solution of 0.4 g. of sodium sulfite in 6 ml. of water was added and the mixture was shaken for 20 minutes. After filtering from the dark osmium compounds the colorless filtrate was concentrated *in vacuo* to a small volume, more water was added and it was extracted thrice with ether. Drying and concentration of the ether gave 211 mg. of colorless oil which could not be induced to crystallize. Chromatography on acid-washed alumina gave a small amount of starting material in the petroleum ether–ether (9:1) eluates and the (−)-2ξ,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-7β-ol-1-one 7-benzoate in the petroleum ether–ether (2:8) eluates. The crude glycol amounted to 94 mg. and after recrystallization from ether–petroleum ether there was obtained 72 mg., m.p. 135–145°.

Hydroxylation of XIVb.—Two hundred milligrams of XIVb was dissolved in 4 ml. of ether and 138 mg. of osmium tetroxide added. After standing at room temperature for 80 minutes the resultant osmate ester was hydrolyzed and the isolation carried out essentially as described for epimer XIVa, yielding 161 mg. of oily crystalline residue. Chromatography on acid-washed alumina yielded 71 mg. of crystalline material in the petroleum ether–ether (9:1) eluates, then a mixture, and finally 38 mg. of crystalline material in the petroleum ether–ether (7:3 and 6:4) eluates. Recrystallization of the early fractions from methanol and ether yielded one isomer of (−)-2ξ,4b-dimethyl-2-(2-methyl-2,3-dihydroxypropyl)-1,2,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-7β-ol-1-one 1,1-dilactol 7-benzoate, m.p. 220–221.5°; $[\alpha]^{27.5}D$ −48 ± 4° (*c* 0.5, chloroform); λ_{max} 5.83 μ.

Anal. Calcd. for $C_{27}H_{32}O_4$: C, 77.11; H, 7.67. Found: C, 77.17; H, 7.81.

The later fractions were recrystallized from ether and methanol to give another isomer of the dilactol structure, m.p. 203–204°. (A mixed m.p. with the isomer above was 183–215°; $[\alpha]^{27.5}D$ −12 ± 4° (*c* 0.5, chloroform); λ_{max} 5.84 μ). The infrared spectra of the isomers in chloroform were quite similar but had some notable differences in the 8 to 15 μ region.

Found: C, 76.18, 76.41, 77.24, 76.96; H, 7.67, 7.45, 8.55, 8.81.

RAHWAY, NEW JERSEY

[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORIES, BROWN UNIVERSITY]

Further Studies on the Chugaev Reaction and Related Reactions

BY GEORGE L. O'CONNOR[1] AND HAROLD R. NACE

RECEIVED NOVEMBER 10, 1952

The pyrolysis of a series of cholesteryl xanthates has been studied. For the series, the first order rate constants have been determined, and from them, the Hammett parameter, ρ. In addition the pyrolyses of several closely related compounds, cholesteryl acetate, methyl trithiocarbonate, ethyl carbonate, phenyl carbamate and benzoate, have been studied. All showed first order rate constants, and the acetate and carbonate pyrolyses had negative entropies of activation and activation energies of 44.1 and 41.0 kcal./mole, respectively. On the basis of these studies it appears that all of these compounds decompose by way of a cyclic six-membered ring transition state similar to the one proposed for the Chugaev reaction. A correlation between the structure of these compounds and their thermal stability appears possible.

Introduction

In a previous study[2] of the pyrolysis of several steroid xanthates it was observed that β-cholestanyl-S-benzyl xanthate decomposed almost twice as fast as the S-methyl xanthate.

Earlier, McAlpine[3] observed that the menthyl-S-isopropyl and S-*p*-nitrobenzyl xanthates pyrolyzed more readily than the S-methyl compound.

On the basis of these observations a comprehensive study has been made of the effect of substitution on the stability of xanthates, and also of a number of analogous esters, with two purposes in mind. In the first place, less stable esters would allow lower pyrolysis temperatures, thus increasing the synthetic utility of the reaction, and, secondly, it was hoped that the study would shed more light on the mechanism of these decompositions.

Alexander[4] observed that in the pyrolysis of carboxylic esters the *cis*-β-hydrogen atom was preferentially eliminated. Hurd,[5] Barton,[6] and Alexander[4] have proposed that these esters decompose by a homogeneous unimolecular reaction involving a cyclic transition state of the type proposed for the Chugaev reaction. Fugassi, *et al.*,[7] investigated the kinetics of the decomposition of *t*-butyl acetate and propionate and obtained first order rates. The reactions appeared to be unimolecular processes with activation energies of 40.5 and 39.2 kcal./mole, respectively, thus supplying additional evidence for a cyclic transition state.

The close analogy between the pyrolysis of xanthate, carbonate and carboxylate esters is further supported by the results reported here based on a kinetic investigation of cholesteryl acetate, chloroacetate, ethyl carbonate, methyl trithiocarbonate, benzoate and phenyl carbamate.

(1) Jesse Metcalf Fellow, Brown University, 1951–1952.

(2) G. L. O'Connor and H. R. Nace, THIS JOURNAL, **74**, 5454 (1952).

(3) I. M. McAlpine, *J. Chem. Soc.*, 1114 (1931).

(4) E. R. Alexander and A. Mudrak, THIS JOURNAL, **73**, 59 (1951); **72**, 3194 (1950); **72**, 1819 (1950).

(5) C. D. Hurd and F. H. Blunck, *ibid.*, **60**, 2419 (1938).

(6) D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 2459 (1949).

(7) C. E. Rudy and P. Fugassi, *J. Phys. Colloid Chem.*, **52**, 357 (1948); E. Warrick and P. Fugassi, *ibid.*, **52**, 1314 (1948).