From another sample of oil, the oxyacetic acid derivative was prepared and was recrystallized from water: white needles; mp 91–92° (lit.[53] mp 90.5–91.5°).

6-Bromothymol from Thymol (16).—As described previously,[55] **16** in dioxane was brominated with dioxane dibromide.[55] The product (46%) distilled as a colorless oil, bp 103–105° (0.5 mm), which crystallized on cooling: mp 54–55° (lit.[55] mp 55–56°); ir, ν_{cap}^{max} 610, 810, 870, 1620, 3400–3600 cm^{-1}; nmr, 7.14 (s, 1, C-5 H), 6.41 (s, 1, C-2 H), 4.83 (s, 1, C-3 OH), 3.05 (septet, 1, J = 7.0 Hz, C-7 H), 2.20 (s, 3, C-10 H), and 1.18 ppm (d, 6, J = 7.0 Hz, C-8 and C-9 H).

The oxyacetic acid derivative was recrystallized from water: white needles; mp 133–134°.

(55) L. A. Yanovskaya, A. P. Terent'ev, and L. I. Belen'kii, *Zh. Obshch. Khim.*, **22**, 1594 (1952); *Chem. Abstr.*, **47**, 8032 (1953).

Anal. Calcd for $C_{12}H_{15}BrO_3$: C, 50.19; H, 5.27; Br, 27.83. Found: C, 49.99; H, 5.27; Br, 27.73.

Registry No.—**1**, 16934-58-0; **2**, 17693-33-3; **8**, 17693-34-4; **9**, 17693-35-5; **10**, 17693-36-6; **11**, 1408-66-4; **12**, 13019-31-3; oxyacetic acid derivative of 6-bromothymol, 17693-39-9.

Acknowledgment.—We wish to thank the National Science Foundation for a grant (GP-5772) supporting part of this work. X-ray diffraction measurements were made using equipment purchased with the support of a U. S. Public Health Service grant (AM-09085) for which we are very grateful.

Experiments Directed toward the Total Synthesis of Terpenes. XIII. The Construction of the Lactone Ring of Rosenonolactone[1]

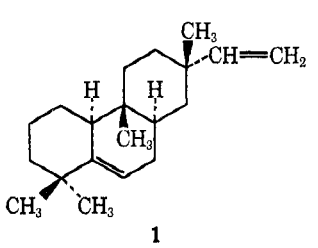
ROBERT E. IRELAND AND LEWIS N. MANDER

Contribution No. 3680 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California

Received June 4, 1968

The use of the lead tetraacetate–iodine transannular oxidation has been explored as a method forthe construction of the lactone bridge of rosenonolactone (**2**). Attempts were made to isomerize the 9β→12 lactone **20**, formed on oxidation of the 9β alcohol **16**, to the requisite 4bβ→12 lactone **6** under acid conditions with no success. The 9β→12 ether **18**, also available from the same precursor on oxidation with lead tetraacetate alone, could only be cleaved so as to generate the chlorodiacetate **27**. Oxidation of the 12-hydroxyacetate **30**, obtained in 20% yield by an alternate synthetic scheme from the aromatic enone **33**, with lead tetraacetate iodine established the desired oxygen bridge in 28% yield. The acetoxylactone **6** could then be obtained in 50% yield by further chromic acid oxidation of the ether.

Our earlier work that led to the total synthesis[2] of (±)-rimuene (**1**) and (±)-13-epirimuene aroused our interest in the closely related, but considerably more complex mold metabolite, rosenonolactone (**2**), and its congeners.[3] While the structural as well as possibly biosynthetic[4] relationship between these substances is clear, rosenonolactone (**2**) poses a much more difficult synthetic problem in view of the higher degree of oxygenation present. Not only are the methyl and vinyl substituents at C-13 in the less readily synthe-



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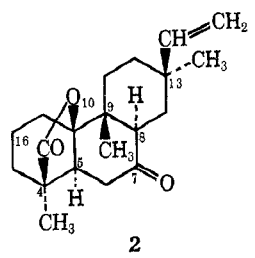
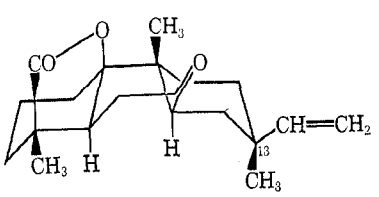
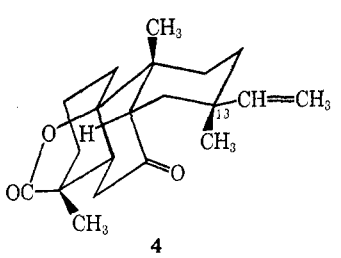


2

sized[2] configuration and a ketone function present in the relatively inaccessible C-7 position, but also there is present a lactone bridge that terminates at the C-10β position and thereby forces the B ring to adopt the boat conformation. In spite of the potential lability conferred on the C-8 hydrogen by the adjacent C-7 ketone the *trans,syn,trans* configuration **3** is not irreversibly convertible into the all-chair *trans,syn,cis* configuration **4**. The strain of the *trans,syn,trans* configuration **3** with the attendant boat conformation of ring B is approximately the same as that of the all-chair *trans,syn,cis* configuration **4** owing to the severe steric congestion of the C-13 methyl group in the latter arrangement. The two configurations have been found[3a] to be present in nearly equal proportions in both mild acidic and basic media, and rosenonolactone (**2**) has conclusively been shown[3b] by X-ray crystal structure analysis of a derivative to be represented by the *trans,syn,trans* configuration **3**. The epimeric



3



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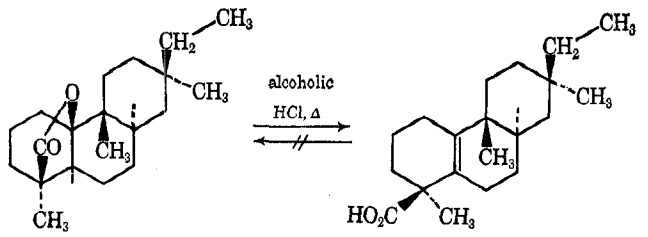
trans,syn,cis configuration **4** is thus reserved for isorosenonolactone. These conformational results are particularly important to a synthetic program, for the establishment of a lactone bridge across a *trans*-fused B/C structure would probably not result in the rosenonolactone structure **2**. In fact, such a transformation has been investigated[3a] with acid **5**, a degradation product of rosenonolactone (**2**), and found

(1) Acknowledgment is made to the Alfred P. Sloan Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) R. E. Ireland and L. N. Mander, *J. Org. Chem.*, **32**, 689 (1967).

(3) (a) G. A. Ellestad, B. Green, A. Harris, W. B. Whalley, and H. Smith, *J. Chem. Soc.*, 7246 (1965); (b) A. I. Scott, S. A. Sutherland, D. W. Young, I. Guglielmetti, D. Arigoni, and G. A. Sim, *Proc. Chem. Soc.*, 19 (1964).

(4) A. J. Birch, R. W. Richards, H. Smith, A. Harris, and W. B. Whalley, *Tetrahedron*, **7**, 241 (1959).



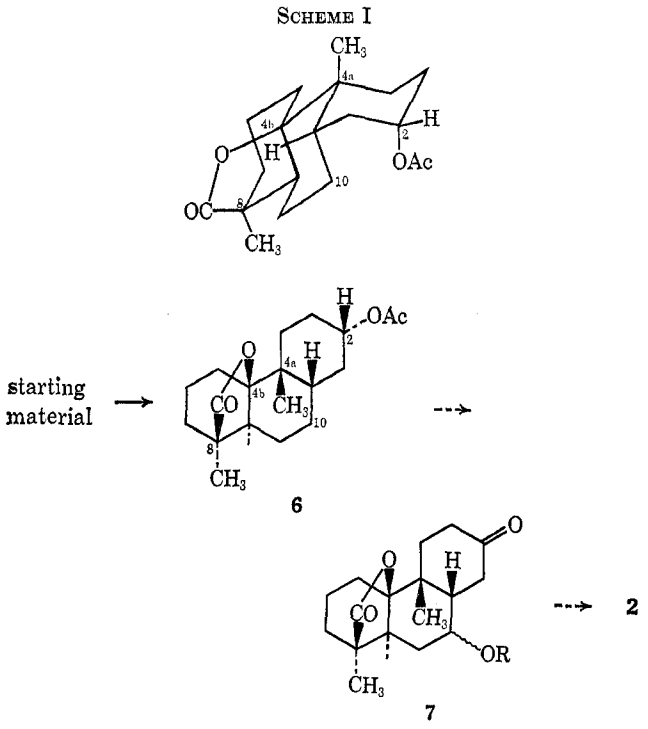
5

to lead to two new lactones,[5] neither of which were related to the metabolite. Thus a synthetic program directed along this pathway would seem fraught with difficulty.

On the other hand, a similar tricyclic structure with a B/C *cis* fusion but lacking the C-13 substituents might be expected to form the all-chair *trans,syn,cis* lactone quite readily. However, in order to maintain the requisite B/C *cis* fusion of the appropriate precursor acid, it would be necessary to alter the C-7 ketone function and provide for its introduction after lactone formation. Such an approach also requires a method for the addition of the methyl and vinyl groups at C-13 as a final stage. Hence, despite the structural similarity between (±)-rimuene (1) and rosenonolactone (2), the synthetic problems are significantly different.

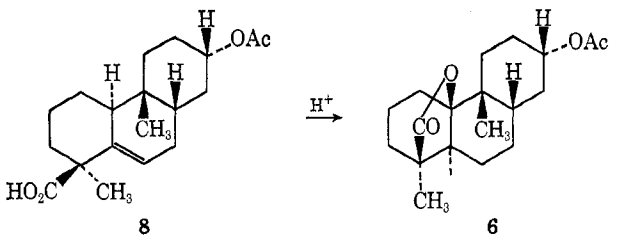
In our synthetic work we have adopted a plan similar to the second structural evaluation above and have succeeded in preparing the key intermediate lactone **6** (Scheme I). Consonant with this approach lactone **6** is a B/C *cis*-fused, *trans,syn,cis* tricyclic substance with an oxygen function placed at C-2[6] so as to provide for the final stages of the synthesis. As well, a suitable oxygen substituent in the α orientation at C-2 is ideally

SCHEME I



arranged to allow transannular oxidation[7] of the C-10 position by virtue of the B/C *cis*-ring fusion. Subsequent modification of this C-2 oxygen function would then allow for the introduction of the methyl and vinyl groups as outlined in our earlier work.[2] Finally, the ultimate goal could be achieved through equilibration of the isorosenonolactone so synthesized and rosenonolactone (2) itself after conversion of the C-10 oxygen function into a ketone.

