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Experiments Directed toward the Total Synthesis of Terpenes. XV. The Synthesis of 3,10-Dimethoxy-6aβ,12bβ-dimethyl-5,6,6a,6bα,7,8,12b,13-octahydropicene, a Potential Intermediate in Triterpene Synthesis[1]

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An approach to the total synthesis of the pentacyclic triterpene alnusenone (1) through the 3-alkoxy-10-hydroxydecahydropicene derivative 4 is outlined, and the initial phases of the scheme were reduced to practice. Three isomers of the 3,10-dimethoxy-6a,12b-dimethyloctahydropicene 6 (R = CH_3) were prepared and characterized. The 6aα,12bβ-dimethyl derivative 14 resulted from the tricyclic unsaturated ketone 11 in 38–50% overall yield by either of two methods. The two isomeric 6aβ,12bβ-dimethyl derivatives 25 and 26 were prepared from the tricyclic α,β-unsaturated ketone 15 by an alternate sequence in 24 and 50% overall yields, respectively. In this latter effort it was found necessary to investigate the course of the catalytic hydrogenation of derivatives of the β,γ-unsaturated keto acid 16, and the effect of the substituents present in the C ring on the stereochemical outcome of this reduction was evaluated.

While the problems associated with the total synthesis of the pentacyclic triterpenes are related to many of those already solved by steroid total syntheses, the triterpene molecule still presents formidable new synthetic challenges in a pentacyclic carbon skeleton with a plethora of angular methyl groups and difficult stereochemical features. Only a relatively few, albeit elegant, forays into this field have been recorded, and notable synthetic success[3] has principally been confined to the hopenone I series, which is derivable[4] from the symmetrical tetracyclic onocerin group. The skeletal substitution patterns of the bulk of the naturally occurring pentacyclic triterpenes, however, lack such potential molecular symmetry and include such familiar examples as β-amyrin, lupeol, and friedelin.[5] The absence of regularity in the substitution patterns of these large molecules precludes their construction by the dimerization sequences[3] that were successful for synthesis in the onocerin series and adds a new dimension to their total syntheses. Some measure of success in the construction of the carbon skeleton of these compounds was first realized by Corey and coworkers[6] with the synthesis of 11,13(18)-oleanadiene from (+)-ambreinolide, and since then two other[6b,c] syntheses of 13(18)-oleanene have been recorded. Unfortunately, the synthetic schemes—all patterned on the AB + DE → ABDE → ABCDE approach—explored in these reports[6] suffer from particularly poor yields in the final stages. Recently, Barton and coworkers[7] have devised a scheme for the partial synthesis of β-amyrin itself from 13(18)-oleanene, and, taken together, these contributions describe a formal total synthesis of that member of this latter group of pentacyclic triterpenes. Other reaction schemes that are potentially more efficient, stereoselective, and versatile than those previously explored[6] may be envisioned for the synthesis of these large, complex, terpenoid molecules. It is with the observations that have resulted from the initial phases of an investigation of one of these approaches that this and the following[8] reports are concerned.

The ultimate objective of this work is the synthesis of

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(3) (a) G. Stork, A. Meisels, and J. E. Davies, *J. Amer. Chem. Soc.*, **85**, 3419 (1963). (b) E. E. van Tamelen, M. A. Schwartz, E. J. Hessler, and A. Storni, *Chem. Commun.*, 409 (1966). Significant earlier efforts that foreshadowed these contributions were by E. Roman, A. J. Frey, P. A. Stadler, and A. Eschenmoser, *Helv. Chim. Acta*, **40**, 1900 (1957); E. J. Corey and R. R. Sauers, *J. Amer. Chem. Soc.*, **81**, 1739 (1959); and F. Sondheimer and D. Elad, *ibid.*, **81**, 4429 (1959).

(4) K. Schaffner, L. Caglioti, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **41**, 152 (1958).

(5) For a general discussion of these and related substances, see J. Simonsen and W. C. J. Ross, "The Terpenes," Vol. V, Cambridge University Press, Cambridge, Great Britain, 1957.

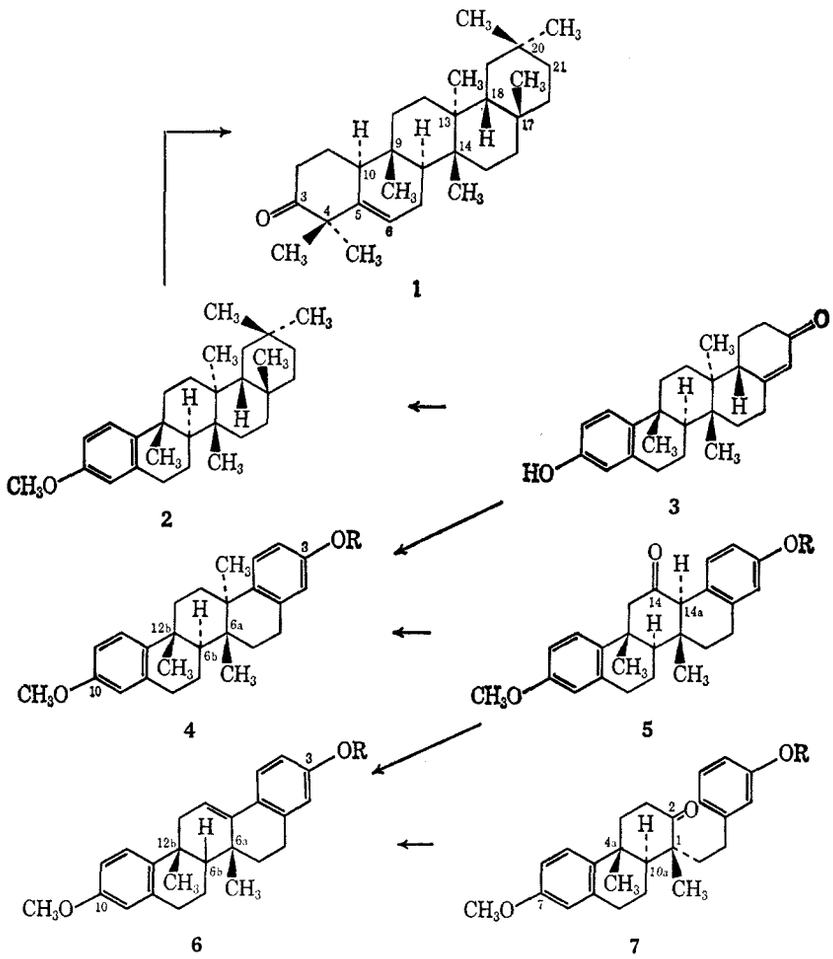
(6) (a) E. J. Corey, H. J. Hess, and S. Proskow, *J. Amer. Chem. Soc.*, **81**, 5258 (1959); (b) J. A. Barltrop, J. D. Littlehailes, J. D. Rushton, and N. A. J. Rogers, *Tetrahedron Lett.*, 429 (1962); (c) E. Ghera and F. Sondheimer, *ibid.*, 3887 (1964).

(7) D. H. R. Barton, E. F. Lier, and J. F. McGhie, *J. Chem. Soc., C*, 1031 (1968).

(8) R. E. Ireland, D. A. Evans, P. Löliger, J. Bordner, R. H. Stanford, Jr., and R. E. Dickerson, *J. Org. Chem.*, **33**, 3729 (1968).

CHART I

THE ESSENCE OF THE SYNTHETIC PLAN



the pentacyclic triterpene alnusenone (1).[9,10] From a synthetic standpoint, the structure of this molecule appeared to offer several advantages over that of the β-amyrin system in spite of the lack of molecular symmetry present. In order to put the present work in better perspective, a brief outline of the general synthetic plan that underlies this effort is in order (see Chart I).

Inasmuch as the A ring of alnusenone (1) bears no angular methyl substituent at either C-5 or C-10, this portion of the molecule represents a synthon[11] that may readily be derived from a methoxylated aromatic ring, such as that present in the pentacyclic ether 2. A procedure by which this transformation can be accomplished is not hard to envision and is, in fact, available from previous work[12] on the total synthesis of (±)-rimuene.

While the substitution pattern of the E ring of alnusenone (1) is identical with that of β-amyrin and contains an angular methyl group at C-17, it too may be envisaged as though it had its roots in a similar aromatic ring. The α,β-unsaturated ketone system in the keto ether 3 that will result when a Birch reduction–hydrolysis sequence is applied to the 3-alkoxy-10-hydroxydecahydropicene 4[13] is ideally situated to provide for the introduction of both the C-17 angular methyl group through a conjugate addition reaction and the C-20 *gem*-dimethyl grouping through subsequent methylation.

Another synthetic advantage of the alnusenone carbon skeleton (1) over that of β-amyrin, which is intimately associated with the utility of the suggested Birch reductions, is the *anti* relationships between the C-9 and C-13 angular methyl groups and the respective adjacent C-10 and C-18 angular hydrogens. It is just such a configurational arrangement about these centers that will result[14] from the Birch reduction of the pen-

(9) S. Chapon and S. David, *Bull. Soc. Chim. Fr.*, 333 (1953); J. M. Beaton, F. S. Spring, and R. Stevenson, *J. Chem. Soc.*, 2616 (1955); J. M. Beaton, F. S. Spring, R. Stevenson, and J. L. Stewart, *Tetrahedron*, **2**, 246 (1958).

(10) The structural formulas containing one or more asymmetric carbon atoms depict one enantiomer but refer to racemic compounds throughout. In the text, (±) prefix will be omitted and intermediates are to be assumed to be racemic. In the discussion, phenanthrene nomenclature and numbering will be used to describe tricyclic compounds, and each racemate is arbitrarily represented by that enantiomer that has the 4a methyl group in the β configuration. The pentacyclic compounds will be described by the picene nomenclature and numbering (A. M. Patterson, L. T. Capell, and D. F. Walker, "The Ring Index," 2nd ed, American Chemical Society, Washington, D. C., 1960, No. 6384), and each racemate is arbitrarily represented by that enantiomer that has the 12b methyl group in the β configuration. In discussions where naturally occurring triterpenes are involved, the nomenclature and numbering suggested by S. Allard and G. Ourisson [*Tetrahedron*, **1**, 277 (1957)] will be used as necessary.

(11) E. J. Corey, *Pure Appl. Chem.*, **14**, 19 (1967).

(12) R. E. Ireland and L. N. Mander, *J. Org. Chem.*, **32**, 689 (1966).

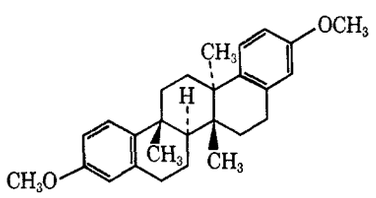
(13) There is ample precedence for the Birch reduction of an anisole-type ring in the presence of a phenolic ring, which remains unaltered in the product; see, for example, J. Fried and N. A. Abraham, *Tetrahedron Lett.*, 3505 (1965).

(14) A. J. Birch, *Quart. Rev.* (London), **12**, 17 (1958).

tacyclic ethers **3** and **4**, which possess the required *trans,anti,trans* backbone in the B, C, and D rings.

A final and compelling virtue of alnusenone (**1**) as a synthetic objective is the reported[9,15] acid-catalyzed rearrangement of this skeleton to the 13(18)-oleanene system. Inasmuch as many of the features of the alnusenone structure (**1**) appear to present fewer synthetic difficulties than those of β-amyrin itself, and in the end a pathway[7] is available whereby the two triterpenes can be linked, an investigation of the preparation of appropriate precursors for the alnusenone (**1**) synthesis was initiated.

