tinuously with ether for 39 hr. The ethereal extract was dried, and the solvent was evaporated to yield 5.84 g. (66.5%) of crude 2-isopropyl-5-oxohexanoic acid, $[\alpha]^{26}D$ +5.45° (*c* 2.58, $CHCl_3$), semicarbazone m.p. 152–155°. The enantiomer is reported[21] to have $[\alpha]D$ −5.0°.

The methyl ester was prepared by allowing the crude acid to react with 50 ml. of methanol and 1 ml. of concentrated sulfuric acid on a steam bath for 6 hr. The reaction mixture was processed in the usual manner and the pure ester was obtained by v.p.c. using a 5 ft. × 0.25 in. Carbowax column at 210°. The ester had $n^{21}D$ 1.4335, $[\alpha]^{25}D$ +10.1° (*c* 2.67 $CHCl_3$), and the semicarbazone melted at 124.0–125.5°.

Anal. Calcd. for $C_{11}H_{21}N_3O_3$ (243.30): C, 54.30; H, 8.70; N, 17.27. Found: C, 54.26; H, 8.54; N, 17.01.

The enantiomer is reported[21] to have $[\alpha]D$ −9° and the semicarbazone m.p. 128.0–129.5°.

Oxidative Rearrangements of Pentacyclic Triterpenes. A Method for the Synthesis of Certain Naturally Occurring Triterpenes from α- and β-Amyrin[1]

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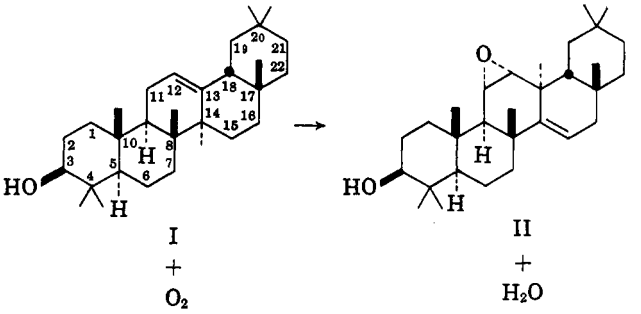
Several new rearrangement reactions of pentacyclic triterpenes are described, a number of which involve rearrangement to a carbon skeleton that is thermodynamically less stable than the initial skeleton. These and related rearrangements provide the basis for a general approach to the partial synthesis of a number of naturally occurring triterpenes, *e.g.*, friedelin. In essence the method involves the coupling of a rearrangement step with an exothermic reaction such as electrophilic addition to a carbon–carbon double bond. Specific illustrations which are presented include the syntheses of 11α,12α-oxidotaraxerol (II), taraxerol, and multiflorenol (XXVI) from β-amyrin.

During a program of studies in the field of pentacyclic triterpenes at the University of Illinois some 10 years ago,[2] it was discovered that ethanolic solutions of a mixture of α- and β-amyrins (obtained from *Manila elemi* resin) upon prolonged exposure to air and sunlight at room temperature deposit a colorless crystalline solid of composition $C_{30}H_{48}O_2$. It was ascertained from subsequent studies that this new substance was *not* present in the original mixture, that it is an oxidation product derived from β-amyrin, and that its formation involves some novel and interesting chemistry. At the outset it was apparent that this product was the result either of carbon rearrangement or functionalization at a saturated carbon, or both, and, since these topics were under active study in our laboratory,[2b,3,4] the incidental discovery assumed a surprising relevance to the pre-existing research program. The new photooxidation product obtained from β-amyrin (I) was eventually shown to be a taraxerene derivative (II) by the chemical studies which are detailed in this paper, and a new kind of oxidative rearrangement was uncovered. The taraxarene skeleton is unstable relative to the