Our first approach to the synthesis of lactone **6** was



8 6

based upon the prognosis that the acid **8** could be induced to lactonize under acidic conditions similar to those used earlier[3a] to lactonize the acid **5**. While we were unable to realize this transformation, the results of the investigation, as outlined in Scheme II, have a distinct bearing on the ultimate solution to the synthetic problem.

Hydrogenation of the readily available[2,8] tricyclic ketone **9** over Raney nickel at atmospheric pressure afforded a mixture of two alcohols. These alcohols were noncrystalline but were readily separated and characterized as their benzoyl derivatives. One benzoate, **12**, obtained in 12% yield, was shown to be the B/C *trans*-fused material by hydrolysis and then oxidation to the corresponding ketone **10**. The latter had been prepared earlier[2] by lithium–ammonia reduction of the same starting enone **9**.

Benzoate **11** was the preponderant product (68% yield) and was taken to be the desired B/C *cis*-fused compound, for hydrolysis and then oxidation gave a ketone that differed from the saturated ketone **10**. The stereochemical assignment that we have made here is well precedented in the work of Cornforth and Robinson[9] with the 8-methoxy analog **33** of ketone **9**. The α orientation of the C-2 oxygen function of benzoate **11** is assumed as a result of the preferred adsorption of the intermediate saturated *cis* ketone on the catalyst on the convex face of the molecule during hydrogenation, and subsequent delivery of the hydrogen to the β face. It is not possible to determine the stereochemistry of this oxygen function more specifically by nmr spectroscopy. Although a broad multiplet characteristic of an axial carbinyl hydrogen signal centered at δ 5.03 ppm indicated the equatorial disposition of the C-2 benzoate, this substituent would be expected to be equatorially oriented in the more stable conformation of either the α- or the β-C-2 configuration owing to the conformational mobility conferred on the molecule by the *cis*-B/C ring fusion.

After hydrolysis of benzoate **11**, and then lithium–alcohol–ammonia reduction of the aromatic ring, acid-

(5) While specific structures were not proposed for the lactones by the authors,[3a] the evidence provided clearly rules out the formation of the *trans,syn,trans* lactone structure.

(6) The phenanthrene numbering system is used for synthetic intermediates throughout the subsequent discusssion.

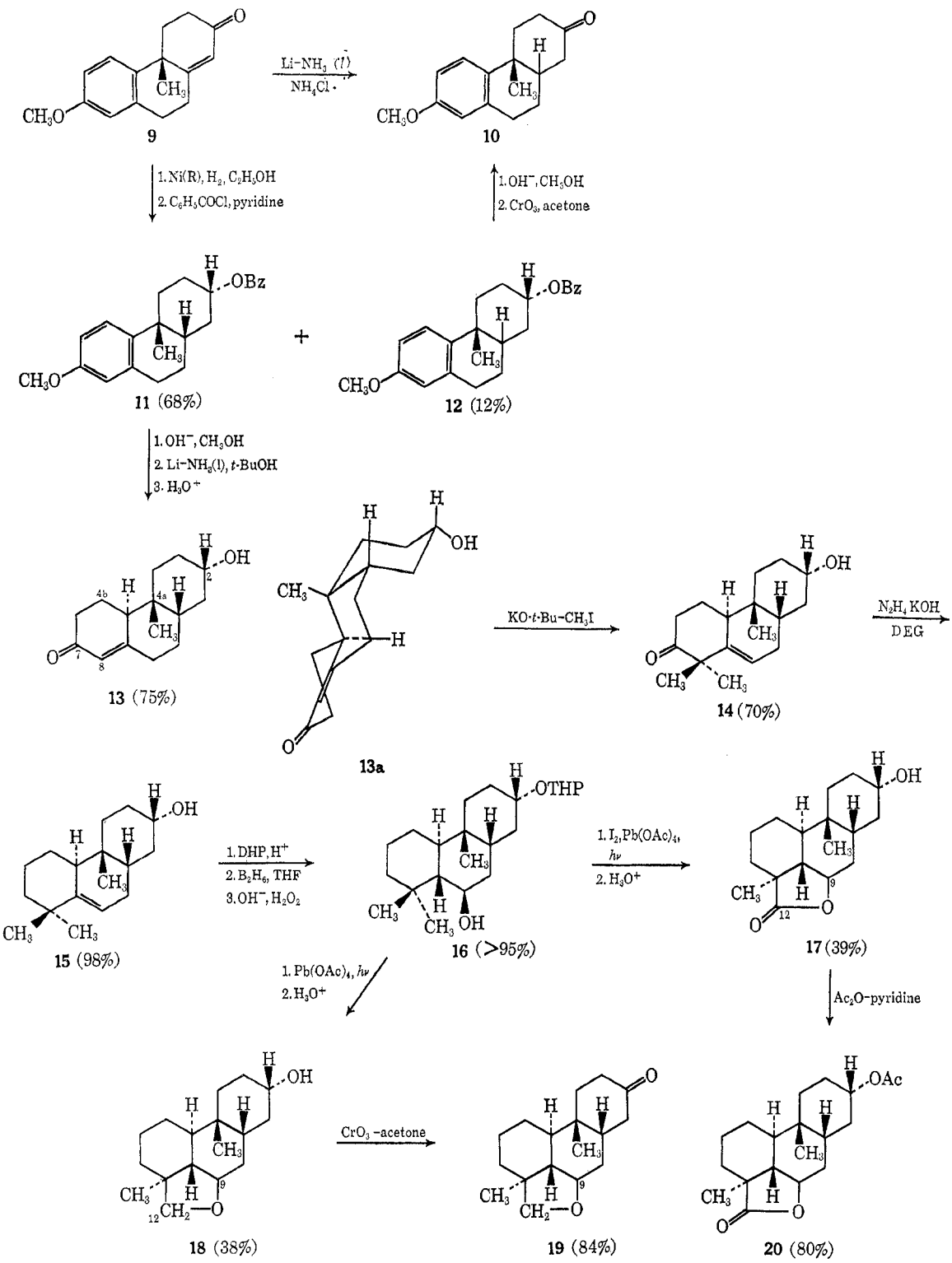
(7) Experiments on closely related model compounds have been conducted in these laboratories (R. Rosich, unpublished work) and found to be moderately successful. Further efforts are in progress.

(8) G. Stork, A. Meisels, and J. E. Davies, *J. Amer. Chem., Soc.*, **85**, 3419 (1963).

(9) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

SCHEME II

THE SYNTHESIS OF 9β→12 ACETOXYLACTONE 20



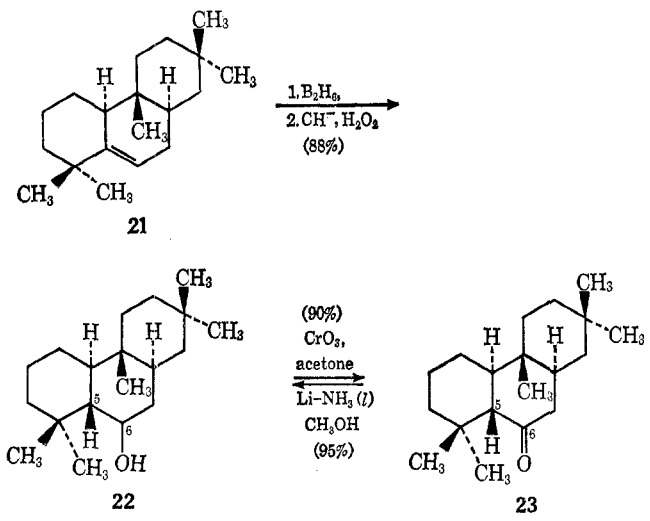
catalyzed hydrolysis of the resulting enol ether produced hydroxy ketone **13** in 75% over-all yield. By virtue of the conjugation of the C-7 carbonyl and the C-4b hydrogen through the double bond, the configuration about C-10 in hydroxy ketone **13** will be such that the compound of the greater thermodynamic stability results and *will therefore depend on the conformation adopted by the B and C rings.* The nmr spectrum of hydroxy ketone **13** indicated that the hydroxyl function at C-2 was equatorial. Based on the reasonable assumption that this C-2 hydroxyl group is also α oriented, the thermodynamically more stable configuration of the molecule is that with the "steroidal" conformation of the B/C ring system and the C-4b hydrogen α oriented, as shown in structure **13a**.

Attempts to introduce suitable substituents into the C-8 position of hydroxy ketone **13** by conventional alkylation procedures were less than satisfactory in our hands. Thus we elected to prepare the 8,8-dimethyl derivative and then to oxygenate the 8β-

methyl group at a later stage by an intramolecular, transannular oxidation.[10] To this end, hydroxy ketone **13** was converted into hydroxy olefin **15** by first methylation[2] in the presence of potassium *t*-butoxide and then reduction by the Huang-Minlon modification[11] of the Wolff–Kishner procedure. The hydroxyl group of olefin **15** was protected as its tetrahydropyranyl ether and then the C-9 hydroxyl group was introduced *via* the standard hydroboration sequence.[12] The stereochemistry of this hydroxylation is, of course, important, as only the 9β-hydroxyl function is useful for the transannular oxidation of the 8β-methyl group. Inspection of a molecular model of hydroxy olefin **15** reveals that the α side of the molecule is encumbered by the axial 8α-methyl group as well as the C-1 methylene group, which bears an axial relationship to ring B. The β face of hydroxy olefin **15** is partially shielded by the axial 4aβ-methyl group, which, however, is in a 1,4 disposition from the C-9 position. *A priori* then, it would appear that the approach to the β side of the 8a,9 double bond should be slightly less encumbered and thus be favored for the establishment of the desired 9β alcohol.

Experimental justification of this conclusion rests on two counts. First, a single crystalline diol is obtained in 90% yield on hydroboration–oxidation of hydroxy olefin **15** itself. This material could not be used further in the synthetic scheme, as both hydroxyl functions are unhindered and no selectivity between them is possible. However, the high yield of a single crystalline diol strongly suggests that one side of the 5,6 double bond is significantly less hindered than the other. The logical conclusion from the analysis of the model is that the unhindered side is the β face.