From the foregoing analysis, it is clear that the prime intermediate objective of this synthetic effort must be the 3-alkoxy-10-hydroxydecahydropicene **4**; however, it is also clear that, during the extended synthesis that will be required to construct the carbon skeleton of this key intermediate **4**, the phenolic A ring may *not* go unprotected. While provision for the selective, reversible protection of this C-10 oxygen function must ultimately be built[8] into the synthesis of any precursor of the decahydropicene **4**, at the outset this problem was considered secondary to the construction of the basic carbon skeleton needed. It is probable that any synthesis devised for the preparation of pentacyclic precursors of the decahydropicene **4** will entail the sequential incorporation of the two aromatic rings and, therefore, will provide ample opportunity to differentiate the two oxygen functions. With this consideration in mind, initial attention was focused on methods suitable for the synthesis of the 3,10-dimethoxydecahydropicene **8** by a



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scheme that could be modified later so as to lead to the desired 3-alkoxy-10-hydroxydecahydropicene **4**. One approach to this synthesis that became the focal point of the present effort is a scheme that passes through the tricyclic ketone **7** (R = CH_3). Acid-catalyzed cyclodehydration of this ketone **7** (R = CH_3) was expected to generate the olefin **6** (R = CH_3), which on hydroboration[16] and oxidation[17] would afford the decahydropicenone **5** (R = CH_3). Methylation at the doubly activated C-14a position of this ketone and then removal of the carbonyl function would complete the construction of the 3,10-dimethoxydecahydropicene **8**. Suitable modification of this sequence at the earlier stages should also provide for the synthesis of the 3-alkoxy-10-hydroxydecahydropicene **4**. The present report is concerned with the synthesis of the ketone **7** (R = CH_3) and its conversion to the olefin **6** (R = CH_3).

Two approaches to the synthesis of the tricyclic ketone **7** (R = CH_3) were investigated in order to ascertain the stereochemical outcome of the substitution of the two groups at C-1. It was felt that the order of addition of the methyl and the 2′-*m*-methoxylphenylethyl groups to the tricyclic nucleus would significantly alter their ultimate stereochemical relationship[18] and that samples in both series would be of value for identification purposes. While the stereochemical outcome of the work that is depicted in the sequel could only be inferred by analogy to previously studied systems during the early stages, subsequent single-crystal X-ray structural analysis[19] on the derived bromo ketone **35**[8] served to make these assignments certain. Therefore, rather than belabor the initial uncertainties, the results are presented in the light of the subsequent firm structural knowledge.

A. 3,10-Dimethoxy-6α,12bβ-dimethyl-5,6,6a,6bα,7,-8,12b,13-octahydropicene.—The synthesis (see Chart II) of one isomer, **13**, of the desired tricyclic ketone **7** (R = CH_3) required the construction of the α,β-unsaturated ketone **11**, in which the 2′-*m*-methoxyphenylethyl side chain was already present, and the addition of the C-1 methyl group was left for a subsequent step. The α,β-unsaturated ketone **11** was readily prepared in 78% yield through the homoannelation of 6-methoxy-1-methyl-2-tetralone (**9**)[3a] with the vinyl ketone **10**[20] in the presence of aqueous methanolic potassium hydroxide. The methylation of this α,β-unsaturated ketone **11** was accomplished either through direct reaction of the ketone with methyl iodide in potassium *t*-butoxide–*t*-butyl alcohol solution or by methylation[21] of the enolate formed on metal–ammonia reduction of the α,β-unsaturated ketone system. The former method required the subsequent catalytic hydrogenation of the remaining olefinic linkage—a process that was attended by some difficulty.

Hydrogenation of the β,γ-unsaturated ketone **12** over palladium on carbon in acetic acid solution resulted in the absorption of considerably more than 1 equiv of hydrogen and afforded a mixture of products that from its spectral properties appeared to contain reduced pentacyclic material as well as the expected saturated tricyclic ketone component. This difficulty was overcome when the ketone group was first reduced with lithium aluminum hydride, and then the double bond was saturated over the palladium catalyst. Oxidation[17] of the resulting alcohol afforded the same tricyclic ketone **13** that resulted from the metal–ammonia methylation sequence.

Cyclization of the saturated tricyclic ketone **13** was possible under the influence of *p*-toluenesulfonic acid in refluxing benzene solution and generated the octahydropicene derivative **14**. This pentacyclic olefin **14** was formed by the reduction–methylation sequence in 50% overall yield from the α,β-unsaturated ketone **11** and in 38% overall yield *via* the longer methylation–hydrogenation route. The degree of the stereoselectivity during the methylation step of the two sequences could not be

(15) A recent mechanistic study of this rearrangement has been made by R. M. Coates, *Tetrahedron Lett.*, 4143 (1967).

(16) G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).

(17) 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).

(18) There is sufficient precedence for this conclusion in the previous synthetic work on the diterpenoid resin acids. In particular, see (a) G. Stork and J. W. Schulenberg, *J. Amer. Chem. Soc.*, **84**, 284 (1962); (b) R. E. Ireland and R. C. Kierstead, *J. Org. Chem.*, **31**, 2543 (1966); and (c) E. Wenkert, A. Afonso, J. B. Bradenberg, G. Kaneko, and A. Tahara, *J. Amer. Chem. Soc.*, **86**, 2038 (1964).

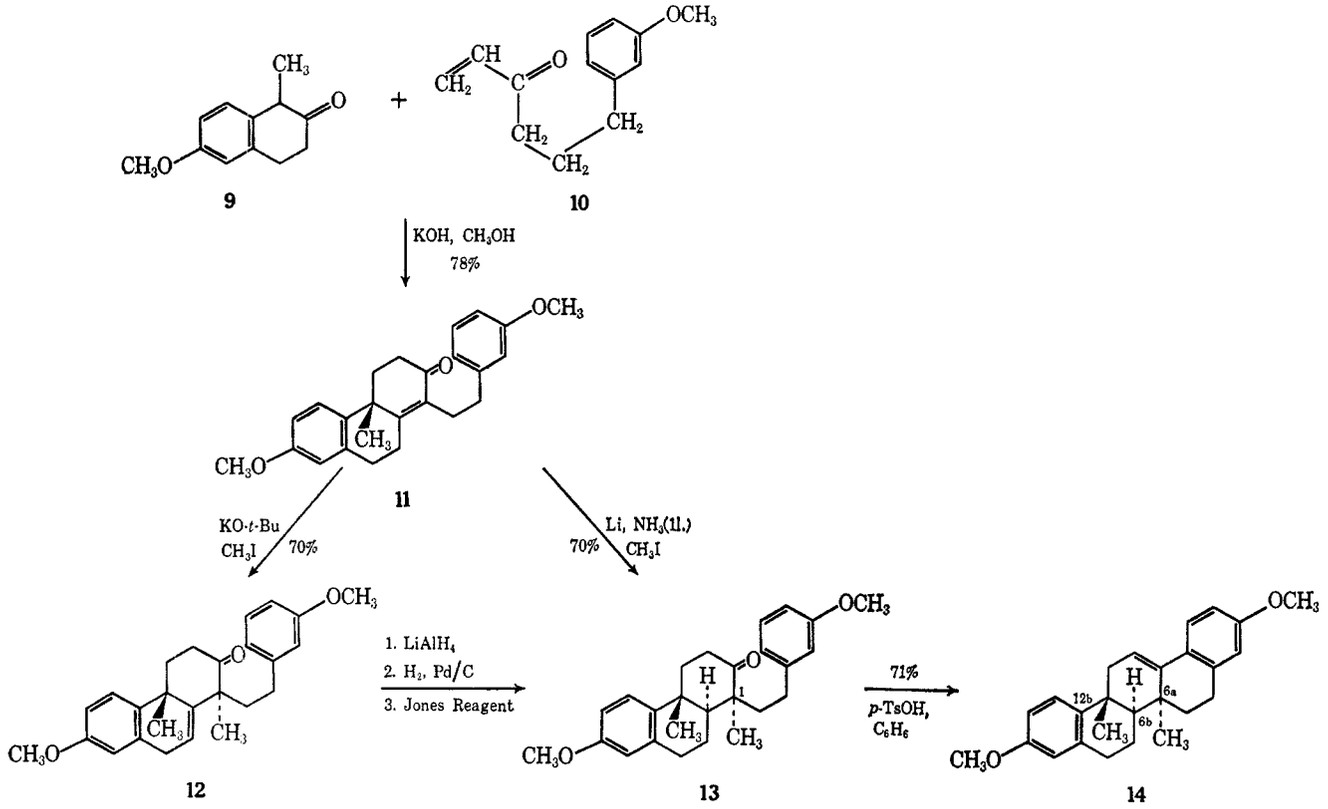
(19) J. Bordner, R. H. Stanford, R. E. Ireland, and R. E. Dickerson, *J. Org. Chem.*, in press.

(20) G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, and H. Smith, *J. Chem. Soc.*, 5072 (1963).

(21) G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Amer. Chem. Soc.*, **87**, 275 (1965).

CHART II

THE SYNTHESIS OF 3,10-DIMETHOXY-6aα,12bβ-DIMETHYL-5,6,6a,6bα,7,8,12b,13-OCTAHYDROPICENE (14)



(38–50% over-all from **11**)

determined accurately, as in each case the product mixtures were difficult to purify, and only the major component was isolated. The overall yields of the pentacyclic olefin **14**, however, are such as to indicate that the methyl group is added predominantly to one side of the tricyclic nucleus in preference to the other. This seems to be the case whether the enolate anion is derived from the α,β-unsaturated ketone **11** directly or is generated by initial saturation of the conjugated double bond in the metal–ammonia reduction. The alkylation[18a,c,22] of closely related tricyclic systems behaves similarly and results primarily in the introduction of the new alkyl group on the α side of the molecule, as well.

The observation that the ketone **13**—and hence, the succeeding transformation products—possesses the *trans* B/C ring fusion was expected as a result of its formation in the metal–ammonia methylation reaction sequence.[21] This reduction procedure invariably generates the *trans* ring juncture in molecules of this type.[12] A corollary of this conclusion is that catalytic hydrogenation of the unsaturated alcohol formed on hydride reduction of the β,γ-unsaturated ketone **12** also generates the *trans* B/C ring fusion, as the same saturated ketone **13** is ultimately obtained.

B. 3,10-Dimethoxy-6aβ,12bβ-dimethyl-5,6,6a,6bβ,-7,8,12b,13-octahydropicene and 3,10-Dimethoxy-6aβ,-12bβ-dimethyl-5,6,6a,6bα,7,8,12b,13-octahydropicene. —An alternate approach to the synthesis of the tricyclic ketone **7** (R = CH_3) originates from the α,β-unsaturated ketone **15**,[23] which already contains the C-1 methyl group and to which the 2′-*m*-methoxyphenylethyl side chain must be added. Investigation of this approach led to the synthesis of the two C-6b epimeric octahydropicenes **25** and **26** *via* the corresponding tricyclic ketones **23** and **24** (**7**, R = CH_3) (see Chart III). The stereochemical difference between these two series is a consequence of the catalytic hydrogenation of the 10(10a) double bond of the unsaturated keto acid **16** and is worthy of further comment.

The unsaturated keto acid **16** was prepared by directed alkylation of the α,β-unsaturated ketone **15** in a procedure that was a slight modification of that described by Stork and Schulenberg.[18a] The desired *cis* relationship between the C-4a and C-1 methyl groups is assured as a result of the Stork–Schulenberg synthesis[18a] of dehydroabietic acid from a similar keto acid, and the recently reported[24] conversion of the keto acid **16** to a derivative of neoabietic acid. Catalytic hydrogenation of the β,γ-unsaturated keto ester derived from treatment of the keto acid **16** with potassium carbonate and methyl iodide in acetone solution was expected to generate the desired *trans* B/C ring fusion. Indeed, the reduction of the 7-demethoxy analog of the keto acid **16** is reported[25] to afford a high yield of a single crystalline saturated keto acid to which the *trans* B/C ring fusion is assigned. Similarly, catalytic hydrogenation of several C-2-deoxy analogs[18a,24] of the keto acid **16** has been shown to generate the *trans* B/C ring fusion, as has the reduction of C-1 *gem*-dimethyl analog.[3a] However, when the ester of the keto acid **16** in acetic

(22) V. Permutti and Y. Mazur, *J. Org. Chem.*, **31**, 705 (1966), and references cited therein.