olean-12-ene (β-amyrin) system as shown by the rearrangement of taraxerol (II minus the epoxide function) to β-amyrin (I) under acid catalysis.[5,6] In the conversion I → II, therefore, there is an intrinsic driving force which overcomes the energetically unfavorable change in the arrangement of carbon and hydrogen and the skeletal rearrangement can be considered as "powered" by the oxidation. Clearly, rearrangements can be differentiated generally with reference to whether the carbon-skeletal change is energetically favorable or unfavorable. The former can be effected merely by the application of a suitable catalytic agent (*e.g.*, an acid), but the latter require coupling to an exergonic (free-energy releasing) reaction which provides the thermodynamic driving force. This distinction serves a useful purpose in the analysis of certain synthetic and biosynthetic problems; it is made here to underscore the broader aspects of the rearrangement I → II, which are also considered in subsequent sections of this paper. The generalization of the idea of oxidatively driven rearrangements leading to less stable carbon skeletons provides a clue to the interesting problem of reversing exergonic rearrangements such as the friedelanol → olean-13,18-ene multigroup rearrangement.[2b] A part of this paper deals with this particular synthetic problem

(1) (a) Submitted in honor of Professor Louis F. Fieser. (b) Presented in part at the Gordon Conference on Natural Products, New Hampton, N. H., Aug. 1960.

(2) Several of the main objectives of these investigations have already been reached and described in publications dealing with structure, synthesis, and stereochemistry in the pentacyclic triterpene series. These include (a) the stereochemistry of the α-amyrin group, E. J. Corey and J. J. Ursprung, *Chem. Ind.* (London), 1387 (1954), and *J. Am. Chem. Soc.*, **78**, 183 (1956); (b) the structure and stereochemistry of friedelin and the multigroup rearrangement from the friedelan to the olean series, E. J. Corey and J. J. Ursprung, *ibid.*, **77**, 3667, 3668 (1955); **78**, 5041 (1956); (c) the total synthesis of pentacyclosqualene, E. J. Corey and R. R. Sauers, *ibid.*, **79**, 3925 (1957); **81**, 1739 (1959); (d) the partial synthesis of α-amyrin from a β-amyrin derivative, E. J. Corey and E. W. Cantrall, *ibid.*, **80**, 499 (1958); **81**, 1745 (1959); and (e) the total synthesis of a β-amyrin derivative, oleana-11,13(18)-diene, E. J. Corey, H.-J. Hess, and S. Proskow, *ibid.*, **81**, 5258 (1959); **85**, 3979 (1963). The last reference in each group is a detailed paper which includes a bibliography of important papers on related topics. (f) For a recent review on pentacyclic triterpenes, see J. Simonsen and W. C. J. Ross, "The Terpenes," Vol. V, Cambridge University Press, London, 1957.

(3) E. J. Corey and W. R. Hertler, *ibid.*, **80**, 2903 (1958); **81**, 5209 (1959).

(4) E. J. Corey and R. W. White, *ibid.*, **80**, 6686 (1959).

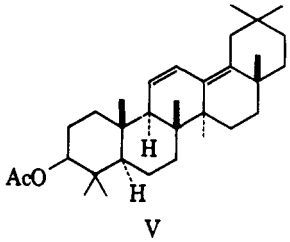
(5) J. M. Beaton, F. S. Spring, R. Stevenson, and J. L. Stewart, *J. Chem. Soc.*, 2131 (1955).

(6) C. J. W. Brooks, *ibid.*, 1675 (1955).

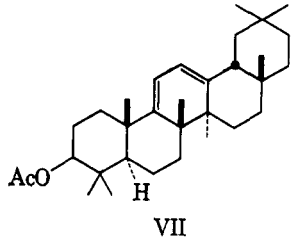
and describes the first partial synthesis of the oleanane–friedelane intermediate, multiflorenol.