Second, as part of an earlier investigation of the structure of rimuene (**1**), the same hydroboration–oxidation sequence was applied to olefin **21**,[13] and there again resulted a single, crystalline alcohol **22** in 88% yield. That alcohol **22** was indeed the 6β isomer was indicated by careful (−10°) Jones oxidation to the corresponding ketone **23** and then equilibration of this ketone with both acid and base. In each case, starting ketone **23** was recovered unchanged. There is ample evidence[14] that low-temperature Jones oxidation does not cause the enolization of similar ketones and that the configuration of a position adjacent to the carbonyl group remains undisturbed. Therefore, the stability of ketone **23** under enolizing conditions indicated that the A/B ring fusion is in the more stable *trans* configuration. In order for this to be the case, the C-5 hydrogen must be β oriented (axial) in ketone **23** and hence also β oriented (axial) in alcohol **22**. The mechanism[15] of the hydroboration reaction involves a *cis* addition of the B–H moiety to the double bond, and this would therefore imply that the C-6 hydroxyl group was also β oriented. Support for this conclusion is found as a result of the chemical reduction of ketone **23**. The alcohol that results from the lithium–ammonia–alcohol reduction in 95% yield is identical with that **22** obtained directly *via* hydroboration–oxidation. This result also indicates alcohol **22** bears an equatorial 6β hydroxyl function.



The stereochemical outcome of the hydroboration–oxidation of olefin **21** provides a close analogy for the result expected on similar treatment of the hydroxyolefin **15**. By virtue of the *trans*-B/C ring fusion in olefin **21** the α face of the molecule is only hindered by the axial 4α methyl group and yet the hydroboration sequence occurs exclusively on the β face. Apparently the hindrance due to the 9β-methyl group is not significant enough to orient the reaction to any extent in the alternate manner. Application of this analogy, together with the formation of only one diol in high yield from the hydroxyolefin **15**, strongly supports the contention that the oxygen function introduced at the C-9 position of olefin **15** is the β-oriented, equatorial alcohol. When the same reaction sequence was carried out on the tetrahydropyranyl ether of the hydroxy olefin **15** in order to provide for the differentiation of the two alcohol functions, a noncrystalline hydroxy ether **16** was obtained in virtually quantitative yield. This material was homogeneous on thin layer chromatography and was taken to be the desired 9β-hydroxy ether **16**. As the lack of crystallinity can most probably be ascribed to the tetrahydropyranyl ether portion of the molecule, hydroxy ether **16** was used directly in the lead tetraacetate oxidation reactions without further purification.

Oxidation of hydroxy ether **16** with lead tetraacetate[9] in benzene and then hydrolysis of the C-2 tetrahydropyranyl ether afforded the cyclic hydroxy ether **18** in 38% yield. That the desired 9β→12 cyclic ether had been formed was obvious from the nmr spectrum of this product, for the resonance assigned to one of the C-8 methyl groups was gone and the new AB quartet of the C-12 oxymethylene at 3.62 ppm appeared.[16] A by-product of this oxidation that resulted in a 5% yield appeared to be the 9α→1α hy-

(10) K. Heusler, J. Kalvoda, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 352 (1963); K. Heusler and J. Kalvoda, *Angew. Chem. Intern. Ed. Engl.*, **3**, 525 (1964).

(11) Huang-Minlon, *J. Amer. Chem. Soc.*, **68**, 2487 (1948).

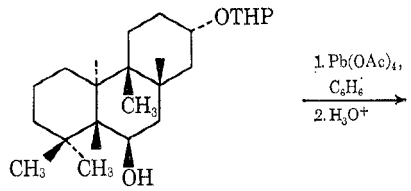
(12) H. C. Brown, K. J. Murray, L. J. Murray, J. A. Snover, and G. Zweifel, *ibid.*, **82**, 4233 (1960).

(13) This olefin was obtained from naturally occurring rimuene (**1**) (kindly supplied by Professor L. H. Briggs of the University of Auckland, Auckland, N. Z.) by oxidation of the C-13 vinyl grouping to an aldehyde and then Wolff–Kishner reduction (see Experimental Section).

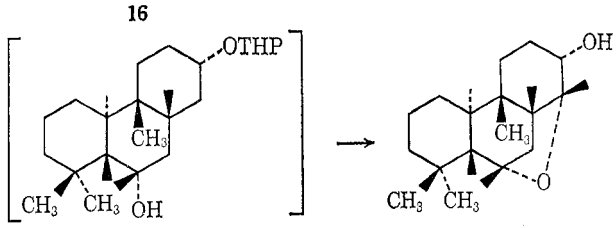
(14) A recent, delicate example is provided by the work of W. S. Johnson, A. van der Gen, and J. J. Swoboda, *J. Amer. Chem. Soc.*, **89**, 170 (1967).

(15) H. C. Brown and G. Zweifel, *ibid.*, **82**, 4708 (1960); **83**, 2544 (1961).

(16) (a) K. Heusler, J. Kalvoda, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 352 (1963); (b) A. Tahara, K. Hirao, and Y. Hamazaki, *Tetrahedron*, **21**, 2133 (1965); (c) E. Wenkert and B. L. Mylari, *J. Amer. Chem. Soc.*, **89**, 174 (1967).



16



24 25 (5%)

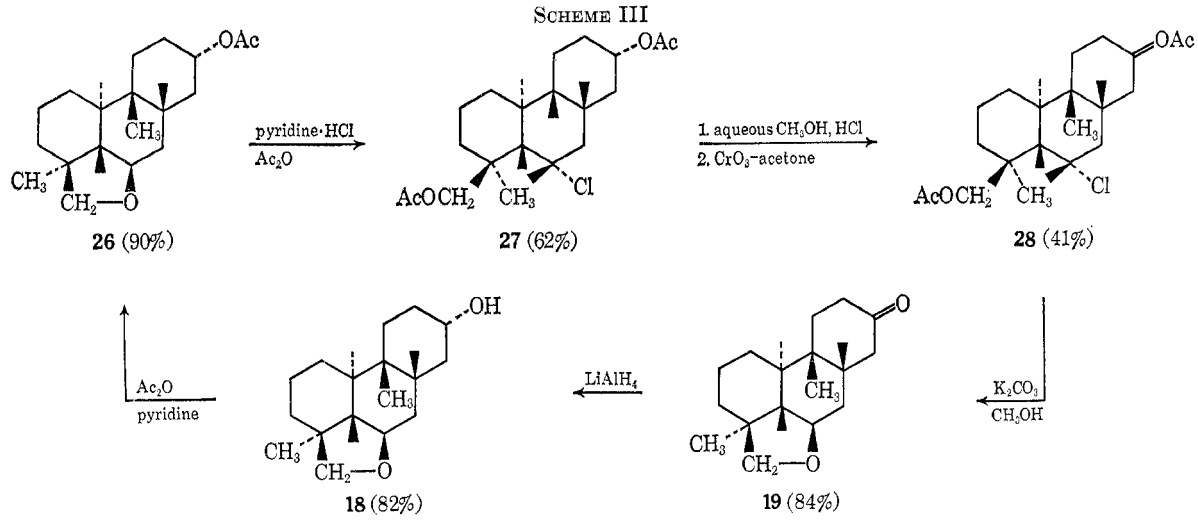
droxy ether **25**. The presence of an ether linkage in the molecule was established by infrared and nmr spectroscopy and yet the nmr spectrum of hydroxy ether **25** still retained the signals due to the two C-8 methyl groups. Isomerization of the starting hydroxy ether **16** under the reaction conditions finds precedence in the work of others[16a,c] and apparently the 9α-oxy radical of the new hydroxy ether **24** attacks the alternate C-1α position in preference to the axial C-8α methyl group. No material related to this latter mode of ether formation could be detected.

The desired hydroxy ether **18** was readily converted into either its acetate **26** or the corresponding ketone **19** by the appropriate means. However, our efforts to oxidize either of these derivatives further to the required lactone were thwarted by more deep-seated molecular changes. We turned our attention to the conversion of the acetoxy ether **26** first to the corresponding diacetoxy olefin by acid-catalyzed ether cleavage (Scheme III). However, on treatment of the acetoxy ether **26** with pyridine hydrochloride in acetic anhydride, a chlorine-containing compound was formed in 62% yield rather than the expected olefin. That this material was the C-9 chlorodiacetate **27** was shown by its reconversion into the starting acetoxy ether **26** by the reaction sequence shown. These results imply that either ether cleavage occurs *via* chloride ion displacement of the C-9 oxygen function or that the intermediate olefin diacetate, if formed, readily adds hydrogen chloride across the 8a,9 double bond. In either case the 9 position for the halogen is ensured and the ready re-formation of the ether bridge under weakly basic conditions strongly suggests that this halogen is α oriented. The suggested α orientation of the C-9 chlorine would also result from either mode suggested above for its generation.

After being unsuccessful in our attempts to transform hydroxy ether **18** into a product of potential further synthetic utility, we investigated the lead tetraacetate–iodine oxidation[10,16] of alcohol **16**. The major product of this reaction was surprisingly hydroxylactone **17** which was isolated in 39% yield after acid-catalyzed hydrolysis of the tetrahydropyranyl ether grouping. The lactone presumably arises from hydrolysis of an *ortho* lactone derivative during work-up. The transfer of two iodine (or acetoxy) radicals in a reaction of this type was not observed until recently,[17] and probably occurs in this reaction as a consequence of the equatorial position of the C-8β methyl group. Oxidation of the mother liquors from the isolation of hydroxylactone **17** afforded the corresponding keto lactone and the keto ether **19**, which is the more normal product expected from the reaction.

Again we found it impossible to isomerize the 9β→12 lactone grouping of the derived acetoxylactone **20** to either an olefinic lactone or the ultimately required 4bβ→12 lactone. The use of a variety of acidic reagents (pyridine hydrochloride, sulfuric acid, boron trifluoride etherate, and triethyloxonium fluoroborate) gave no useful result. In each case the starting acetoxylactone **20** was either recovered unchanged or so grotesquely maltreated that the identification of the products was not possible. These transformations having failed, we turned our attention to the possibility of the direct formation of the desired 4bβ→12 lactone bridge and based our approach on the results of the foregoing investigation.

SCHEME III



26 (90%) **27** (62%) **28** (41%)

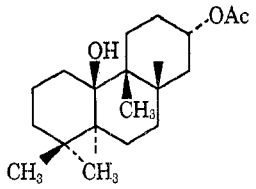
18 (82%) **19** (84%)

The two substrates on which an oxygen bridge can be formed between C-4b and C-12 *via* the transannular oxidation sequence are 4bβ-hydroxyacetate **29** and 12-hydroxyacetate **30**. Efforts[18] to prepare analogs of

(17) For related polyoxidation by the lead tetraacetate–iodine reagent, see ref 16c.