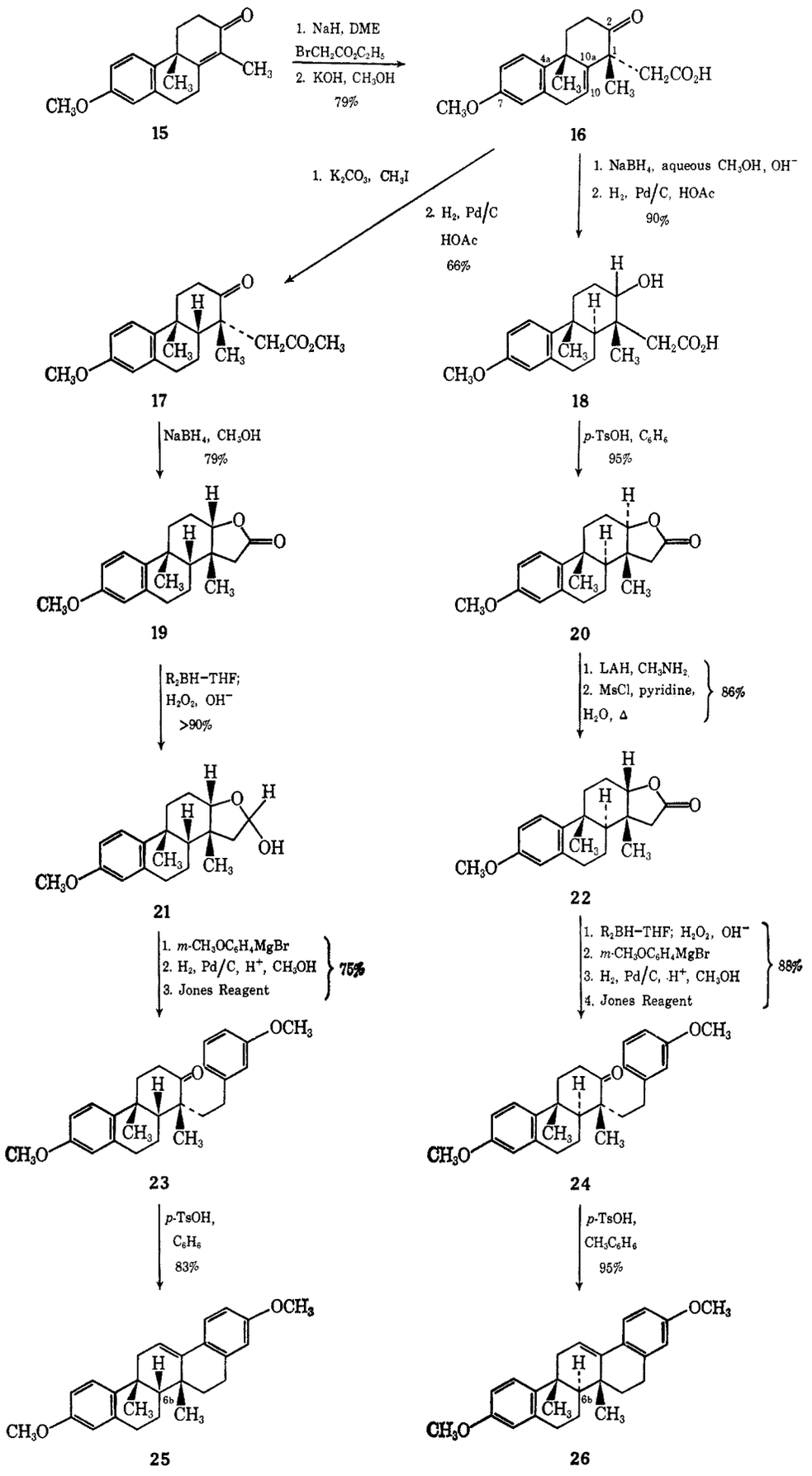
(23) M. Fetizon and J. Delobelle, *Compt. Rend.*, **245**, 850 (1957).

(24) A. Ogiso and S. W. Pelletier, *Chem. Commun.*, 94 (1967).

(25) V. R. Ghatak, D. K. Datta, and S. C. Ray, *J. Amer. Chem. Soc.*, **82**, 1728 (1960).

CHART III

THE SYNTHESIS OF THE EPIMERIC OCTAHYDROPICENES 25 AND 26



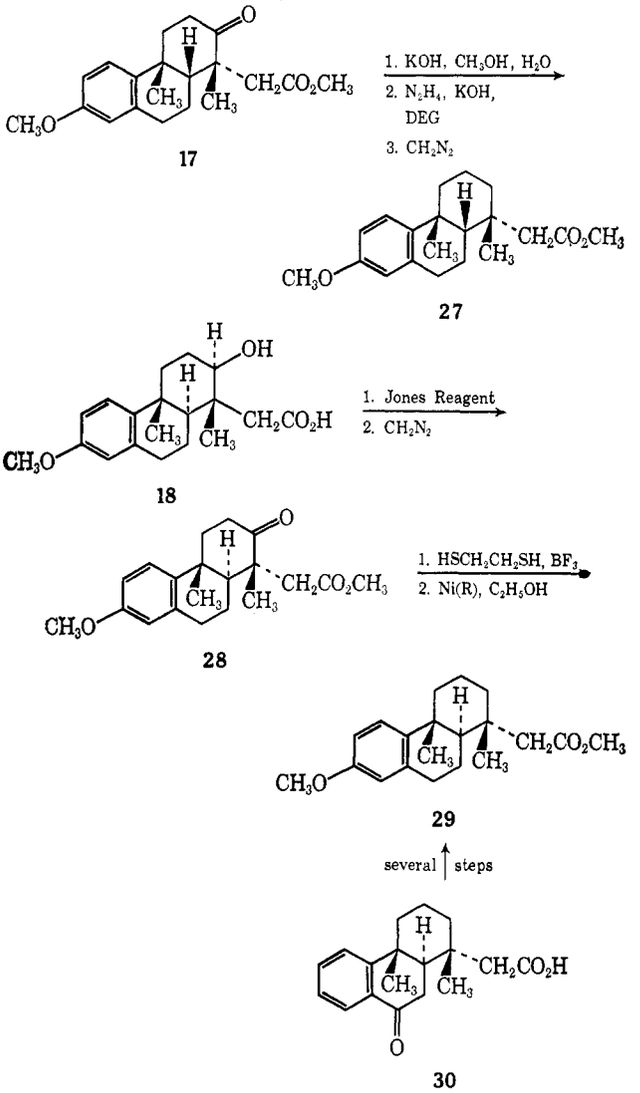
acid solution was hydrogenated over 10% palladium on carbon, there resulted a mixture which was shown by gas–liquid chromatographic analysis to consist of two isomeric saturated keto esters in a ratio of 8:1. When the conditions reported by Ghatak and coworkers[25] were used, the two isomeric keto esters were still formed, but now in a ratio of 3:1. When the former conditions were used on a preparative scale, the saturated keto ester **17** was isolated in 66% yield and shown to be the major component of the mixture by peak enhancement experiments on the gas–liquid chromatograph. Initially, this isomer was assumed to be the *trans* B/C ring fused material and was carried[8] on through the synthetic scheme. Ultimately, X-ray structural analysis[19] of the bromo ketone **35**[8] derived from this keto ester **17** unequivocally demonstrated that it was indeed the *cis* B/C ring fused material.

If the report by Ghatak and coworkers[25] is neglected, the principal structural difference between the keto acid **16** and similar molecules that are reported[3a,24] to produce *trans* B/C ring fused products on catalytic hydrogenation is the presence of the C-2 ketone group. When this carbonyl group is not present and that center is tetrahedral, hydrogenation appears to take place exclusively from the α side of the molecule. The same α orientation was observed earlier in this work when it was found that catalytic hydrogenation of the alcohol derived from the unsaturated ketone **12** produced by B/C *trans* fused saturated ketone **13** after oxidation of the resulting saturated alcohol. Therefore, in order to modify the stereochemical outcome of the catalytic hydrogenation of the 10(10a) double bond of the keto acid **16**, the C-2 ketone group was first reduced with sodium borohydride to the β (equatorial) alcohol,[26] and then the hydrogenation was effected over 10% palladium on carbon as before. In this case, there was formed in 95% yield a single saturated product which was shown to be the desired B/C *trans* fused hydroxy acid **18** by conversion to the C-2-deoxy ester **29**[24] and direct comparison (see Chart IV) with an authentic sample prepared from the keto acid **30**[27] by an alternate synthesis.[28] Furthermore, after esterification and then oxidation of the saturated hydroxy acid **18**, the resulting saturated keto ester **28** was shown by peak enhancement experiments on the gas–liquid chromatograph to have an identical retention time with that of the minor component formed on hydrogenation of the ester of the unsaturated keto acid **16**.

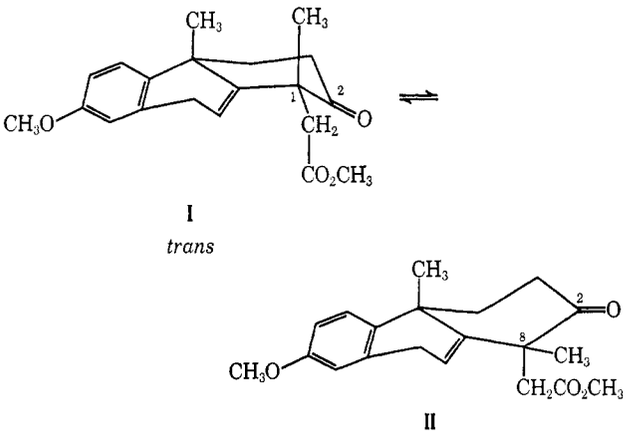
These results indicate that the stereochemical outcome of the saturation of the 10(10a) double bond in tricyclic molecules such as these is quite dependent on the character of ring C and its substituents. This may be a function of the conformation of the molecule that

CHART IV

IDENTIFICATION OF *cis* AND *trans* PRODUCTS FROM CATALYTIC HYDROGENATION OF UNSATURATED KETO ACID **16**



undergoes the hydrogenation reaction. In the case of the keto acid **16**, hydrogenation may be taking place to a significant extent through the quasiboat conformation II. In contrast to the quasichair conformation I



I

trans

II

cis and *trans*

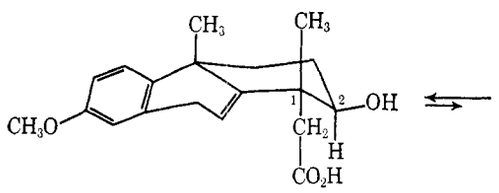
in which one side of the molecule is quite free from steric hindrance, the quasiboat conformation II is hindered on both sides and might be expected to undergo hydro-

(26) The configuration of the C-2 hydroxyl group was determined by lactonization of the hydroxy acid **16** in 89% yield in benzene solution in the presence of *p*-toluenesulfonic acid. These conditions have been shown to avoid isomerization of the hydroxyl-bearing carbon in similar cases [J. A. Marshall, N. Cohen, and A. R. Hochsteller, *J. Amer. Chem. Soc.*, **88**, 3408 (1966)]. The C-2 hydrogen resonance in the nmr spectrum of this lactone appeared as a broad multiplet centered at δ 3.77 ppm ($W_{1/2}$ = 15 Hz). This signal is characteristic (N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Systems," Holden-Day, Inc., San Francisco, Calif., 1966, p 80) of the pattern of an axial hydrogen, and therefore the hydroxyl group on the carbon must be equatorial.

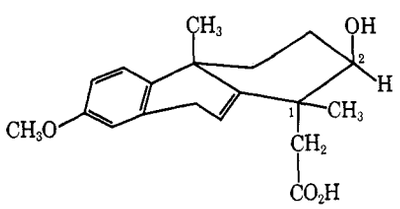
(27) R. E. Ireland and R. C. Kierstead, *J. Org. Chem.*, **31**, 2543 (1966).

(28) F. F. Giarrusso and R. E. Ireland, *ibid.*, **33**, 3560 (1968).

genation considerably less stereoselectively. The likelihood that at equilibrium a significant portion of the keto ester exists in the quasiboat conformation II is enhanced by virtue of the greater flexibility of the carbonyl-containing C ring compared with a more saturated analog[29] and the destabilization of the quasichain conformation I as a result of the eclipsing of the equatorial C-1 acetic acid side chain and the C-2 carbonyl oxygen.[30] The situation is entirely different in the case of the hydroxy acid formed on reduction of the keto acid **16** with sodium borohydride. Here the quasichair conformation III is certainly more stable than the corresponding quasiboat conformation IV,



III
trans



IV
cis and *trans*

and, since the trigonal C-2 carbonyl group is no longer present, the energy barrier for the interchange between conformations will certainly be greater. The greater ease and stereoselectivity of the hydrogenation of this hydroxy acid compared with the foregoing keto ester is probably a result of reaction through the quasichain conformation III.

The B/C *cis* fused keto ester **17** and the B/C *trans* fused hydroxy acid **18** were separately converted to the corresponding octahydropicenes **25** and **26**, respectively, by virtually the same reaction sequences. The principle involved first the conversion of the carboxyl group to an aldehyde function and then the incorporation of the required *m*-methoxyphenyl residue through use of the Grignard reaction. Subsequent hydrogenolysis of the benzylic-type hydroxy group and then acid-catalyzed cyclodehydration of the derived ketones **23** and **24** succeeded in each case to provide an efficient route to the desired pentacyclic materials. The apparent efficiency of the sequence (the *cis,syn* pentacyclic diether **25** was available in 44% overall yield from the B/C *cis* fused keto ester **17** and the *trans,anti* pentacyclic diether **26** was prepared in 68% overall yield from the B/C *trans* fused hydroxy acid **18**) requires no further emphasis, but the utility of the C-2 oxygen function in the conversion of the carboxyl grouping to an aldehyde is worthy of mention.

(29) The chair–boat energy barrier is at least 4 kcal/mol less in cyclohexanone than it is in cyclohexane: (a) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Amer. Chem. Soc.*, **84**, 386 (1962); (b) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, p 186.

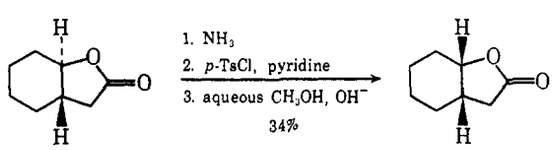
(30) This "2-alkyl ketone" effect is significant for alkyl groups larger than the methyl group; *cf.* ref 29b, pp 112–113.

In each case, it was planned to generate the aldehyde function by the disiamyl borane reduction[31] of the γ-lactone formed between a C-2 hydroxyl group and the C-1α acetic acid side chain. The resulting γ-lactol that is formed in this manner would serve not only to stabilize the air-sensitive aldehyde group during isolation and manipulation, but also, on treatment with excess *m*-methoxyphenylmagnesium bromide, to regenerate the aldehyde group necessary for the addition of this Grignard reagent.

Application of this scheme to the B/C *cis* fused keto ester **17** followed the expected plan exactly. Reduction of the keto ester **17** with sodium borohydride generated the α (equatorial) hydroxyl group at C-2, and on work-up of the reaction mixture the desired γ-lactone **19** was formed spontaneously. Reduction[31] of this *cis* locked γ-lactone **19** with disiamylborane, followed by oxidation with hydrogen peroxide and treatment with aqueous base, produced the expected γ-lactol **21** in virtually quantitative yield. In general, no purification of the γ-lactol **21** was necessary before it was converted directly to the ketone **43** by the three-stage process outlined (see Chart III). The greater than 68% yield of the ketone **23** from the lactone **19** was gratifying.

The B/C *trans* fused hydroxy acid **18** also bore a C-2 equatorial (β) hydroxyl group,[26] and hence the equatorial C-1α acetic acid side chain was *trans* to this hydroxyl group. This relationship was amply demonstrated by the lack of spontaneous γ-lactone formation, and it was not until the hydroxy acid **18** was heated under reflux in benzene solution in the presence of *p*-toluenesulfonic acid that the γ-lactone **20** was formed. The disiamylborane reduction[31] of this *trans* locked γ-lactone **20** did not behave according to plan and resulted only in the formation of the corresponding diol from overreduction. Even careful control of the reaction conditions and the number of equivalents of reducing agent used did not prevent overreduction, and none of the γ-lactol was formed. Apparently, the strain of the *trans* locked γ-lactol system was great enough to assure the continual availability of some open-chain hydroxyaldehyde in the reaction mixture, and thus account for the observed formation of the diol.

In view of the results obtained above in the B/C *cis* fused series, the obvious solution to this problem was to employ the corresponding *cis* locked γ-lactone **22** in the reduction sequence. A convenient procedure for the epimerization of the C-2 hydroxyl group—with concomitant formation of the desired *cis* locked γ-lactone **22**—was found in the report[32] of the analogous transformation of the *trans*-lactone **31** to its *cis* isomer **32**.



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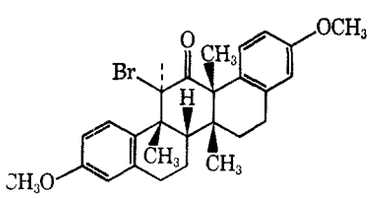
After some experimentation, the procedure detailed by Brewster and Kucera[32] was modified as outlined (see Chart III), with the resulting increase of the overall

(31) H. C. Brown and A. W. Moerikofer, *J. Amer. Chem. Soc.*, **85**, 2063 (1963).

(32) J. H. Brewster and C. H. Kucera, *ibid.*, **77**, 4546 (1955).

yield of the process from 34% to 86%. With the availability of the *cis* locked γ-lactone **22** assured by this sequence, the disiamylborane reduction[31] was investigated, and it was gratifying to find that once more the *cis* locked γ-lactol was the sole product in greater than 90% yield. Again, the γ-lactol need not be purified, and application of the foregoing Grignard reduction–oxidation sequence to the crude reduction product resulted in an 88% yield of the B/C *trans* fused ketone **24** (**7**, R = CH_3). Thus, the sequence for the conversion of each of the *cis* and *trans* fused acetic acid derivatives **17** and **18** was complete and was found to *require* as intermediates the *cis* locked γ-lactones **19** and **22**, respectively.

Final conversion of each of the ketones **23** and **24** (**7**, R = CH_3) to their octahydropicene counterparts **25** and **26** made available two further isomers in the latter series. Subsequent conversion[8] of the *cis,syn* isomer **25** to the bromo ketone **33** and complete definition of its structure through single-crystal X-ray structural anal-



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ysis[19] makes certain the structural assignments presented here. By virtue of their mode of synthesis, the two isomers **25** and **26** can differ only in the configuration about the C-6b carbon, and, as the diether **25** is the *cis,syn* fused (C-6bβ hydrogen) isomer, the diether **26** must be the *trans,anti* fused (C-6bα hydrogen) isomer. Since the isomeric diether **14** must also possess a B/C *trans* ring fusion (C-6bα hydrogen) (*vide supra*) and is not identical with the B/C *trans* fused diether **26**, this diether must have the *trans,syn* structure **14** assigned to it above. Further transformations of these pentacyclic substances in the direction of natural triterpenes is under investigation.

Experimental Section[33]

A. 3,10-Dimethoxy-6aα,12bβ-dimethyl-5,6,6a,6bα,7,8,12b,-13-octahydropicene Series. 7-Methoxy-1-(2′-*m*-methoxyphenylethyl)-4aβ-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (11).—To a stirred solution of 5.30 g (0.028 mol) of 6-methoxy-1-methyl-2-tetralone (**9**)[32a] in 30 ml of methanol under a nitrogen atmosphere at 0° was slowly added a solution of 2.15 g of potassium hydroxide in 2.9 ml of water and 10 ml of methanol. After stirring for 30 min at 0°, the mixture was cooled to −20°, and a solution of 5.69 g (0.029 mol) of 6-(*m*-methoxyphenyl)-1-hexen-3-one (**10**)[20] in 10 ml of methanol was added dropwise with stirring. After addition was complete, the cooling bath was removed, and the viscous reaction mixture was stirred at room temperature for an additional 3 hr. The mixture was then heated at boiling under reflux for 3.5 hr, cooled, diluted with water, and made acid to test paper with 10% aqueous hydrochloric acid. The product was isolated by ether extraction, and the ethereal extract was washed with water and saturated aqueous sodium hydroxide solution and dried (Na_2SO_4). After evaporation of the solvent, there remained 11.3 g of viscous, yellow oil which was chromatographed on 400 g of Merck alumina. Elution of the column with 1.6 l. of 1:1 ether–benzene and 400 ml of ether afforded 8.19 g (78%) of the desired α,β-unsaturated ketone **11** as a light yellow oil. While all attempts to induce this material to crystallize were fruitless, it was sufficiently pure for further experimentation and exhibited a single spot on tlc in 10% ether–hexane on silica gel. The analytical sample was obtained by evaporative distillation of a small portion of this material at 100° bath temperature (0.005 mm): uv λ_{max} (95% EtOH) 224 (ε 20,700) and 243 mμ (ε 15,600); ir (CCl_4) 1662 cm^{-1} (conjugated C=O); nmr ($CDCl_3$) δ 1.43 (s, 3, C-4aβ $3H_3$), 3.73 (s, 6, $2ArOCH_3$), and 6.70 and 7.08 (m, 7, ArH).

Anal. Calcd for $C_{25}H_{28}O_3$: C, 79.76; H, 7.50. Found: C, 79.90; H, 7.58.

In subsequent preparations of the α,β-unsaturated ketone **11** by this procedure, or when the corresponding Mannich base methiodide[20] of the hexenone **10** was used, the yields varied from 65 to 75%.

1α,4aβ-Dimethyl-7-methoxy-1β-(2′-*m*-methoxyphenylethyl-3,4,4a,9-tetrahydro-2(1H)-phenanthrone (12)—Into a mixture of 4.65 g (0.012 mol) of the α,β-unsaturated ketone **11** and 1.79 g of commercial potassium *t*-butoxide under a nitrogen atmosphere was directly distilled from sodium hydride *ca.* 150 ml of glyme, and the mixture was stirred and heated at boiling under reflux for 0.5 hr. After this period, the solvent was allowed to distil until no trace of *t*-butyl alcohol was detected in the distillate by glpc on a 6-ft 10% SE-30 on Chromosorb P column at room temperature. Anhydrous glyme was added periodically during the distillation in order to maintain the volume of the reaction mixture at *ca.* 150 ml. The reaction mixture was then cooled in an ice bath, and 7.0 g of methyl iodide was added all at once. After stirring for 3 hr at room temperature and then 1 hr under reflux, the reaction mixture was cooled, diluted with water, and made acidic with 10% aqueous hydrochloric acid. The product was isolated by extraction with ether, and the ethereal solution was washed with water and saturated aqueous sodium chloride solution and dried (Na_2SO_4). After evaporation of the solvents at reduced pressure, 4.9 g of a viscous, oily product remained.

Chromatography of this crude product on 250 g of Merck acid-washed alumina (deactivated with 1% water) afforded the β,γ-unsaturated ketone in two main portions. The first portion (1.19 g eluted with 400 ml of 20% ligroin–benzene) was a mixture of mono- and dimethylated ketone as judged from its nmr spectrum. Rechromatography of this portion on 50 g of the same support afforded 0.50 g of a clear, colorless oil that was considered to be the pure monomethylated ketone **12** from its nmr spectrum.

The second portion of the initial chromatogram amounted to 2.88 g of pure monomethylated ketone **12** and was eluted with 1.2 *l.* of 20% ligroin–benzene. Thus, a total of 3.30 g (70%) of monomethylated ketone **12** was obtained as a clear, colorless oil. The analytical sample was prepared by evaporative distillation of a portion of this material at 300–230° bath temperature (0.005 mm): ir (CCl_4) 1710 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.18 (s, 3, C-1α CH_3), 1.28 (s, 3, C-4aβ CH_3), 3.78 (s, 6, $2ArOCH_3$), 5.95 (m, 1, C-10 H), and 6.70 and 7.12 (m, 7, ArH).

Anal. Calcd for $C_{26}H_{30}O_3$: C, 80.08; H, 7.78. Found: C, 79.97; H, 7.74.

1α,4aβ-Dimethyl-3,4,4a,9,10,10aα-hexahydro-7-methoxy-1β-(2′-*m*-methoxyphenylethyl)-2(1H)-phenanthrone (13). a. From Catalytic Hydrogenation of the Ketone 12.—A solution of 2.50 g (6.4 mmol) of the β,γ-unsaturated ketone **12** in 50 ml of dry ether was treated with 250 mg of lithium aluminum hydride at room temperature for 0.5 hr. The excess hydride was destroyed with excess 10% aqueous hydrochloric acid and the product was isolated by ether extraction. After the ethereal solution was washed with water, dried (Na_2SO_4), and evaporated, the crude product was dissolved in 50 ml of glacial acetic acid and then stirred for 48 hr in an atmosphere of hydrogen at room temperature and pressure in the presence of 250 mg of 10% palladium on carbon. The catalyst was then removed by filtration through Celite, and the acetic acid was evaporated at reduced pressure.