(18) T. A. Spencer, K. K. Schmiegel, and K. L. Williamson, *J. Amer. Chem. Soc.*, **85**, 3785 (1963); T. A. Spencer, K. K. Schmiegel, and W. W. Schmiegel, *J. Org. Chem.*, **30**, 1626 (1965).

the former alcohol **29** have been recorded and have not yet met with success. For this reason and the fact that it is not obvious that the highly hindered 4bβ-



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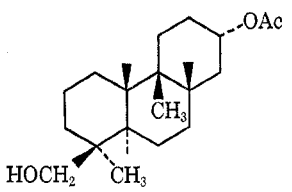
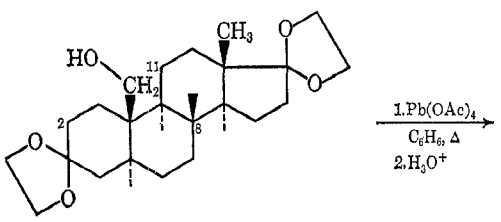


30

hydroxyl group would participate in the oxidation reaction, we chose to approach the oxygen bridging problem through the 12-hydroxyacetate **30**. There was reason to believe that in spite of the neopentyllike character of this latter alcohol, the transannular oxidation would proceed in the desired direction in at least moderate yield. Thus the oxidation of the steroidal alcohol **31** with lead tetraacetate in boiling benzene and then hydrolysis is recorded[19] to generate a mixture of products in 70% yield of which the ethers **32** represent



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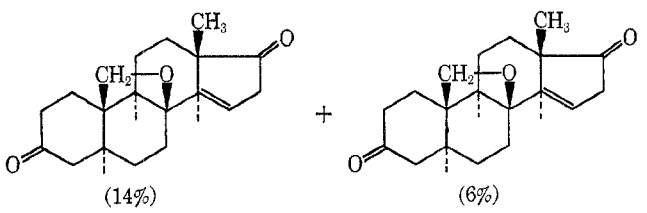


(14%) (6%)

30% (20% yield). While attack of the oxy radical on the C-8 hydrogen represented the major mode of reaction, abstraction of the C-11 hydrogen as well as fragmentation also compete. It therefore seemed to us that, while the prognosis for a high yield of the desired 4bβ→12 ether in the oxidation reaction was poor, the synthetic value of the end result warranted the loss. To this end we prepared the hydroxyacetate **30** according to the scheme outlined in Scheme IV.

Ketoacetate **34**, required as the starting point of this scheme, was prepared according to the procedures of Cornforth and Robinson.[9] The introduction of the C-8 substituents was accomplished stereoselectively through methylation of the aldehyde derived from condensation of the ketoacetate **34** with methoxymethylenetriphenylphosphorane. The stereoselective equatorial methylation of the intermediate aldehyde was expected on the basis of previous experience,[2,20] and indeed we were unable to detect any of the axially methylated product by either gas chromatography or nmr spectroscopy of the crude methylation product.

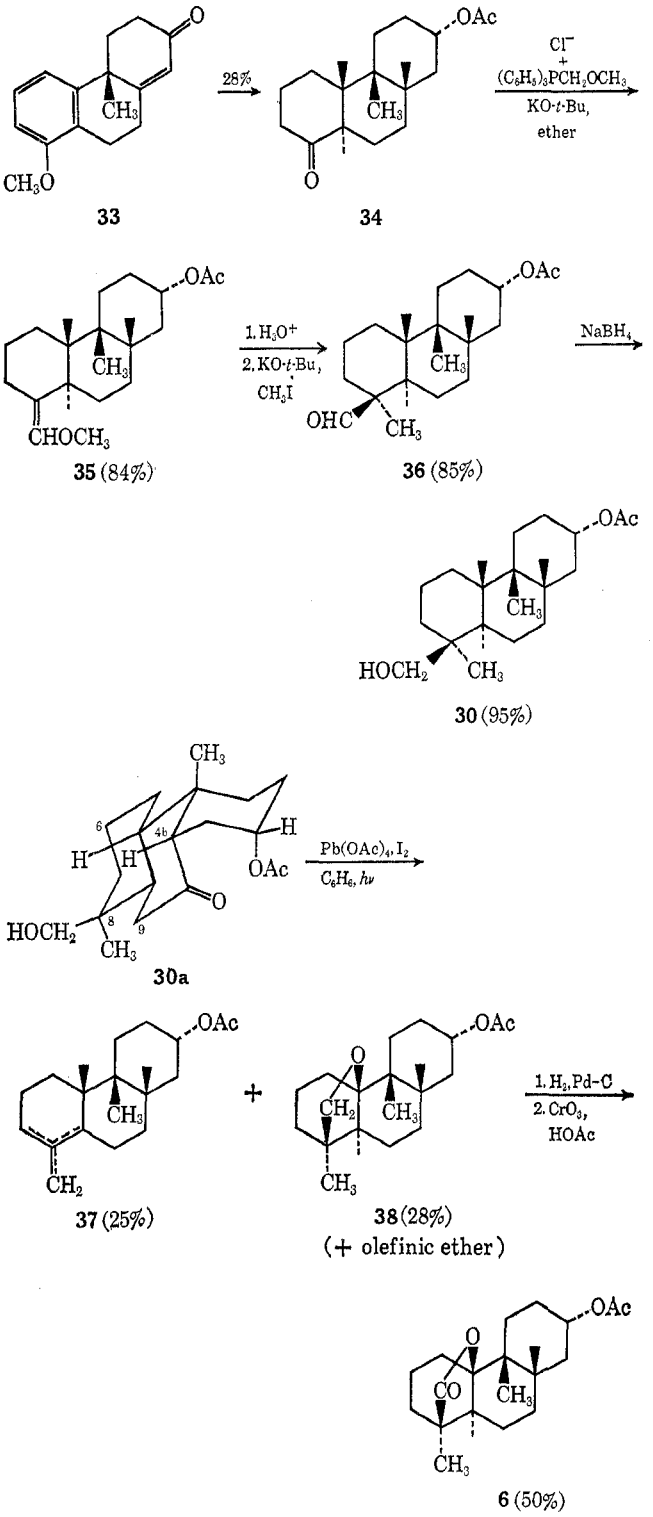
The required hydroxyacetate **30** was readily pre-

(19) D. Hauser, K. Heusler, J. Kalvoda, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **47**, 1961 (1964).

(20) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Amer. Chem. Soc.*, **89**, 1483 (1967); H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968).

SCHEME IV

THE SYNTHESIS OF THE 4bβ→12 ACETOXYLACTONE **6**



pared by sodium borohydride reduction of the aldehyde **36**, and subjected to the lead tetraacetate–iodine oxidation. The tertiary hydrogen at C-4b is ideally situated for abstraction by the C-12 oxy radical, as is shown in the conformational formula **30a** and indeed a mixture of 4bβ→12 ethers **38** was isolated in 28% yield after chromatography of the filtered reaction mixture on alumina. A 25% yield of a mixture of olefinic acetates **37** which result from the fragmentation mode of reaction was also isolated. A pure sample

of the saturated acetoxy ether for characterization purposes was obtained from the mixture of ethers **38** but in practice it was found more expedient to hydrogenate the mixture first, and then isolate the crystalline saturated acetoxy ether. The material obtained in this manner (25% over-all yield) was then directly subjected to chromic acid oxidation and the long sought acetoxylactone **6** isolated after chromatography on Florisil in 50% yield. The yield of this final transformation leaves as much to be desired as does that of the lead tetraacetate oxidation reaction. However, in neither case was an investigation initiated to optimize the reaction conditions, and further experimentation may improve these results. Such a project is underway, together with the accumulation of sufficient material for an assault on the natural product, rosenonolactone **2**, itself.

Experimental Section[21]

2α-Benzoyloxy-4aβ-methyl-7-methoxy-1,2,3,4,4a,9,10,10aβ-octahydrophenanthrene (11).—A solution of 6.5 g (0.027 mol) of enone **9**[2,3] in 40 ml of ethanol was added to a suspension of 1.2 g of W-2 Raney nickel[22] in 10 ml of ethyl acetate and the mixture stirred at room temperature and atmospheric pressure under an atmosphere of hydrogen until the theoretical amount (1200 ml) of hydrogen had been absorbed (*ca.* 5 hr). The mixture was then treated with 10 g of Celite and filtered through a pad of Celite; the Celite was washed with two 50-ml portions of methanol; and the combined filtrates were evaporated to dryness at 50° under reduced pressure. The resulting yellow gum which amounted to 6.6 g could not be crystallized and was dissolved in 20 ml of dry pyridine. This solution was cooled to 0°, treated dropwise with 4 g (0.030 mol) of benzoyl chloride and then stirred at room temperature for 3 hr. The mixture was poured onto ice, and the resulting aqueous mixture extracted with 200 ml of ether and then 25 ml of benzene. The combined organic extracts were washed successively with two 50-ml portions of 2% aqueous sulfuric acid, water, two 10-ml portions of 1% sodium hydroxide, water and then dried over anhydrous sodium sulfate. The filtrate that remained after removal of the drying agent was concentrated at 50° under reduced pressure, and the resulting residue was chromatographed on 150 g of Woelm alumina (activity I).

Elution of the column with 750 ml of 10% benzene–petroleum ether afforded 6.3 g (68%) of *cis* benzoate **11**, mp 95–98°. After two crystallizations of a sample of this material from ether–hexane, *cis* benzoate **11** was obtained analytically pure and melted at 98.5–100°: ir (Nujol) 1710, 1585, 710 ($C_6H_5CO_2$–), 1601, 1573, 1270 (CH_3OAr), 1375, 1140, 800 cm^{-1} (distinctive skeletal bonds); nmr ($DCCl_3$) δ 1.18 (s, 3, C-4aβ-CH_3), 3.75 (s, 3, CH_3OAr), and 5.03 (m, 1, –CHOBz).

Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.82; H, 7.48. Found: C, 78.83; H, 7.53.

Continued elution with 50 ml of the same solvent concentration afforded 1.1 g (12%) of *trans* benzoate **12**, mp 89–92°. The analytical sample, obtained after two crystallizations from ether–hexane, melted at 92–94°: ir (Nujol) 1710, 1580, 710 ($C_6H_5CO_2$–), 1601, 1575 (sh) 1270 (CH_3OAr), 1375, 1350, 1165, 800 cm^{-1} (distinctive skeletal bands); nmr ($DCCl_3$) δ 1.30 (s, 3, C-4aβ-CH_3), 3.75 (s, 3, CH_3OAr), and 5.18 (m, 1, –CHOBz).

Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.82; H, 7.48. Found: C, 78.95; H, 7.53.

(21) Melting points were determined on a Kofler hot stage; infrared spectra were recorded with a Perkin–Elmer spectrophotometer, Model 237; and ultraviolet spectra were recorded with a Perkin-Elmer ultraviolet spectrophotometer, Model 202. A Varian Associates Model A-60A nuclear magnetic resonance spectrometer was used for nmr spectra except where marked with an asterisk, when the spectra were determined on an HA-100 spectrometer. We thank Professor S. Chan for carrying out these latter measurements. Petroleum ether, unless otherwise noted, refers to the fraction boiling in the range 30–60°. Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich.

(22) Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p 181.

Hydrolysis (aqueous methanolic potassium hydroxide) of a 500-mg sample of benzoate **12** and then oxidation (Jones reagent[23]) of the resulting oily alcohol afforded 122 mg (71%) of the *trans* ketone **10**,[2] mp 99–100°. A mixture of this material and a sample of the authentic *trans* ketone **10**,[2] mp 100–102°, melted at 99–101°.

2α-Hydroxy-4aβ-methyl-1,2,3,4,4a,4bα,5,9,10,10aβ-decahydro-7(6H)-phenanthenone (13).—A solution of 6.3 g (0.018 mol) of *cis* benzoate **11** in 20 ml of ether was treated with 216 ml of 1 *N* sodium hydroxide–92% aqueous methanol solution, and the mixture was heated under reflux for 3 hr and then allowed to stand at room temperature for 6 hr. Most of the methanol was then removed at 50° under reduced pressure; the residue was diluted with water; and the resulting aqueous mixture was extracted with two 200-ml portions of 10:1 ether–benzene. The combined organic extracts were washed with two 30-ml portions of water, dried (Na_2SO_4), and evaporated to dryness at 50° under reduced pressure. The resulting colorless oil amounted to 4.4 g and was not further purified but used directly in the subsequent reduction reaction.

A solution of 4.4 g (0.081 mol) of the crude hydroxy ether in 40 ml of dry tetrahydrofuran was slowly added to a stirred solution of 4.107 g (0.58 g-atom) of lithium wire in 500 ml of dry liquid ammonia and 80 ml of dry tetrahydrofuran. After the addition was complete, 80 ml of dry *t*-butyl alcohol diluted with 10 ml of dry tetrahydrofuran was added dropwise over a 20-min period and the reaction mixture was stirred until the deep blue color of the unreacted lithium had dissipated (*ca.* 7 hr). The reaction mixture was then treated with 40 ml of methanol and stirred under a stream of nitrogen until most of the ammonia had evaporated. The residue was partitioned between water and 50:50 ether–benzene; the organic layer was separated, washed with four 30-ml portions of water, and then evaporated to dryness at 60° under reduced pressure.

This residue was dissolved in 100 ml of hot methanol, treated with 50 ml of 5 *N* aqueous hydrochloric acid, and the mixture was heated under reflux for 3 hr. Most of the methanol was then removed at 50° under reduced pressure. The residue was diluted with water, and the resulting aqueous solution extracted with two 150-ml portions of chloroform. The combined organic layers were washed with water, dilute aqueous potassium carbonate solution and dried (Na_2SO_4). After removal of the solvent at 50° under reduced pressure, the pale orange semicrystalline residue (4.15 g) was crystallized from acetone–hexane. The material obtained in the first crop from this crystallization was the hydroxy ketone **13**, mp 149–153°, and amounted to 2.92 g (75%). The analytical sample, obtained after two further crystallizations of a portion of this material from acetone, melted at 153–155°: ir ($HCCl_3$) 3600, 3420 (free and bonded OH), 1655 (>C=O), 1615 cm^{-1} (conjugated >C=C<); nmr ($DCCl_3$) δ 0.85 (s, 3, C-4aβ-CH_3), 3.65 (m, 1, $w/2$ ~15 Hz, >CHOH) and 5.95 (s, 1, >C=CH–).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.04; H, 9.35.

2α-Hydroxy-4aβ,8,8-trimethyl-1,2,3,4,4a,4bα,5,8,10,10aβ-7-(6H)-phenanthrone (14).—To a stirred, nitrogen protected solution of 3.40 g (0.015 mol) of hydroxy ketone **13** in 100 ml of dry benzene and 50 ml of dry *t*-butyl alcohol was added 5.10 g (0.045 mol) of powdered potassium *t*-butoxide, and the mixture was stirred at room temperature for 5 min. To this clear, pale orange solution was then added 12.6 g (0.090 mol) of methyl iodide all at once, and the reaction mixture stirred for 16 hr at room temperature. The suspension was then diluted with 100 ml of water; 100 ml of ether was added; and the organic layer was separated. The ethereal solution was washed with four 30-ml portions of water, dried (Na_2SO_4), and then evaporated to dryness at 40° under reduced pressure. The colorless, syrupy residue deposited 2.65 g (70%) of the methylated hydroxy ketone **14**, mp 118–121°, on standing overnight at 0° in ether–petroleum ether. The analytical sample obtained after one further crystallization of this material from ether–petroleum ether melted at 120–122°: ir (Nujol) 3420 (OH), 1698 (>C=O), 1655 cm^{-1} (conjugated >C=C<); nmr* ($HCCl_3$) δ 0.82, 1.27, 1.28 (s, 9, $3CH_3C$←), and 5.68 (m, 1, >C=CH–).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.87; H, 9.97.

(23) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, **39**, (1946); see also C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

2α-Hydroxy-4aα,8,8-trimethyl-1,2,3,4,4a,4bα,5,6,7,8,10,10aβ-dodecahydrophenanthrene (15).—A solution of 2.55 g (0.0097 mol) of the hydroxy ketone **14**, 10 ml of 97% hydrazine, and 10 g of potassium hydroxide in 150 ml of diethylene glycol was heated at 112° (bath temperature) under a nitrogen atmosphere for 1 hr. The bath temperature was raised to 215° during which time excess hydrazine was allowed to distil. The mixture was then stirred and heated at 215° for 2.5 hr, cooled, and diluted with an equal volume of water. The aqueous mixture was extracted with two 150-ml portions of 50:50 ether–petroleum ether, and the combined organic layers were washed with two 30-ml portions of water, dried (Na_2SO_4), and evaporated to dryness at 40° under reduced pressure. The colorless crystalline residue, which amounted to 2.42 g, was crystallized from petroleum ether and afforded 2.36 g (98%) of alcohol **15**, mp 132–134°. The analytical sample, obtained after one further crystallization of a portion of this material from ether–hexane, also melted at 132–134°: ir (Nujol) 3280 (OH), 3048 (>C=CH–), 1655 cm^{-1} (>C=C<); nmr ($DCCl_3$) δ 0.76, 1.01, 1.07 (s, 9, $3CH_3C\leftarrow$), and 5.40 (m, 1, >C=CH–).

Anal. Calcd for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 82.13; H, 11.33.

2α,9β-Dihydroxy-4aβ,8,8-trimethyl-*trans,anti,cis*-perhydrophenanthrene.—A solution of diborane in tetrahydrofuran was prepared under a nitrogen atmosphere at 0–5° through the addition of 1.5 g of boron trifluoride etherate to a suspension of 0.30 g of sodium borohydride in 25 ml of tetrahydrofuran. To this mixture was added a solution of 150 mg (0.60 mmol) of hydroxy olefin **15** in 25 ml of tetrahydrofuran; the reaction mixture was stirred at room temperature overnight. The cooled (ice bath) reaction mixture was then treated with 10 ml of 2.5 *N* aqueous potassium hydroxide, followed by 10 ml of 30% hydrogen peroxide, and the suspension heated under reflux for 1 hr. The cooled mixture was diluted with benzene; the organic layer was separated, washed with two 50-ml portions of water, dried (Na_2SO_4), and evaporated to dryness at 50° under reduced pressure. After crystallization of the resulting colorless, crystalline residue from ether–petroleum ether, there was obtained 142 mg (90%) of the diol, mp 175–176°. The analytical sample, obtained after one further crystallization of a portion of this material from the same solvent mixture, also melted at 175–176°: ir (Nujol) 3250 cm^{-1} (OH); nmr ($DCCl_3$) δ 0.90, 0.99, 1.18 (s, 9, $3CH_3C\leftarrow$).

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.55; H, 11.23.

Tetrahydropyranyl 9β-Hydroxy-4aβ,8,8-trimethyl-*trans,anti,cis*-perhydro-2α-phenanthryl Ether (16).—A solution of 2.2 g (0.009 mol) of hydroxy olefin **15** in 30 ml of dihydropyran containing 5 mg of *p*-toluenesulfonic acid was stirred at room temperature for 35 min and then 1 g of anhydrous potassium carbonate was added. After this mixture was stirred for 2 min, 100 ml of water and 300 ml of 5:1 ether–benzene were added; the organic layer was separated, washed with 50 ml of water, and then dried over anhydrous sodium sulfate. The residue that resulted after removal of the solvent at 30° under reduced pressure was adsorbed on 60 g of alumina (Merck) and the tetrahydropyranyl ether eluted with 250 ml of 2% ether–petroleum ether. There was obtained 2.85 g of colorless oil which could not be induced to crystallize, but which showed no hydroxyl absorption in the 3400-cm^{-1} region of the infrared spectrum. This was taken to be the required ether and used directly in the following experiment.

A solution of diborane in tetrahydrofuran was prepared under a nitrogen atmosphere at 0–5° through the addition of 5.0 g of boron trifluoride ether to a suspension of 1.10 g of sodium borohydride in 50 ml of dry tetrahydrofuran. After 5 min a solution of the tetrahydropyranyl ether above in 50 ml of dry tetrahydrofuran was added and the mixture was stirred in an ice bath for 16 hr. The reaction mixture was allowed to warm to room temperature over a 1-hr period and then 30 ml of 10% aqueous sodium hydroxide was cautiously added to the ice-cooled solution, followed immediately by 30 ml of 30% hydrogen peroxide. The mixture was then heated under reflux for 1 hr, cooled, diluted with benzene, and the organic layer was separated. The benzene solution was washed with two 50-ml portions of water, dried (Na_2SO_4) and then the solvents were removed at 30° under reduced pressure. The residual, viscous, colorless oil amounted to 2.96 g and could not be induced to crystallize. This material showed strong hydroxyl absorption in the 3400-cm^{-1} region and no double-bond absorption in the 1600-cm^{-1} region of the infrared spectrum. Hydrolysis of a small portion in acetone–3 *N* hydrochloric acid afforded the diol, mp 175–176°, obtained above. The noncrystallinity was ascribed to the asymmetry in the tetrahydropyranyl ether portion of the molecule, and the material was used in subsequent experiments without further purification: ir (film) 3450 (OH), and 1135, 1115 cm^{-1} (acetal).