(33) All melting points were determined on a Kofler hot stage and are uncorrected. All boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer infrared spectrometer Model 237B and ultraviolet spectra were taken on a Cary recording spectrometer Model 11M. Nuclear magnetic resonance spectra were taken on a Varian Associates Model A-60A nuclear magnetic resonance spectrometer. Ligroin, unless otherwise noted, refers to the petroleum ether fraction boiling in the range of 30–60°. All gas chromatographic analyses were carried out on a F & M Model 810 gas chromatograph which was equipped with a 6-ft 5% silicon gum rubber (SE-30) on Chromosorb P support. The term "dry tetrahydrofuran" refers to purification of the commercial material by distillation from lithium aluminum hydride under anhydrous conditions. "Dry benzene" was obtained by distillation of the solvent from calcium hydride. All microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

The crude, saturated alcohol, which showed no signal due to a vinyl hydrogen in its nmr spectrum, was then oxidized with a slight excess of Jones reagent[17] in acetone solution, and the ketonic product was isolated by ether extraction. The material (2.00 g) obtained in this fashion was an oil and difficult to purify. In practice, it was best to carry this crude ketone **13** directly to the pentacyclic olefin **14**, as complete purification at this stage resulted in an inordinate loss of material.

A small sample of the crude ketone **13** was purified by tlc on a silica gel plate of 1.5 mm × 20 cm × 20 cm in 50% ligroin–ether. The major band that represented the ketone **13** was eluted with ether, and while it was not possible to induce it to crystallize, the material was analytically pure. This sample showed only a single spot on analytical tlc and impurities of <2% on glpc on a 6-ft 10% SE-30 on Chromosorb P column at 300° (t_R = 5.5 min): ir (film) 1705 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.23 (s, 3, C-1α CH_3), 1.31 (s, 3, C-4aβ CH_3), 3.73 (s, 3, $ArOCH_3$), 3.77 (s, 3, $ArOCH_3$), and 6.70 and 7.10 (m, 7, ArH).

Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.55; H, 8.22. Found: C, 79.53; H, 8.34.

b. From Lithium–Ammonia Reduction–Methylation of the Ketone 11.—A solution of 1.02 g (2.82 mmol) of the α,β-unsaturated ketone **11** and 209 mg (2.82 mmol) of dry *t*-butyl alcohol in 30 ml of dry glyme was added dropwise to a solution of 42 mg (6.1 g-atoms) of lithium in 100 ml of dry ammonia containing 25 ml of dry glyme. The resulting reaction mixture was allowed to stir under a nitrogen atmosphere for 15 min, and then a solution of 6 ml of methyl iodide in 10 ml of dry glyme was added all at once, whereupon the dark blue color of the reaction mixture was quickly discharged. The ammonia was allowed to evaporate overnight, and the product was isolated by extraction with 1:1 ether–benzene. After the organic extract was washed with water and dried (Na_2SO_4), evaporation of the solvents at reduced pressure afforded 1.0 g of a light brown oil that on glpc analysis (6-ft 10% SE-30 on Chromosorb P column at 300°) indicated the presence of three components. The major component (70%) was shown to be the desired reduced–methylated ketone **13** by peak enhancement, and another component (15%) was identified as the starting unsaturated ketone **11**. The third component (*ca.* 10–12%) was considered to be the corresponding reduced unmethylated ketone. This crude product was best carried on to the cyclization reaction directly, but a small sample was purified by preparative tlc on a 1.5 mm × 20 cm × 20 cm silica gel plate in 50% ligroin–ether. In this fashion, from 250 mg of crude product there was obtained 130 mg of the pure ketone **13** as a glass that gave identical infrared and nmr spectra with those of the material from the foregoing catalytic hydrogenation. The behavior of the two samples on glpc and tlc was also identical.

3,10-Dimethoxy-6aα,12bβ-dimethyl-5,6,6a,6bα,7,8,12b,13-octahydropicene (14).—A solution of 1.00 g of the crude ketone **13** (from either of the above sources) and 105 mg of *p*-toluenesulfonic acid monohydrate in 30 ml of benzene was heated at reflux in a nitrogen atmosphere for 90 min. After cooling, the mixture was passed through 20 g of Merck alumina with the aid of added benzene and afforded 0.8 g of pale yellow, crystalline solid. Two crystallizations of this material from methylene chloride–hexane gave 525 mg (38–50% overall yield from ketone **11** depending on the sequence used) of colorless pentacyclic olefin **14**: mp 203–204°; uv λ_{max} (CH_2Cl_2) 250 mμ (ϵ 20,400); ir (Nujol) 1648 cm^{-1} (C=C); nmr δ 1.06 (s, 3, C-6aα CH_3), 1.19 (s, 3, C-12bβ CH_3), 3.77 (s, 6, $2ArOCH_3$), 6.0 (m, 1, C-14 **H**), and 6.68 and 7.20 (m, 6, ArH).

Anal. Calcd for $C_{26}H_{30}O_2$: C, 83.38; H, 8.07. Found: C, 83.20; H, 8.22.

B. 3,10-Dimethoxy-6aβ,12bβ-dimethyl-5,6,6a,6bα,7,8,12b,13-octahydropicene Series. 1β,4aβ-Dimethyl-1,2,3,4,4a,9-hexahydro-7-methoxy-2-oxo-1α-phenanthreneacetic Acid (16).—Dimethoxyethane (350 ml) was distilled from lithium aluminum hydride directly into a reaction flask which had been purged with nitrogen. Sodium hydride (6.9 g, 0.17 mol), as a 59.4% dispersion in mineral oil, and unsaturated ketone **15** (35.9 g, 0.14 mol) was added to the reaction flask. The solution was heated at reflux under nitrogen for 6 hr. The deep red reaction mixture was cooled to 0°, and 50.0 g (0.3 mol) of ethyl bromoacetate was added dropwise to the stirred solution at a rate which maintained the temperature at 5°. After the addition was complete, the reaction was stirred at 0° for 2 hr and allowed to warm slowly to room temperature overnight. Water (1.5 l.) was then added, and the aqueous layer was extracted with benzene. The organic layer was washed with water and saturated brine solution, and then dried (Na_2SO_4). Removal of the solvent and excess ethyl bromoacetate under reduced pressure afforded an orange oil. The crude keto ester was saponified directly without further purification with 23.5 g (0.42 mol) of potassium hydroxide in 325 ml of methanol and 30 ml of water. This solution was heated at reflux in a nitrogen atmosphere for 3 hr. The cooled reaction mixture was diluted with water, and the aqueous layer was extracted with 50% benzene–ligroin. The red, aqueous layer was poured onto ice and 10% hydrochloric acid, and the precipitated acid was extracted with chloroform. The organic layer was washed with water until neutral and dried (Na_2SO_4), and the solvent was removed at reduced pressure. There remained a yellow solid which on crystallization from ethanol afforded 29.7 g (79%) of the desired keto acid **16**, mp 176–180°, as a pale yellow solid. Several additional recrystallizations from ethanol afforded material of analytical purity: mp 179–180°; ir ($CHCl_3$) 3500 and 3575 (OH), 1775 (γ-lactone C=O), and 1705 cm^{-1} (keto acid C=O).

Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.52; H, 7.12.

It is apparent from the above infrared data that the unsaturated keto acid exists in two tautomeric forms in chloroform—free keto acid and hydroxylactone.

Methyl 1β,4aβ-Dimethyl-1,2,3,4,4a,9-hexahydro-7-methoxy-2-oxo-1α-phenanthreneacetate.—To a solution of 1.0 g (3.19 mmol) of unsaturated keto acid **16** in 20 ml of acetone under a nitrogen atmosphere was added 0.665 g (4.8 mmol) of anhydrous potassium carbonate and 3.0 ml of methyl iodide. While the reaction was heated at reflux for 5 hr, every 1.5 hr an additional 3.0 ml of methyl iodide was added. After the solvent was removed at reduced pressure, the residue was partitioned between ether and 10% aqueous potassium carbonate solution. The organic layer was separated, washed with water until neutral and saturated brine solution, and dried (Na_2SO_4). Removal of the solvent at reduced pressure afforded a pale orange oil which crystallized on cooling. Crystallization of this material from a hexane–ethanol mixture gave 961 mg (93%) of pale orange crystals, mp 83–87°. After a small sample was purified by preparative thin layer chromatography on silica gel (1:1 ether–hexane) and recrystallized twice from ethanol, the analytically pure ester was obtained as colorless prisms: mp 87–88°; ir ($CHCl_3$) 1735 (ester C=O), 1710 (C=O), and 1610 and 1500 cm^{-1} (ArH); nmr ($CDCl_3$) δ 1.32, 1.38 (s, 3 each, C-1β and C-4aβ CH_3), 3.42 (s, 3, CO_2CH_3), 3.79 (s, 3, $ArOCH_3$), 5.89 (t, 1, J = 4 Hz, C-10 **H**), 6.67 (s, 1, C-8 **H**), 6.76 (q, 1, J_o = 8 Hz, J_m = 3 Hz, C-6 **H**), and 7.27 (d, 1, C-5 **H**); nmr (C_6H_6) δ 1.24 and 1.12 (s, 3 each, C-1β and C-4aβ CH_3).

Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 73.20; H, 7.27.

Ethyl 1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aβ-octahydro-2-oxo-1α-phenanthreneacetate.—To a solution of 1.02 g (3.24 mmol) of the unsaturated keto acid **16** in 40 ml of ethanol was added 0.392 g (3.5 mmol) of potassium *t*-butoxide followed by 1.2 g (6.3 mmol) of triethyloxonium fluoroborate. The reaction was allowed to stir at room temperature for 2.5 hr and then diluted with 200 ml of 1:1 ether–benzene. After the organic layer was washed with saturated brine solution and dried (Na_2SO_4), the solvents were removed at reduced pressure. There remained 1.22 g of the unsaturated ethyl ester as a yellow oil, the infrared spectrum of which had bands at 1710 and 1735 cm^{-1}. This material was hydrogenated without further purification.

According to the procedure of Ghatak and coworkers,[25] a solution of the unsaturated ester in 5.0 ml of glacial acetic acid was added to a slurry of 78 mg of prereduced platinum oxide in 5.0 ml of glacial acetic acid. The reaction mixture was stirred under 1 atm of hydrogen, and after 1 hr the theoretical amount of hydrogen was consumed. The catalyst was removed by filtration and the acetic acid was evaporated at reduced pressure. As the presence of 30–40% of unreduced olefin in this crude product was indicated by glpc, the entire mixture was recycled under the above conditions, and hydrogenation was continued for 12 hr. After removal of the catalyst and solvent as before, the residue showed the absence of any starting olefin on glpc and the presence of the *cis* fused keto ester and the *trans* fused keto ester in a 3:1 ratio. Attempts to reproduce this experiment on a larger scale were only partially successful. If the hydrogenation was allowed to proceed until all of the olefin was consumed, a significant amount of the lactone **19** was produced from overreduction of the ketone carbonyl. From one of these reductions, however, a 44% yield

of the crystalline saturated ethyl ester was isolated. Recrystallization of a small quantity of this material from 20% ether–hexane afforded an analytical sample of this ester: mp 99–100°; ir ($CHCl_3$) 1735 (ester C=O) and 1715 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.21 (s, 6, C-1β and C-4aβ CH_3) and 3.78 (s, 3, $ArOCH_3$).

Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.37; H, 8.18.

Methyl 1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aβ-octahydro-2-oxo-1α-phenanthreneacetate (17).—A solution of 30.3 g (0.092 mol) of the methyl ester of the unsaturated keto acid **16** in 130 ml of acetic acid was hydrogenated in the presence of 7.0 g of 10% palladium on charcoal in a Paar shaker under an initial pressure of 53 psi of hydrogen. A reaction time of 24 hr was required for complete hydrogenation. The catalyst was filtered, and the reaction mixture was diluted with 1.0 l. of chloroform. The resulting solution was washed with water, 10% sodium bicarbonate, and then water until neutral. After the organic layer was washed with saturated brine solution and dried (Na_2SO_4), evaporation of the solvent at reduced pressure afforded 31.1 g of a colorless oil. The presence of the *cis* and *trans* fused saturated keto esters **17** and **28** in an 8:1 ratio was indicated by glc. The crude product was dissolved in a 1:1 ether–hexane solution and allowed to stand at 5° in the refrigerator for 2 weeks. During this period, a white solid slowly crystallized from the solution. When the solid was filtered and air dried, there was obtained 20.0 g (66%) of crystalline *cis* fused keto ester **17**, mp 67–70°. A small sample of this material was further purified for analysis by preparative tlc on silica gel in 1:1 ether–hexane. Recrystallization of the chromatographed material once from ether–hexane afforded colorless prisms: mp 69–71°; ir ($CHCl_3$) 1730 (ester C=O), 1705 (C=O), and 1610 and 1500 cm^{-1} (ArH); nmr ($CDCl_3$) δ 1.20 (s, 6,C-1β and C-4aβ CH_3), 2.28 (s, 2, C-1α CH_2CO), 3.50 (s, 3, CO_2CH_3), 3.77 (s, 3, $ArOCH_3$), 6.67 (s, 1, C-8 **H**), 6.72 (q, 1, J_o = 12 Hz, J_m = 3 Hz, C-6 **H**), and 7.29 (d, 1, J = 9 Hz, C-5 **H**); nmr (C_6H_6) δ 0.99 (s, 3, C-4aβ CH_3) and 1.26 (s, 3, C-1β CH_3).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.78; H, 7.90.

The nmr and ir spectra of the mother liquors of the first crystallization indicated the presence of the methyl pseudoester [ir ($CHCl_3$) 1775 cm^{-1} (γ-lactone C=O)] as well as the *cis* fused ester **17** and the *trans* fused ester **28**. Apparently, this compound was formed during the period when the crude hydrogenation mixture was crystallizing, for there was no spectral evidence for this material in the crude product.

The *trans* fused ester **28** was identified in these mother liquors by peak enhancement experiments on the gas chromatograph using the pure, authentic ester **28** prepared as described below.

1β,4aβ-Dimethyl-1-methoxy-1,2α,3,4a,9-hexahydro-2β-hydroxy-1α-phenanthreneacetic Acid.—To a solution of 20.1 g (0.064 mol) of unsaturated keto acid **16** in 300 ml of dry tetrahydrofuran was added portionwise 1.32 g (0.035 mol) of sodium borohydride over a 5-min period while the mixture was stirred at 25°. After the solution had stirred for 10 hr, the system was purged with nitrogen, and a solution of 60 ml of 10% aqueous potassium hydroxide in 60 ml of methanol was added. Stirring was continued for an additional 8 hr, and then the unsaturated hydroxy acid was liberated by pouring the reaction mixture into a slurry of ice and 1.0 *N* hydrochloric acid. This aqueous solution was made acidic to congo red paper with concentrated hydrochloric acid, and the crystalline product was collected by filtration and air dried for 24 hr. There was obtained 19.3 g (96%) of the desired unsaturated hydroxy acid, which was sufficiently pure for use in subsequent reactions. Recrystallization of a small sample of this material from ethanol yielded colorless crystals of analytical purity: mp 188–190°; ir (Nujol) 3660 (broad OH), 1700 (acid C=O), and 1610, 1575, and 1500 cm^{-1} (ArH).

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.28, H, 7.55.

Esterification of a small sample of this crude unsaturated hydroxy acid with ethereal diazomethane afforded the corresponding methyl ester as an oil. The analytical sample was prepared by evaporative distillation of this material at 120° bath temperature (0.05 mm): ir ($CHCl_3$) 3600 and 3450 (free and bonded OH) and 1725 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 1.27 (S, 6, C-1β and C-4aβ CH_3), 2.72 (d, 2, J = 5 Hz, C-1α CH_2CO), 3.32 (d, 2, J = 5 Hz, C-9 CH_2), 3.52 (s, 3, CO_2CH_3), 3.77 (s, 3, $ArOCH_3$), 5.97 (t, 1, J = 5 Hz, C-10 **H**), 6.65 (s, 1, C-8 **H**), 6.72 (q, 1, J_o = 8.0 Hz, J_m = 3.0 Hz, C-6 **H**), and 7.23 (d, 1, J = 8 Hz, C-5 **H**).

Anal. Calcd for $C_{22}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.65; H, 7.98.

Lactonization of Unsaturated Hydroxy Acid 16.—A solution of 201 mg (0.636 mmol) of hydroxy acid **16** and 25 mg of *p*-toluenesulfonic acid monohydrate in 25 ml of benzene was heated at reflux for 1 hr, cooled, and diluted to 200 ml with ether. The organic layer was separated and extracted with 10% aqueous potassium carbonate solution and water, dried (Na_2SO_4), and evaporated at reduced pressure. Trituration of the crystalline residue with ether afforded 170 mg (89%) of the corresponding lactone as colorless crystals, mp 134–136°. A small sample, recrystallized four times from acetone–hexane, gave constant-melting material: mp 137–139°; ir (Nujol) 1787 (γ-lactone C=O) and 1615, 1575, and 1500 cm^{-1} (ArH); nmr ($CDCl_3$) δ 1.33 (s, 3, C-4aβ CH_3), 1.40 (s, 3, C-1β CH_3), 2.50 (s, 2, C-1α CH_2CO), 3.34 (d, 2, J = 4.0 Hz, C-9 CH_2), 3.78 (s, 3, $ArOCH_3$), 3.86 (m, 1, $W_{1/2}$ = 15 Hz, axial C-2 CHO), and 4.02 (t, 1, J = 4 Hz, C-10 **H**).

Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.46; H, 7.40.

1β,4aβ-Dimethyl-2β-hydroxy-7-methoxy-1,2α,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetic Acid (18).—A solution of 3.16 g (10 mmol) of the unsaturated hydroxy acid **16** in 250 ml of glacial acetic acid was stirred at 25° under 1 atm of hydrogen in the presence of 0.5 g of 10% palladium on charcoal until *ca.* 260 ml of hydrogen was absorbed. The catalyst was filtered, and the filtrate was partitioned between chloroform and water. The organic layer was separated and extracted with water and then dried (Na_2SO_4). Evaporation of the solvent at reduced pressure afforded 3.12 g. The analytical sample, obtained after two crystallizations of a portion of this material from ethanol, melted at 186–188°: ir (Nujol) 3330 (broad OH) and 1695 cm^{-1} (acid C=O).

Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.70; H, 8.28.

Esterification of a small portion of the crude (mp 184–186°) hydroxy acid **18** in tetrahydrofuran with ethereal diazomethane afforded the corresponding methyl ester as a colorless oil, which produced a single peak on glpc analysis at 280°. The analytically pure ester was obtained after preparative tlc on silica gel in ether and evaporative distillation at 120° bath temperature (0.05 mm): ir ($CHCl_3$) 3500 (broad OH) and 1728 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 0.97 (s, 3, C-1β CH_3), 1.18 (s, 3, C-4aβ CH_3), 2.50 (d, 2, J = 11 Hz, C-1 α CH_2CO), 3.61 (s, 3, $ArOCH_3$), 3.74 (s, 3, $ArOCH_3$), 6.58 (s, 1, C-8 **H**), and 7.14 (d, 1, J_o = 8.5 Hz, C-5 **H**).

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26: H, 8.49. Found: C, 72.28; H. 8.64.

1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aβ-octahydro-2-oxo-1α-phenanthreneacetic Acid.—A solution of 7.30 g (0.023 mol) of the keto ester **17** in 145 ml of methanol containing 8 ml of water and 3.0 g (0.053 mol) of potassium hydroxide was stirred at room temperature under a nitrogen atmosphere for 14 hr. After dilution of the reaction mixture with water, the aqueous solution was washed with 50 ml of ether and made acid to congo red paper with concentrated hydrochloric acid. The precipitate was extracted with ether, and the ethereal solution was washed with water and saturated aqueous sodium chloride solution and dried (Na_2SO_4). Removal of the solvent at reduced pressure left 5.84 g (78%) of the crystalline keto acid, mp 211–213°, which was sufficiently pure for use in subsequent reactions. The analytical sample, prepared by crystallization of a sample of this material from ethanol, melted at 213–216°: ir (Nujol) 3340 (broad OH) and 1725 cm^{-1} (broad C=O of CO_2H and ketone).

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.00; H, 7.78.

Methyl 1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aβ-octahydro-1α-phenanthreneacetate (27).—To a solution of 4.37 g (0.014 mol) of the above keto acid and 2.05 ml of 85% hydrazine hydrate in 40 ml of diethylene glycol was added 3.14 g of potassium hydroxide, and the mixture was heated at 110° for 1 hr. The temperature was then raised to 207° and heating was continued for an additional 2 hr. The reaction mixture was cooled, diluted with 400 ml of water, and washed with 50 ml of ether. The aqueous layer was separated, made acid to congo red paper with concentrated hydrochloric acid, and extracted with ether. The ethereal extract was washed with water and saturated aqueous sodium chloride solution and dried (Na_2SO_4). After removal

of the solvent at reduced pressure, there remained 3.10 g (76%) of a solid acid that was not further purified, but dissolved in 40 ml of ether and treated with excess ethereal diazomethane. The yellow oil obtained after evaporation of the solvent and excess reagent was washed through 30 g of silica gel with 250 ml of 1:1 ether–benzene. Removal of these solvents and evaporative distillation of the residue at 110° bath temperature (0.05 mm) afforded 2.80 g (88%) of the methyl ester **27** as a clear, colorless oil. The analytical sample was obtained by evaporative redistillation of a portion of this material under the same conditions: ir ($CHCl_3$) 1725 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 1.10 (s, 3, C-1β CH_3), 1.14 (s, 3, C-4aβ CH_3), 2.74 (s, 2, C-1α CH_2CO), 3.50 (s, 3, CO_2CH_3), 3.73 (s, 3, $ArOCH_3$), 6.58 (s, 1, C-8 **H**), 6.65 (q, 1, J_o = 12 Hz, J_m = 3 Hz, C-6 **H**), and 7.17 (d, 1, J = 8 Hz, C-5 **H**).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.81; H, 8.87.

Methyl 1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aα-octahydro-2-oxo-1α-phenanthreneacetate (28).—A solution of 5.00 g (0.016 mol) of the hydroxy acid **18** in 500 ml of dry acetone was cooled to 0° and then treated with 7.9 ml (4.0 mequiv) of Jones reagent.[17] After the mixture was stirred at 0° for 0.5 hr, 1500 ml of water was added and the product was isolated by ether extraction. The ethereal extract was washed with water and saturated aqueous sodium chloride solution and then dried (Na_2SO_4). After removal of the solvent at reduced pressure, the crude keto acid that remained [4.80 g (97%), mp 174–177°] was sufficiently pure for use in subsequent reactions. The analytical sample, obtained after two crystallizations of a portion of this material from acetone–hexane, melted at 177–179°: ir ($CHCl_3$) 3460, 3340 (OH of pseudoacid), and 1750 cm^{-1} (γ-lactol C=O); nmr ($CDCl_3$) δ 1.20 (s, 3, C-4aβ CH_3), 1.22 (s, 3, C-1β CH_3), 2.60 (d, 2, J = 3 Hz, C-1α CH_2CO), and 3.77 (s, 3, $ArOCH_3$).

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.16; H, 7.63.

The methyl ester **28** was prepared from 200 mg (0.63 mmol) of this keto acid by treatment of an ethereal solution with excess ethereal diazomethane. After evaporation of the reaction mixture, evaporative distillation of the resulting oil at 110° bath temperature (0.05 mm) afforded 183 mg (88%) of a clear, colorless oil that needed no further purification for combustion analysis. Both tlc on silica gel in 10% ether–ligroin and glpc on a 6-ft 10% SE-52 on Chromosorb P column at 280° indicated the presence of a single component: ir ($CHCl_3$) 1725 (ester C=O) and 1700 cm^{-1} (ketone C=O); nmr ($CDCl_3$) δ 1.11 (s, 3, C-4aβ CH_3), 1.30 (s, 3, C-1β CH_2CO), 3.60 (s, 3, CO_2CH_3), 3.77 (s, 3, $ArOCH_3$), 6.62 (s, 1, C-8 **H**), 6.72 (q, 1, J_o = 12 Hz, J_m = 3 Hz, C-6 **H**), and 7.27 (d, 1, J = 9 Hz, C-5 **H**); nmr (C_6H_6) δ 1.06 (s, 3, C-4aβ CH_3) and 0.92 (s, 3, C-1β CH_3).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.59; H, 7.82.