Lactone (9β→12) of 8β-Carboxy-2α,9β-dihydroxy-4a,β,8α-dimethyl-*trans,anti,cis*-perhydrophenanthrene (17).—After a stirred suspension of 10.0 g (22.6 mmol) of lead tetraacetate and 10.0 g of calcium carbonate in 500 ml of cyclohexane was heated under reflux for 0.5 hr, a solution of 2.52 g (7.2 mmol) of the hydroxy ether **16** in 100 ml of cyclohexane was added, followed immediately by 2.54 g (10.0 mmol) of iodine. The reaction mixture was heated under reflux for 1 hr by the heat from two 250-W incandescent lamps. The cooled mixture was filtered, and the filter cake washed thoroughly with ether. The combined filtrate was washed with 100 ml of 1% aqueous potassium carbonate solution, dried (Na_2SO_4), and the solvent was removed at reduced pressure at 60°. The residue was dissolved in 50 ml of acetone, treated with 10 ml of 3 *N* hydrochloric acid, and the mixture was stirred at room temperature for 3 hr. The reaction mixture was then diluted with 100 ml of water and extracted with two 100-ml portions of 5:1 ether–benzene. The combined organic extracts were washed with 50 ml of water, 50 ml of 1% aqueous potassium carbonate, and then dried (Na_2SO_4). The solvents were removed at reduced pressure at 60° and the residue was crystallized from ether. In this manner there was obtained 780 mg (39%) of hydroxylactone **17**, mp 225–227°, as colorless prisms. The analytical sample, mp 226–227°, was obtained by recrystallization of a portion of this material from acetone: ir (Nujol) 3520 (OH), 1780 cm^{-1} (γ-lactone >C=O); nmr* ($DCCl_3$) δ 0.98, 1.17 (s, 6, $2CH_3C\leftarrow$), 3.62 (m, 1, >CHOH), and 4.48 (m, 1, >CHOCO–).

Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.54; H, 9.40.

Acetoxylactone **20** was prepared by treatment of 700 mg (2.52 mmol) of the hydroxylactone **17** in 5 ml of pyridine with 10 ml of acetic anhydride. After dilution with water and extraction with ether–benzene, acetoxylactone **20** was crystallized from ether–hexane. In this manner there was obtained 646 mg (80%) of lactone **20**, mp 140–142°, as colorless prisms. The analytical sample, mp 140–142°, was obtained after one further crystallization of a portion of this material from the same solvent mixture: ir (Nujol) 1780 (γ-lactone >C=O) and 1735, 1250 cm^{-1} (–OCO-CH_3); nmr* ($DCCl_3$) δ 0.99, 1.19 (s, 6, $2CH_3C\leftarrow$), 2.07 (s, 3, CH_3CO–), and 4.42 and 4.70 (m, 2, 2–CHO–).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.28; H, 8.94.

When a solution of 100 mg of acetoxylactone **20** in 20 ml of formic acid was heated under reflux for 4 hr, cooled, diluted with water, and the product isolated by extraction with 1:1 ether–benzene, there was obtained 94 mg of a crystalline compound which appeared to be the bisformate of the corresponding dihydroxy acid. The nmr spectrum of this material in $DCCl_3$ showed two low-field singlets of one proton integration each at 466 and 476 cps.

A solution of this bisformate in 50 ml of methanol was hydrolyzed by heating to reflux for 0.5 hr after the addition of 1 ml of 1% aqueous potassium hydroxide. The product was isolated after acidification of the cooled reaction mixture and extraction with ether. The crystalline residue obtained after evaporation of the ether was recrystallized from acetone and amounted to 88 mg of the corresponding dihydroxy acid, mp 215–218°.

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.71; H, 9.53.

Acetylation of this material (75 mg) with 1 ml of acetic anhydride in 1 ml of pyridine resulted in the reformation of acetoxylactone **20** (65 mg), mp 140–142°, which was identified by comparison of infrared spectra and mixture melting point determination, mmp 140–142°.

Hydroxy Ether 18.—To a warm solution of 9.0 g (20.9 mmol) of lead tetraacetate in 300 ml of benzene was added 10.0 g of calcium carbonate and then a solution of 2.96 g (8.6 mmol) of the hydroxy ether **16** in 50 ml of benzene. The mixture was stirred and heated under reflux with one 250-W incandescent lamp for 2.5 hr. After cooling, the reaction mixture was filtered, and the filtrate was washed with diluted aqueous sodium bicarbonate and the dried (Na_2SO_4). After removal of the solvent at reduced pressure at 50°, the residue was chromatographed on 90 g of alumina (Merck). After an initial 215 mg of unidenti-

fied material was eluted with 1200 ml of 3% ether–petroleum ether, there was eluted 157 mg (5%) of an oil which afforded 98 mg of a crystalline hydroxy ether after brief treatment with aqueous hydrochloric acid. This material was tentatively identified as hydroxy ether **25** on the basis of the proton magnetic resonance spectrum which indicated the presence of three methyl groups. The analytical sample, obtained after two crytallizations of this ether from petroleum ether–ether, melted at 178–180°: ir (Nujol) 3240 cm^{-1} (OH); nmr* ($DCCl_3$) δ 0.89, 0.95 (s, 9, $3CH_3C\leftarrow$), and 4.42 and 4.00 (m, 3, $-CH_2O-$ and $-CHO-$).

Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.24; H, 10.65.

Continued elution of the column with 3500 ml of 20% ether–petroleum ether afforded 1.707 g of a new ether, which on hydrolysis in aqueous hydrochloric acid resulted in 1.02 g (38%) of the desired hydroxy ether **18**, mp 174–176°. The analytical sample of this material, mp 175–177°, was obtained after two crystallizations from petroleum ether–ether: ir (Nujol) 3410 cm^{-1} (OH); nmr ($DCCl_3$) δ 0.94, 1.02 (s, 6, $2CH_3C\leftarrow$), and 3.62 (q, 2, $-CH_2O-$).

Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.24; H, 10.46.

Continued elution of the chromatographic column with 750 ml of ether afforded 722 mg of the starting hydroxytetrahydropyranyl ether **16** as an oil which was identified by comparison of the infrared spectrum with that of authentic material.

Acetate **26** of the hydroxy ether **18** was prepared by treatment of 1.00 g (0.004 mol) of alcohol **18** with 5 ml of acetic anhydride in 5 ml of pyridine. After the reaction mixture was heated at 85° for 40 min, cooled, and diluted with ice and water, the product was isolated by ether extraction. The ethereal extract was washed successively with water, dilute hydrochloric acid, 1% aqueous sodium hydroxide, water, and dried (Na_2SO_4). Removal of the ether at 50° at reduced pressure afforded an oil which crystallized on trituration with ether. This material was crystallized two times from methanol and amounted to 1.06 g (87%) of the desired acetate **26**: mp 109.5–5–111°; ir (film) 1735 and 1245 cm^{-1} (OAc); nmr* ($DCCl_3$) δ 0.95, 1.03 (s, 6, $2CH_3C\leftarrow$), 2.05 (s, 3, CH_3CO-), 3.64 (m, 3, $-CH_2OCH-$), and 4.68 (m, 1, $w/2 \sim 15$ Hz, $-CHOAc$).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.25; H, 9.83.

Keto Ether 19.—A solution of 1.00 g (0.004 mol) of the hydroxy ether **18** in 30 ml of acetone was cooled to 5° and treated with Jones reagent over a 10-min period until the color of the reagent persisted. Excess reagent was destroyed with isopropyl alcohol; the reaction mixture was diluted with water, and the product isolated by extraction with 1:1 ether–benzene. The organic layer was washed successively with 1% aqueous sodium hydroxide, water, and then dried (Na_2SO_4). The solvents were removed at 50° at reduced pressure, and the solid residue was crystallized from ether–hexane. In this manner there was obtained 880 mg (84%) of keto ether **19**, mp 122–124°. The analytical sample was obtained after one further crystallization from ether–hexane and had the same melting range and ir (Nujol) 1710 cm^{-1} (>C=O).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.88; H, 9.98.

8β-Acetoxymethyl-2α-acetoxy-9α-chloro-4aβ,8α-dimethyl-*trans*,-*anti*,*cis*-perhydrophenanthrene (27).—A solution of 1.10 g (3.60 mmol) of acetoxy ether **26** in 25 ml of acetic anhydride containing 0.60 g (5.22 mmol) of pyridine hydrochloride was heated under reflux for 5 hr and then cooled and poured onto crushed ice. After 15 min the product was isolated by extraction with two 150-ml portions of 1:1 petroleum ether–ether. The combined organic extract was washed successively with water, 1% aqueous sodium hydroxide, water, and then dried (Na_2SO_4). After removal of the solvent at 50° at reduced pressure, the solid residue was crystallized from petroleum ether. The crystalline material collected imparted a green color to a gas flame when burned on a copper loop and amounted to 0.75 g (62%) of diacetoxy chloride **27**, mp 128–129.5°. This material was not purified for analysis: ir (Nujol) 1735 and 1250 cm^{-1} (OAc); nmr ($DCCl_3$) δ 0.95, 1.00 (s, 6, $2CH_3C\leftarrow$), 2.10 (s, 6, $2CH_3CO-$), 3.42 (q, 2, $-CH_2OAc$), and 4.4–5.2 (m, 2, >CHCl and >CHOAc).

Anal. Calcd for $C_{21}H_{33}ClO_4$: C, 65.50; H, 8.65. Found: C, 65.71; H, 8.71.

8β-Acetoxymethyl-9α-chloro-4aβ,8α-dimethyl-*trans*,*anti*,*cis*-2-perhydrophenanthrone (28).—In a typical experiment, 72 mg (1.85 mmol) of diacetoxy chloride **27** was hydrolyzed in a solution of 10 ml of 3 *N* aqueous hydrochloric acid and 50 ml of methanol stirred at room temperature for 20 hr. The reaction mixture was then diluted with water and the product isolated by ether extraction. The ethereal extract was washed with dilute aqueous potassium carbonate until neutral, water, and dried (Na_2SO_4). Removal of the ether at 50° at reduced pressure and a crystallization of the solid residue from ether–hexane afforded 320 mg (51%) of a monoacetate, mp 190–193°. The infrared spectrum of the mother liquor from this crystallization indicated that the remainder of the material was primarily chloroidiol.