Methyl 1β,4aβ-Dimethyl-2,2-ethylenedithio-7-methoxy-1,2,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetate.—A solution of 145 mg (0.44 mmol) of the keto ester **28** in 1.5 ml of ethanedithiol was treated with 0.25 ml of redistilled boron trifluoride ethereate, and the reaction mixture was stirred under a nitrogen atmosphere for 1 hr. The mixture was then diluted with 30 ml of ether, and the ethereal solution was washed with 1.0 N aqueous sodium hydroxide and water and dried ($MgSO_4$). After removal of the solvents, the solid residue was crystallized from ether–hexane. In this manner there was obtained 130 mg (73%) of the thioketal, mp 156–158°, in one crop; preparative tlc of the mother liquors from this crystallization on silica gel in 2:1 ether–hexane afforded an additional 12 mg of material of the same purity. The analytical sample, obtained after one further crystallization of a portion of this material from ether–hexane, melted at 157.5–159.0°: ir ($CHCl_3$) 1725 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 1.20 and 1.22 (s, 6, C-4aβ CH_3 and C-1β CH_3), 3.59 (s, 3, CO_2CH_3), and 3.75 (s, 3, $ArOCH_3$).

Anal. Calcd for $C_{22}H_{30}S_2O_3$: C, 64.98; H, 7.44; S, 15.77. Found: C, 64.86; H, 7.38; S, 15.74.

Methyl 1β,4aβ-Dimethyl-7-methoxy-1,2,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetate (29).—A solution of 75 mg (0.18 mmol) of the above thioketal in 7 ml of ethanol was treated with *ca.* 1 g of Raney nickel,[34] and the mixture was heated at reflux for 4 hr. The mixture was then cooled and filtered through Celite to remove the nickel, and the filter cake was washed with a 10-ml portion of hot ethanol. Removal of the solvents at reduced pressure afforded 52 mg (90%) of the ester **29**, mp 76–78°, as a white, crystalline solid. This material was purified for analysis by preparative tlc on silica gel in 2:1 ether–hexane and afforded 48 mg of analytically pure ester **29**: mp 82.5–83.0°; ir ($CHCl_3$) 1725 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 1.03 (s, 3 C-1β CH_3), 1.16 (s, 3, C-4aβ CH_3), 2.28 (s, 2, C-1α CH_2CO), 3.60 (s, 3, CO_2CH_3), 3.75 (s, 3, $ArOCH_3$), 6.58 (s, 1, C-8 **H**), 6.64 (q, 1, J_o = 12 Hz, J_m = 3 Hz, C-6 **H**), and 7.16 (d, 1, J = 9 Hz, C-5 **H**).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.73; H, 8.83.

The melting point of a mixture of a sample of the ester **29** prepared as above and one obtained from the keto acid **30**[27] by introduction of the C-2 methoxyl group *via* nitration[28] was 82–83°.

Lactone of 1β,4aβ-Dimethyl-2α-hydroxy-7-methoxy-1,2β,3,4,4a,9,10,10aβ-octahydro-1α-phenanthreneacetic Acid (19).—To a solution of 10.3 g (0.031 mol) of saturated keto ester **16** in 500 ml of methanol cooled to −5° was added 1.26 g of sodium borohydride in small portions so that the temperature was maintained between −5 and 0°. After the addition was completed, the solution was stirred at −5° for 2.5 hr. Water was added, and the aqueous solution was extracted with ether. The organic layer was washed with water and saturated brine solution and dried (Na_2SO_4). Removal of the solvent at reduced pressure afforded 9.1 g of a solid, which after crystallization from acetone–hexane afforded 7.35 g (79%) of the crystalline lactone **19**, mp 142–145°. The analytical sample, obtained after three additional recrystallizations from ethanol, melted at 144–147°: ir ($CHCl_3$) 1774 (γ-lactone C=O) and 1613 and 1500 cm^{-1} (ArH); nmr ($CDCl_3$) δ 1.20 (s, 6, C-1β and C-4aβ CH_3), 3.74 (s, 3, $ArOCH_3$), 4.16 (m, 1, $W_{1/2}$ = 14 Hz, axial C-2 CHO), 6.59 (s, 1, C-8 **H**), and 7.14 (d, 1, J = 8 Hz, C-5 **H**).

Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.93; H, 7.98.

Hemiacetal of 1β,4aβ-Dimethyl-2α-hydroxy-7-methoxy-1,2β-3,4,4a,9,10,10aβ-octahydro-1α-phenanthreneacetaldehyde (21).—To an ice-cooled solution of 0.132 mol of disiamylborane[33] in 285 ml of dry tetrahydrofuran under nitrogen was added dropwise 10.1 g (0.034 mol) of lactone **19** in 75 ml of dry tetrahydrofuran over a 15-min period. The reaction was stirred at 0° for 2 hr and at room temperature for 15 hr, and then cooled to 0°. The excess borane was decomposed with 25 ml of water, and then, after a solution of 60 ml of 30% hydrogen peroxide adjusted to pH 8 was added, the reaction was allowed to stir at room temperature for 1 hr. Concentration of the reaction mixture at reduced pressure left a semicrystalline solid which was dissolved in 500 ml of benzene and washed with 5% aqueous potassium hydroxide solution and water and dried (Na_2SO_4). After removal of the solvent at reduced pressure, the white crystalline residue was dried at 0.05 mm and room temperature for 8 hr. Gas chromatographic analysis of the crude product indicated that the reduction had proceeded to give a single compound in greater than 90% yield, and this material was suitable for subsequent reactions with further purification. Recrystallization of the crude product from acetone–hexane yielded 8.0 g (77%) of colorless crystals, mp 175–180°. An analytically pure sample of this hemiacetal **21**, mp 178–181°, was obtained after two further crystallizations of a portion of this material from the same solvent mixture: ir ($CHCl_3$) 3590 and 3360 cm^{-1} (OH).

Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.59; H, 8.57.

1β,4aβ-Dimethyl-3,4,4a,9,10,10aβ-hexahydro-7-methoxy-1α-(2′-*m*-methoxyphenylethyl)-2(1H)-phenanthrone (23). Grignard Addition.—To a solution of 63.5 mmol of *m*-methoxyphenylmagnesium bromide in 70 ml of 1:1 ether–tetrahydrofuran was added 6.4 g (21.2 mmol) of hemiacetal **21** in 50 ml of dry tetrahydrofuran slowly over a 0.5-hr period. The deep red solution was heated at reflux for 5 hr, cooled, and poured onto ice and solid ammonium chloride. The aqueous solution was extracted with 1:1 ether–benzene, and the combined organic layers were washed with 5 N hydrochloric acid solution, and water until neutral, dried (Na_2SO_4), and concentrated at reduced pressure. On chromatography of the residue on 300 g of alumina (Merck), the desired diol [7.8 g (88%)] was eluted with 1.5 l. of 10% methanol–ether as an oil. This material was not further purified but used directly in the succeeding reactions.

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

Hydrogenation.—A solution of 7.8 g of the above diol in 125 ml of methanol and 0.5 ml of 60% perchloric acid was stirred under 1 atm of hydrogen in the presence of 0.90 g of 10% palladium on charcoal. After 7 hr, the theoretical amount of hydrogen was absorbed. The catalyst was then removed by filtration, 1.0 g of anhydrous potassium carbonate was added to the filtrate, and the reaction mixture was concentrated at reduced pressure. The residue was taken up in 200 ml of ether, washed with water, and dried (Na_2SO_4). Removal of the solvent at reduced pressure yielded a colorless oil, 7.5 g, which was oxidized without further purification.

Oxidation.—To a stirred, ice-cooled solution of 7.5 g of alcohol in 125 ml of acetone was added dropwise 7 ml of Jones reagent[17] over a 15-min period. The reaction was stirred at 0° for 0.5 hr and then poured into ice and water. The aqueous solution was extracted with 1:1 benzene–ether, and the combined organic layers were washed with water and dried (Na_2SO_4). After removal of the solvents at reduced pressure, the residue was chromatographed on 200 g of alumina (Merck). Elution of the column with 1.2 l. of 75% benzene–ligroin afforded 6.22 g (75% based on the hemiacetal **21**) of the ketone **23**, mp 76–77°, as a colorless, crystalline solid. Crystallization of this material from ethanol did not change the melting point: ir (Nujol) 1705 (C=O), 1610, 1580, 1500 (aromatic bands), and 1035 and 1048 cm^{-1} (COC); nmr ($CDCl_3$) δ 1.22 (s, 6, C-1β and C-4aβ CH_3) and 3.71 and 3.75 (s, 3 each, $ArOCH_3$).

Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22. Found: C, 79.43; H, 8.15.

3,10-Dimethoxy-6aβ,12bβ-dimethyl-5,6,6a,6β,7,8,12b,13-octahydropicene (25).—A solution of 2.39 g (6.1 mmol) of the ketone **23** and 116 mg of *p*-toluenesulfonic acid monohydrate in 400 ml of benzene was heated at reflux under a Dean–Stark water separator in a nitrogen atmosphere for 12 hr. The course of the reaction was followed by thin layer chromatography, and the reaction was stopped as soon as all of the starting ketone had been consumed. If the reaction was allowed to proceed beyond this point, a second hydrocarbon was gradually produced at the expense of the desired product. The benzene solution was cooled, washed with 5% aqueous potassium hydroxide solution and water, and then dried (Na_2SO_4). Evaporation of the solvent at reduced pressure and then recrystallization of the solid residue from ether–hexane afforded 1.96 g (83%) of the picene **25**, mp 113–115°. Two additional crystallizations from the same solvent yielded analytical material with no change in melting point: uv λ_{max} (CH_2Cl_2) 250 mμ (ϵ 18,900); ir ($CHCl_3$) 1610, 1500 (aromatic bands), and 1260 and 1035 cm^{-1} (COC); nmr ($CDCl_3$) δ 1.15 (s, 3, C-6aβ CH_3), 1.44 (s, 3, C-12bβ CH_3), 3.73 (s, 6, $2ArOCH_3$), 5.87 (t, 1, J = 4.0 Hz, C-14 **H**), 6.57 (s, 2, C-4 and C-9 **H**), 6.67 (q, 2, C-2 and C-11 **H**), 7.22 (d, 1, J = 8 Hz, C-12 **H**), and 7.35 (d, 1, J = 8 Hz, C-1 **H**).

Anal. Calcd for $C_{26}H_{30}O_2$: C, 83.38; H, 8.07. Found: C, 83.40; H, 8.22.

When the ketone **23** was cyclized with either anhydrous hydrogen fluoride or polyphosphoric acid, an undefinable mixture of several hydrocarbons was formed from which none of the picene derivative **25** could be isolated.

Lactone of 1β,4aβ-Dimethyl-2β-hydroxy-7-methoxy-1,2α,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetic Acid (20).—A solution of 204 mg (0.64 mmol) of hydroxy acid **19** and 20 mg of *p*-toluenesulfonic acid monohydrate in 20 ml of benzene was heated at reflux for 0.75 hr. The product was isolated as previously described for the lactonization of the unsaturated hydroxy acid **16**. There was obtained 189 mg (98%) of colorless crystalline solid, which glpc indicated to consist of a single component to the extent of at least 98%. Crystallization of this material from acetone–hexane afforded 120 mg (62%) of colorless prisms, mp 122–125°. A sample recrystallized twice more from the same solvent system afforded analytically pure lactone **20**: mp 124.5–126°; ir ($CHCl_3$) 1785 cm^{-1} (γ-lactone C=O); nmr ($CDCl_3$) δ 1.07 (s, 3, C-1β CH_3), 1.22 (s, 3, C-4aβ CH_3), 3.75 (s, 3, $ArOCH_3$), 3.87 (m, 1, $W_{1/2}$ = 17 Hz, axial C-2 CHO), 6.61 (s, 1, C-8 **H**), and 7.14 (d, 1, J = 8.0 Hz, C-5 **H**).

Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.07; H, 8.03.

Reduction of 304 mg (1.01 mmol) of the lactone **20** with 4.0 mmol of disiamylborane[31] according to the same procedure as that previously described for the reduction of the lactone **19** afforded a crude, colorless. crystalline solid. Crystallization of this material from hexane–acetone gave 104 mg (36%) of the corresponding diol, mp 132.5–134°. No evidence was found for the presence of the expected hemiacetal, even when the reduction was carried out at lower temperature or with less disiamylborane. The analytical sample of the diol was obtained by one further crystallization of a sample of this material from hexane–acetone and melted at 131–132°: ir ($CHCl_3$) 3350 cm^{-1} (broad OH); nmr ($CDCl_3$) δ 0.93 (s, 3, C-1β CH_3), 1.20 (s, 3, C-4aβ CH_3), 2.90 (t, 2, C-9 CH_2), 3.64 (m, 5, C-2 **H**, CH_2OH and 2O**H**), and 3.76 (s, 3, $ArOCH_3$); nmr ($CDCl_3$ + pyridine) 3.64 (m, 3, C-2 **H** and CH_2OH) and 4.50 (m, 2, O**H**).

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.11; H, 9.33.

N-Methyl 1β,4aβ-Dimethyl-2β-hydroxy-7-methoxy-1,2α,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetamide.—To a 50-ml three-necked flask equipped with a dropping funnel and Dry Ice condenser was added 10 ml of dry tetrahydrofuran and 41 mg (1.08 mmol) of finely pulverized lithium aluminum hydride. Anhydrous monomethylamine was slowly distilled into the reaction vessel with stirring until all of the lithium aluminum hydride had reacted. The reaction mixture was stirred for 2 hr, the Dry Ice condenser was removed, and the excess methylamine was allowed to distil from the reaction flask at room temperature. A solution of 164 mg (0.546 mmol) of lactone **20** in 5 ml of dry tetrahydrofuran was added dropwise over a 5-min period. After the reaction mixture had stirred at room temperature for 12 hr, it was diluted with 100 ml of water, and the aqueous solution was extracted with 200 ml of 1:1 ether–benzene. The organic layer was separated and washed with 1 *N* hydrochloric acid and water and dried (Na_2SO_4). After the solvents were evaporated at reduced pressure, there was obtained 170 mg (94%) of the crystalline amide. This material was sufficiently pure for subsequent reactions. An infrared spectrum of this amide showed the presence of a carbonyl band at 1640 cm^{-1} and the absence of any band due to γ-lactone carbonyl at 1785 cm^{-1}. Crystallization of the crude product from ethanol gave 135 mg (75%) of the amide as white needles, mp 212–215°. An analytical sample of the hydroxyamide, prepared by two additional crystallizations from ethanol, had a melting range of 212–214°: ir (Nujol) 3320–3300 (broad NH and OH) and 1640 and 1630 cm^{-1} (amide C=O).

Anal. Calcd for $C_{20}H_{29}NO_3$: C, 72.47; H, 8.82; N, 4.23. Found: C, 72.63; H, 8.80; N, 4.19.

Lactone of 1β,4aβ-Dimethyl-2α-hydroxy-7-methoxy-1,2β,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetic Acid (22).—To 350 ml of dry pyridine was added 16.0 g (0.048 mol) of the above hydroxyamide. The stirred solution was cooled to 0°, and 22.5 g (0.196 mol) of methanesulfonyl chloride was added dropwise over a 15-min period while the temperature was maintained between 0 and 5°. After the addition was completed, the orange-colored reaction mixture was stirred for 21 hr at room temperature. The mixture was then treated with 25 ml of water and the solution was heated to 85° and then allowed to cool to room temperature over a 1-hr period. The pyridine solution was dissolved in 50% ether–benzene, and the mixture was extracted with water, followed by 10% hydrochloric acid, until the aqueous washes were acidic. The organic layer was then washed with 10% aqueous potassium hydroxide and water until neutral, and dried (Na_2SO_4). After removal of the solvents at reduced pressure, the light orange residue crystallized on cooling. Trituration with cold ether afforded 10.75 g (74%) of the lactone **22**, mp 116.5–118°, as a white crystalline solid. Chromatography of the mother liquors on 100 g of neutral alumina (Woelm Activity III) afforded an additional 2.04 g (14%) of slightly less pure lactone **22**, mp 114–115°, on elution with 1 l. of 50% benzene–ligroin. A small sample recrystallized twice from acetone–hexane gave orthorhombic crystals: mp 118–120°; ir ($CHCl_3$) 1760 cm^{-1} (γ-lactone C=O); nmr ($CDCl_3$) δ 1.02 and 1.03 (s, 3 each, C-4aβ and C-1β CH_3), 3.77 (s, 3, $ArOCH_3$), 4.33 (m, 1, $W_{1/2}$ = 3.0 Hz, equatorial C-2 CHO), 6.62 (s, 1, C-8 **H**), and 7.20 (d, 1, J = 8.5 Hz, C-5 **H**).

Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.02; H, 7.95.

Hemiacetal of 1β,4aβ-Dimethyl-2α-hydroxy-7-methoxy-1,2β,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetaldehyde.—A solution of 8.8 g (29.4 mmol) of the lactone **32** was added dropwise under nitrogen to a stirred, ice-cooled solution of 118 mmol of disiamylborane in 224 ml of dry tetrahydrofuran. After the addition was completed, the solution was stirred for 15 hr at room temperature. The product was isolated as in the previously described procedure for the reduction of the lactone **19** above. There was obtained 8.9 g (100%) of a white crystalline solid

which was shown to consist of a single component by glpc. The crude hemiacetal was sufficiently pure for subsequent reactions. A small sample, recrystallized twice from acetone–hexane, gave hemiacetal of analytical purity: mp 174.5–178°; ir ($CHCl_3$) 3570–3360 cm^{-1} (broad OH), no absorption due to carbonyl in the 1700-cm^{-1} region.

Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.41; H, 8.60.

1β,4aβ-Dimethyl-3,4,4a,9,10,10aα-hexahydro-7-methoxy-1α-(2′-*m*-methoxyphenylethyl)-2(1H)-phenanthrone (24).—The general procedures followed in the subsequent experiments were similar to those which were used in the synthesis of the isomeric C-10aβ ketone **23**.

Grignard Addition.—To a solution of 0.04 mol of *m*-methoxyphenylmagnesium bromide in 60.0 ml of 2:1 ether–tetrahydrofuran was added 3.8 g (12.6 mmol) of the above hemiacetal in 50 ml of dry tetrahydrofuran. The red solution was heated at reflux for 6 hr, cooled, and then poured onto ice and solid ammonium chloride. The crude diol was isolated and purified by chromatography as previously described. This diol was carried onto the next experiment without characterization.

Hydrogenolysis.—A solution of the diol obtained in the previous experiment in 250 ml of methanol and 1.0 ml of 60% perchloric acid was stirred under 1 atm of hydrogen in the presence of 0.50 g of 10% palladium on charcoal. After the theoretical quantity of hydrogen was absorbed, the catalyst was filtered and the product was isolated as previously described. The resulting alcohol was used in the following oxidation without purification.

Oxidation.—The unpurified alcohol from the preceding experiment was dissolved in 125 ml of acetone and treated with 4.0 ml of Jones reagent[17] for 0.5 hr at 0°. The reaction was worked up in the previously described manner, and the resulting product was chromatographed on 150 g of alumina (Merck). Elution with 900 ml of 50% benzene–ligroin afforded material which on trituration in cold ether gave 4.33 g (88% from lactone **22**) of the colorless, crystalline ketone **23**, mp 108–111°. Recrystallization of a small sample from methanol for analysis afforded material which melted at 109.5–111°: ir ($CHCl_3$) 1700 (C=O), 1610 and 1500 (aromatic bands), and 1035 cm^{-1} ($ArOCH_3$); nmr ($CDCl_3$) δ 1.16 (s, 3, C-1β CH_3), 1.25 (s, 3, C-4aβ CH_3), and 3.80 (s, 6, 2 $ArOCH_3$).

Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22. Found: C, 79.43; H, 8.20.

3,10-Dimethoxy-6aβ,12bβ-dimethyl-5,6,6a,6bα,7,8,12b,13-octahydropicene (26).—A solution of 2.163 g (5.52 mmol) of ketone **24** and 0.80 g of *p*-toluenesulfonic acid monohydrate in 500 ml of toluene was heated at reflux under a Dean–Stark water separator in a nitrogen atmosphere. The progress of the reaction was followed by glpc. After 31 hr, all of the ketone had been transformed to a single product which was stable to further acid treatment. The reaction mixture was cooled, washed with 10% aqueous potassium hydroxide solution, water until neutral, and saturated brine solution, and dried (Na_2SO_4). Removal of the solvent at reduced pressure yielded a crystalline residue which on trituration with methanol afforded 1.90 g (97%) of the pentacyclic olefin **26**, mp 185–188°. Recrystallization of a small sample from ethanol–benzene for analysis gave material melting at 188.5–191°: ir (Nujol) 1650 (weak C=C), 1610, 1574, and 1500 (aromatic bands), and 1030 and 1040 cm^{-1} ($ArOCH_3$); nmr ($CDCl_3$) δ 1.00 (s, 3, C-6aβ CH_3), 1.32 (s, 3, C-12bβ CH_3), 3.78 (s, 6, 2 $ArOCHH_3$), 5.91 (m, 1, C-14 **H**), 6.67 (m, 2, C-4 and C-9 **H**), 7.27 (d, 1, J = 9.0 Hz, C-12 **H**), and 7.43 (d, 1, J = 9.0 Hz, C-1 **H**).

Anal. Calcd for $C_{26}H_{30}O_2$: C, 83.38; H, 8.07. Found: C, 83.24; H, 8.05.

Registry No.—**11**, 21343-29-3; **12**, 21347-62-6; **13**, 21347-63-7; **14**, 21347-64-8; **16**, 21371-73-3; **17**, 21373-64-8; **18**, 21347-65-9; **19**, 21347-66-0; **20**, 21347-67-1; **21**, 21347-68-2; **22**, 21371-74-4; **23**, 21347-69-3; **24**, 21347-70-6; **25**, 21343-13-5; **26**, 21343-14-6; **27**, 21343-15-7; **28**, 21343-16-8; **29**, 21343-17-9; methyl ester of **16**, 21343-18-0; ethyl ester of **17**, 21343-19-1; 1α,4aβ-dimethyl-7-methoxy-1,2α,3,4,4a,9-hexahydro-2β-hydroxy-1-α-phenanthreneacetic acid, 21343-20-4; methyl ester of **21**, 21343-21-5; lactone of **16**, 21343-22-6; methyl ester of **18**, 21343-23-7; 1β-4aβ-dimethyl-7-methoxy-1,2,3,-4,4a,9,10,10aβ-octahydro-2-oxo-1α-phenanthreneacetic acid, 21343-24-8; free acid of **28**, 21343-25-9; methyl 1β,4aβ-dimethyl-2,2-ethylenedithio-7-methoxy-1,2,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetate, 21343-26-0; corresponding diol of **20**, 21343-27-1; N-methyl 1β,4aβ-dimethyl-2β-hydroxy-7-methoxy-1,2α,3,4,4a,9,10,10aα-octahydro-1α-phenanthreneacetamide, 21343-28-2.

Experiments Directed toward the Total Synthesis of Terpenes. XVI. The Structure and Stereochemistry of Two Decahydropicene Derivatives

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The conversion of the *cis,syn*-octahydropicene **5** and the *trans,anti*-octahydropicenes **12a** and **12b** to the *cis,-syn,cis*-decahydropicene **7** and *trans,anti,trans*-decahydropicenes **16a** and **16b** is described. In the former case, the structure and stereochemistry of the ketone **7** was established by single-crystal X-ray structural analysis of the derived bromo ketone **8**. While the stereochemistry of the latter series of ketones **16a** and **16b** is that required for the synthesis of the triterpene alnusenone **1**, the yield in the transformation was too low to make either material a viable synthetic intermediate.

In the preceding paper in this series,[3] a plan was presented for the construction of the pentacyclic triterpene alnusenone (**1**) which entailed the construction of the trimethyl decahydropicene derivative (**2**). One approach to the synthesis of this key intermediate **2** envisaged the introduction of the angular methyl group at C-14a through methylation of the ketone **3** derived by oxidation of the pentacyclic olefin **4**. The preparation of three stereoisomers of this latter material **4** was initially accomplished,[3] and the results of the further transformations of two of these stereoisomeric olefins is the subject of the present report.

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