The analytical sample of the monoacetate, obtained after one further crystallization of the material from acetone–hexane, melted at 191–194: ir (Nujol) 3460 (OH), 1725 and 1255 cm^{-1} (OAc); nmr ($DCCl_3$) δ 0.91, 0.98 (s, 6, $2CH_3C\leftarrow$), 2.01 (s, 3, CH_3CO_2-), 3.42 (m, 3, CH_2OAc and >CHOH), and 4.8 (m, 1, >CHCl).

Anal. Calcd for $C_{19}H_{31}ClO_3$: C, 66.84; H, 9.40. Found: C, 67.09; H, 9.30.

This monoacetate was shown to be the primary acetate and not the expected secondary acetate by oxidation to the acetoxy ketone **28**. Thus when 310 mg (0.90 mmol) of the monoacetate in 30 ml of acetone was treated dropwise at 5° with sufficient Jones reagent to impart a red-brown coloration to the solution, there was isolated after dilution with water and ether extraction a crystalline ketonic (infrared spectrum) product. Crystallization of this material from ether–hexane afforded 250 mg (80%) of acetoxy ketone **28**: mp 125–126°; ir (Nujol) 1735 and 1250 (OAc), and 1710 cm^{-1} (>C=O); nmr ($DCCl_3$) δ 1.0, 1.04 (s, 6, $CH_3C\leftarrow$), 2.03 (s, 3, CH_3CO_2-), 3.45 (m, 2, $-CH_2OAc$), and 4.9 (m, 1, >CHCl).

Anal. Calcd for $C_{19}H_{29}ClO_3$: C, 67.23; H, 8.57. Found: C, 66.95; H, 8.69.

Keto Ether 19.—A solution of 230 mg (0.67 mmol) of acetoxy ketone **28** in 100 ml of methanol and 5 ml of 10% aqueous potassium carbonate was diluted with sufficient water to maintain homogeneity and then heated under reflux for 0.5 hr. After cooling, the reaction mixture was diluted with water, and the product was isolated by extraction with 5:1 ether–benzene. The organic extract was washed with water, and then dried (Na_2SO_4). Removal of the solvents at 50° at reduced pressure and then crystallization of the residue from ether–petroleum ether afforded 150 mg (84%) of the keto ether **19**, mp 120–123°, as pale yellow prisms. One further crystallization of a sample of this material from ether–hexane gave material that melted at 122–124° alone or on admixture with authentic keto ether **19**, mp 122–124°, prepared as described above.

Reduction of 220 mg of this keto ether with 200 mg of lithium aluminum hydride in 40 ml of ether afforded 180 mg (82%) of the hydroxy ether **18** after one crystallization from ether–petroleum ether. This material melted at 174–176° alone or on admixture with a specimen of the authentic hydroxy ether, mp 174–176°, prepared as described above.

Norrimuene Aldehyde (2β,4aβ,8,8-Tetramethyl-1,2,3,4,-4a,4bα,5,6,7,8,10,10aα-dodecahydrophenanthrene-2α-carboxaldehyde).—A solution of 386 mg (1.42 mmol) of crude rimuene[12] in 10 ml of purified dioxane was treated with 360 mg (1.42 mmol) of osmium tetroxide, and the reaction mixture was allowed to stand at room temperature overnight. The black solution was then saturated with hydrogen sulfide, and, after standing at room temperature for 1 hr, the black suspension was filtered. The black filter cake was washed with ether, and the combined filtrate was evaporated at reduced pressure on the steam bath. The resulting colorless oil which amounted to 442 mg was dissolved in 20 ml of ether and treated with 30 ml of an ethereal solution of paraperiodic acid which contained 50 mg of acid/50 ml of solution. After the reaction mixture had been stirred at room temperature for 45 min, the precipitated iodic acid was removed by filtration, and the ethereal filtrate was washed with two 25-ml portions of 4% aqueous sodium hydroxide, water, saturated salt solution, and then dried (Na_2SO_4). Evaporation of the ether at reduced pressure on the steam bath left a light yellow oil which readily crystallized on scratching. When this material was crystallized from methanol, there was collected 254 mg (66%) of the desired aldehyde, mp 85–86.5°, in two crops. The analytical sample, obtained after one further crystallization of a portion of this aldehyde from methanol, also melted at 85.5–86°: ir (film) 3040, 1650 (>C=CH–) and 2680, 1725 cm^{-1} (–CHO).

Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.40; H, 11.17.

Norrimuene (2,2,4aβ,8,8-Pentamethyl-1,2,3,4,4a,4bα,5,6,7,8,-10,10aα-dodecahydrophenanthrene) (21).—A solution of 513 mg (1.88 mmol) of the above aldehyde and 1 ml (1.03 g, 20 mmol) of 98–100% hydrazine hydrate in 10 ml of diethylene glycol was heated under reflux under a nitrogen atmosphere at 100° for 0.5 hr and 140° for 0.5 hr. After this time 2.2 g (20 mmol) of potassium hydroxide was added, and the temperature was raised to 190° and maintained there for 4 hr. The reaction mixture was then cooled, diluted with water, and the product was isolated by extraction with petroleum ether. The organic extract was washed with water, dried (Na_2SO_4), and then concentrated to *ca.* 5 ml. This solution was adsorbed on 10 g of alumina (Woelm activity I) from which olefin **21** was eluted with 35 ml of petroleum ether. After evaporative distillation of this material at 80° (0.02 mm), there was obtained 472 mg (97%) of olefin **21** which crystallized on cooling to 0° and scratching, exhibited a single peak on gas–liquid partition chromatography on a 10% glycol succinate–Chromosorb P column (6 ft) and did not need further purification for combustion analysis. The material could be recrystallized with difficulty from methanol and formed needles which melted at 37.5–38°: ir (film) 3050 and 1650 cm^{-1} (>C=CH–); nmr ($DCCl_3$) δ 0.65, 0.90, 1.01, 1.06 (s, 15, $5CH_3C\leftarrow$), and 5.48 (m, 1, >C=CH–).

Anal. Calcd for $C_{19}H_{32}$: C, 87.62; H, 12.38. Found: C, 87.50; H, 12.32.

9β-Hydroxy-2,2,4aβ,8,8-pentamethyl-*trans,anti,trans*-perhydrophenanthrene (22).—To a solution of 260 mg (1 mmol) of olefin **21** in 8 ml of tetrahydrofuran was added 10 ml (5.00 mmol) of a 0.5 *M* solution of diborane in tetrahydrofuran, and the reaction mixture stirred under a nitrogen atmosphere for 1 hr at room temperature. After treatment of this mixture with 10 ml of 10% aqueous sodium hydroxide and then 10% of 30% aqueous hydrogen peroxide, the reaction mixture was heated under reflux for an additional 1.5 hr. After cooling, water was added, and the product was isolated by ether extraction. The ethereal extract was washed with water, saturated salt solution, and then dried (Na_2SO_4). Evaporation of the ether at reduced pressure on the steam bath afforded a solid alcohol which was chromatographed on 24 g of Florisil.

Elution of the column with 75 ml of petroleum ether afforded 12 mg (5%) of recovered olefin **21**, which was identified by comparison of its infrared spectrum with that of an authentic sample.

Continued elution of the column with 300 ml of benzene afforded 243 mg (88%) of crystalline alcohol **22**, mp 150–151°. The analytical sample, obtained after one crystallization from petroleum ether, melted at 150.5–151.5°: ir ($HCCl_3$) 3600 and 3450 cm^{-1} (free and bonded OH); nmr ($DCCl_3$) δ 0.72, 0.90, 0.95, 1.19 (s, 15, $5CH_3C\leftarrow$), 3.60 (m, 1, >CHOH).

Anal. Calcd for $C_{19}H_{34}O$: C, 81.95; H, 12.31. Found: C, 81.87; H, 12.31.

9-Keto-2,2,4aβ,8,8-pentamethyl-*trans,anti,trans*-perhydrophenanthrene (23).—A solution of 162 mg (0.58 mmol) of alcohol **22** in 7 ml of acetone was cooled to 15° and treated with 0.17 ml (0.68 mequiv of oxidant) of Jones reagent. After addition of the oxidant the reaction mixture was stirred for 3 min and diluted with ice and water. The product was isolated by ether extraction, and the ethereal extracts were then washed with 10% aqueous potassium bicarbonate, water, saturated salt solution, and dried (Na_2SO_4). Removal of the ether at reduced pressure on the steam bath afforded 155 mg (90%) of crystalline ketone **23**, mp 109–110°. Recrystallization of this material from methanol gave 145 mg (84%) of the ketone **23**, mp 110.5–111.0°, softened at 108°, which was not further purified for analysis: ir ($HCCl_3$) 1701 cm^{-1} (>C=O); nmr ($DCCl_3$) δ 0.89, 0.91, 1.08, 1.12 (s, 15, $5CH_3C\leftarrow$).

Anal. Calcd for $C_{19}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.65; H, 11.58.

Adsorption of a 47-mg sample of this ketone **23** on 4 g of basic alumina and then elution of the material from the column after standing 1 hr with 35 ml of 25% benzene–petroleum ether gave 46 mg of recovered ketone **23**, mp 111–112°, softening at 108°. A mixture of this sample of ketone and that obtained from oxidation prior to this base treatment, mp 110.5–111°, softening 108°, melted at 110.5–111.5°, softening 108°. Similar results were observed when this ketone was equilibrated in either 2% sodium methoxide in methanol or 3% sulfuric acid in acetic acid.

Reduction of ketone **23** with lithium in liquid ammonia afforded only alcohol **22**. Thus, to a solution of 100 mg (14 mmol) of lithium in 50 ml of liquid ammonia was added a solution of 74 mg (0.24 mmol) of ketone **23** in 12 ml of ether, and the reaction mixture was stirred for 45 min. Then the blue color was discharged with excess methanol, and the ammonia was evaporated in an air jet on the steam bath. The resulting sludge was partitioned between water and ether, and the ethereal layer was separated and washed successively with water, 3 *N* hydrochloric acid, water, saturated salt solution, and dried (Na_2SO_4). After evaporation of the ether at reduced pressure on the steam bath, the solid residue was crystallized from petroleum ether. In this manner there was obtained 70 mg (95%) of alcohol **22**, mp 151–152°, alone or on admixture with a sample of the alcohol, mp 150.5–151.5°, obtained directly from hydroboration–oxidation of olefin **21**.

2α-Acetoxy-8-methoxymethylene-4aβ-methyl-*trans,syn,cis*-perhydrophenanthrene (35).—A solution of methoxymethylenetriphenylphosphorane in 80 ml of dry ether was prepared by treatment of 3.06 g (10 mmol) of methoxymethylenetriphenylphosphonium chloride suspended in ether with 1.12 g (10 mmol) of potassium *t*-butoxide. To this solution at room temperature under a nitrogen atmosphere was added a solution of 1.2 g (4.3 mmol) of acetoxy ketone **34**[9] in 20 ml of dry ether, and the reaction mixture was stirred for 20 hr. Then the reaction mixture was decomposed with 20 ml of water, 20 ml of benzene was added, and the organic layer was separated, washed with three 20-ml portions of water, and then dried (Na_2SO_4). The solvents were removed at reduced pressure at 50°, and the residue was partitioned between petroleum ether and aqueous methanol (1:3). The aqueous layer was separated and extracted with petroleum ether. The combined petroleum ether extract was washed with water, dried (Na_2SO_4), and the solvent removed at 50° at reduced pressure. The residue was then chromatographed on 35 g of alumina (Merck). After a small amount of aromatic material was eluted with 600 ml of petroleum ether, elution with 1650 ml of benzene afforded 1.109 g (84%) of methoxymethylene derivative **35**, mp 101–103°. The analytical sample, prepared by crystallization of a portion of this material from petroleum ether, melted at 102.5–104.5°: ir (film) 1735, 1245 (OAc) and 1765 cm^{-1} (>C=CHOCH$_3$); nmr ($DCCl_3$) δ 1.00 (s, 3, $CH_3C\leftarrow$), 2.01 (s, 3, CH_3CO_2–), 3.56 (s, 3, CH_3OR), 5.00 (m, 1, $w/2$ = 8 Hz, >CHOAc), and 5.67 (s, 1, CH_3OCH=C<).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.54; H, 9.84.

2α-Acetoxy-4aβ,8α-dimethyl-*trans,syn,cis*-perhydrophenanthryl-8β-carboxaldehyde (36).—A solution of 1.10 g (3.54 mmol) of acetoxy ether **35** in 100 ml of ether previously saturated with 62% perchloric acid was stirred at room temperature for 1 hr. After dilution of the reaction mixture with 50 ml of benzene, the whole was washed successively with two 30-ml portions of water, 30 ml of saturated aqueous sodium bicarbonate solution, and then dried (Na_2SO_4). Removal of the solvents at 50° at reduced pressure afforded 1.04 g of aldehyde [ir (film) 2695, 1730 (–CHO) and 1740, 1240 cm^{-1} (–OAc)] which was not purified further but used directly in the following methylation experiment.

A solution of the above aldehyde in 100 ml of 1:1 benzene–*t*-butyl alcohol under a nitrogen atmosphere was treated with 2.4 g (21.4 mmol) of solid potassium *t*-butoxide, and the mixture was stirred for 10 min at room temperature. To this solution was then added 5.6 g (40.0 mmol) of methyl iodide in one portion, and the reaction mixture stirred at room temperature for 16 hr. Another portion of 1.2 g (10.7 mmol) of potassium *t*-butoxide was then added, and this was followed immediately with 2.8 g (20.0 mmol) of methyl iodide. After stirring for an additional 2 hr, the reaction mixture was treated with water, 100 ml of ether was added, and the organic layer was separated, washed with four 30-ml portions of water, and then dried (Na_2SO_4). The residue obtained after removal of the solvents at reduced pressure at 50° was reacetylated in 5 ml of pyridine containing 5 ml of acetic anhydride. After heating for 1 hr at 90°, this solution was diluted with water, and the product was isolated by ether extraction. The ethereal extract was washed with water, 3 *N* hydrochloric acid, water, and then dried (Na_2SO_4). The residue that remained after evaporation of the ether at reduced pressure at 50° was chromatographed on 40 g of Florisil. After several early fractions that contained small amounts of oily material, there was eluted 976 mg of crystalline product with 5.6 l. of 5–10% ether–petroleum ether. Recrystallization of this material from petroleum ether afforded 934 mg (85%) of aldehyde **36**, mp 83–86°. The analytical sample, obtained after one further crystallization from the same solvent, melted at 84–86°: ir (Nujol) 2700, 1715 (–CHO) and 1735, 1240 cm^{-1} (–OAc); nmr (CCl_4) δ 1.05, 1.06

(s, 6, $2CH_3C\leftarrow$), 1.97 (s, 3, CH_3CO_2-), 4.92 (m, 1, $w/2$ = 7 Hz, >CHOAc), and 9.69 (s, 1, -CHO).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.29; H, 9.74.

2α-Acetoxy-4aβ,8α-dimethyl-8β-hydroxymethyl-*trans,syn,cis*-perhydrophenanthrene (30).—A solution of 918 mg (3.0 mmol) of the aldehyde **36** in 50 ml of methanol was treated with 1.0 g of sodium borohydride, and the reaction mixture was stirred at 20°. After 45 min, the mixture was diluted with 50 ml of water, and the product isolated by extraction with two 100-ml portions of ether–benzene (5:1). The combined ethereal extract was washed with two 30-ml portions of water, dried (Na_2SO_4), and then the solvents were removed at reduced pressure at 50°. After the solid residue was crystallized from ether–petroleum ether, there was obtained 878 mg (95%) of the acetoxy alcohol **30**, mp 151–153°. The analytical sample, obtained after one further crystallization from the same solvent mixture, also melted at 151–153°: ir (Nujol) 3250 (OH) and 1735, 1245 cm^{-1} (OAc); nmr ($DCCl_3$) δ 0.98, 1.01 (s, 6, $2CH_3C\leftarrow$), 2.02 (s, 3, CH_3CO_2-), 3.61 (m, 2, $-CH_2OH$), and 5.00 (m, 1, $w/2$ = 7 Hz, >CHOAc).

Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.78; H, 10.56.

Acetoxy Ether 38.—A solution of 1.5 g (3.4 mmol) of lead tetraacetate in 100 ml of warm benzene was stirred with 1 g of calcium carbonate for 15 min and then filtered from the solids. To this colorless solution was added 3.0 g of calcium carbonate and then 720 mg (2.34 mmol) of acetoxy alcohol **30** in 200 ml of benzene, and the suspension was stirred and heated under reflux with a 250-W tungsten lamp. After 1 hr irradiation was also effected with a 250-W GE Purple X lamp arranged at a distance of 2 in. from the reaction vessel. After a total reaction time of 4 hr, the reaction mixture was cooled, filtered, diluted with ether, and washed successively with 100 ml of water, 100 ml of 1% aqueous sodium hydroxide, 100 ml of water, and then dried (Na_2SO_4). The solvents were then removed at reduced pressure at 50°, and the residue was chromatographed on 35 g of alumina (Merck). Elution of the column with 1800 ml of 1% ether–petroleum ether afforded 159 mg (25%) of an oily product that appeared to be a mixture of acetoxy olefins **37** [ir (film) 1740 (OAc), and 1645, 880 cm^{-1} (>C=C<)].

Further elution of the column with 3000 ml of 3% ether–petroleum ether and 1500 ml of 5% ether–petroleum ether gave 203 mg (28%) of a mixture of acetoxy ether **38** and an olefinic acetoxy ether ($\Delta^{8a,9}$). The early fractions were essentially pure acetoxy ether **38** and an analytically pure sample, mp 92–95°, was prepared by crystallization of these from pentane at −70°; ir (film) analysis showed no absorption in the 3600–3200-cm^{-1} region, and 1735, 1240 cm^{-1} (OAc).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.38; H, 9.78.

The mother liquors from this crystallization and the later chromatographic fractions were combined, and the entire mixture was dissolved in 10 ml of acetic acid in which was suspended 100 mg of 10% palladium on carbon. This suspension was stirred in an atmosphere of hydrogen at room temperature for 3 hr, filtered to remove the catalyst, and the filtrate was evaporated to dryness at 60° and reduced pressure. After crystallization of the residue from pentane, there was obtained 190 mg (26%) of pure acetoxy ether **38**, mp 92–95°. The melting point of this material was not changed when mixed with the analytical sample obtained above.

Acetoxylactone 6.—A solution of 200 mg (0.65 mmol) of acetoxy ether **38** in 15 ml of glacial acetic acid was warmed to 65–70° and treated dropwise with sufficient Jones reagent to impart a lasting coloration due to excess reagent to the solution. After heating was continued for 10 min, the reaction mixture was cooled, treated with a few drops of methanol to destroy excess oxidant, and then diluted with water. This aqueous suspension was extracted with 200 ml of 5:1 ether–benzene, and the ethereal extract was then washed with water, sufficient 1% aqueous sodium hydroxide to remove all acidic components, water, and then dried (Na_2SO_4). Removal of the solvents at 50° reduced pressure left a solid residue [195 mg, $\nu_{max}^{Nujol\ mull}$ 1770 cm^{-1} (lactone), 1730 cm^{-1} (OAc)] which was chromatographed on 8 g of Florisil. Elution with 1200 ml of 4% ether–benzene afforded 104 mg (50%) of acetoxylactone **6**, mp 174–177°. The analytical sample was obtained by crystallization of this material from ether–hexane and melted at 176–178°: ir (Nujol) 1770 (γ-lactone >C=O) and 1735, 1245 cm^{-1} (OAc); nmr ($CDCl_3$) δ 1.05 (s, 3, C-4aβ-CH_3), 1.11 (s, 3, C-4α-CH_3), 2.00 (s, 3, CH_3CO_2-), and 4.92 (m, 1, $w/2$ = 10 H_3, >CHOAc).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 73.35; H, 9.41. Found: C, 73.42; H, 9.37.

Registry No.—**2**, 508-71-4; **6**, 18181-45-8; **11**, 18181-46-9; **12**, 18181-47-0; **13**, 18181-48-1; **14**, 18181-49-2; **15**, 18181-50-5; 2α,9β-dihydroxy-4aβ,8,8-trimethyl-*trans,anti,cis*-perhydrophenanthrene, 18181-51-6; **16**, 18181-52-7; **17**, 18181-53-8; **18**, 18181-54-9; **19**, 18181-28-7; **20**, 18181-29-8; dihydroxy acid derivative of **20**, 18181-30-1; norrimuene aldehyde, 1910-13-0; **21**, 18181-32-3; **22**, 18181-33-4; **23**, 18181-34-5; **25**, 18181-35-6; **26**, 18181-36-7; **27**, 18181-37-8; primary monoacetate of **27**, 18181-38-9; **28**, 18181-39-0; **30**, 18181-40-3; **35**, 18181-41-4; **36**, 18181-42-5; **38**, 18181-43-6.