Evidence for the Structure of the Photooxidation Product, $C_{30}H_{48}O_2$, from β-Amyrin.—The earliest procedure for the preparation of this photoproduct was as follows. The crude mixture of α- and β-amyrins obtained from *Manila elemi* resin[7] was dissolved in sufficient 95% ethanol to maintain a clear solution at 15°, treated with aqueous hydrochloric acid to produce a reading of pH 2–3 with wetted pH test paper, and exposed to direct summer sunlight (Urbana, Ill.) through Pyrex. After 10–12 weeks a heavy colorless, crystalline precipitate resulted from which the pure photoproduct could be isolated. Longer periods were required during other seasons. The yield of this material based on the β-amyrin initially present was 10%. Approximately 15% yield of this compound, which will be called β-U in this discussion, could be obtained by the irradiation of acidified ethanolic solutions of pure β-amyrin for 2–3 weeks with an ultraviolet lamp (Hanovia Model 7420, 325 w., target distance *ca.* 40 cm.) through Pyrex. The purified β-U, m.p. 285–288° (with some decomposition), exhibited hydroxyl absorption in the infrared but no bands due to carbonyl, and analysis indicated the presence of two oxygens as $C_{30}H_{48}O_2$. Reaction of β-U with acetic anhydride–pyridine afforded a monoacetate showing acetoxy absorption but no hydroxyl absorption in the infrared and no other carbonyl. Oxidation of β-U with chromic acid afforded a monoketone, $C_{30}H_{46}O_2$ (III), which was converted by Wolff–Kishner reduction (W–K) to a nonhydroxylic, nonketonic compound, $C_{30}H_{48}O$ (IV). It is clear, therefore, that β-U is a hydroxy ether. The presence of a carbon–carbon double bond in β-U and the above derivatives is indicated by the fact that all these substances produce a yellow coloration with tetranitromethane. In addition the n.m.r. spectrum of IV exhibits a signal due to a single olefinic proton as a quartet centered at δ 5.53 (δ = p.p.m. shift downfield from internal tetramethylsilane).

Reaction of β-U acetate with anhydrous hydrogen iodide in acetic acid afforded an acetoxydiene, m.p. 227–228°, with ultraviolet absorption at 242, 251, and 261 mμ which proved to be identical with an authentic sample of the known 3β-acetoxyoleana-11,12;13,18-diene (V); thus the secondary hydroxyl of β-U is at C-3 as in β-amyrin.



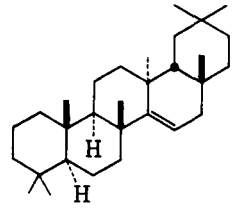
V



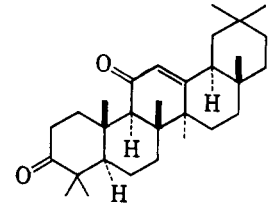
VII

Treatment of β-U acetate with anhydrous hydrogen bromide in acetic acid, on the other hand, gave an acetoxybromodiene VI, m.p. 221–222°, with ultraviolet absorption at 283 mμ (ε 8600). The bromine substituent was unaffected by heating at reflux with silver acetate in acetic acid, but it was replaced by hydrogen by the action of lithium aluminum hydride in boiling dioxane to yield a product which was identified as 3β-acetoxyoleana-9,11;12,13-diene (VII) by comparison with an authentic specimen. The n.m.r. spectrum of the acetoxybromodiene VI revealed the presence of only one olefinic proton as a sharp singlet at δ 5.8, and, consequently, the bromine substituent must be attached to the diene chromophore at C-11 or C-12; the latter position seems somewhat more likely because of the sharpness of the olefinic peak, but a definite assignment has not yet been made. From these data it is possible to conclude that the ether oxygen function in β-U is attached to C-11 or C-12 (or both) and that the D/E ring fusion of β-U is *cis* as in β-amyrin; *i.e.*, it is in the thermodynamically less stable arrangement.

The ether function in β-U is unaffected by treatment with lithium aluminum hydride in ether at reflux for 100 hr., a fact which initially seemed to argue against the assignment of a 1,2-epoxide function. However, it was discovered that the ether function was susceptible to cleavage by prolonged heating (5 days) with lithium aluminum hydride at reflux in dioxane or by treatment with a large excess of lithium in hot anhydrous ethylenediamine. Both reactions produced a diol (VIII) which was converted by acetylation to a diacetate and by oxidation with chromic acid to a diketone (IX). Wolff–Kishner reduction of the diketone led to a hydrocarbon, m.p. 238–241°, which was identical with an authentic specimen of taraxerene (skimmiene) X.[8,9] This transformation established that β-U possesses the taraxerol carbon skeleton of X and not the oleanene skeleton of β-amyrin. That the diol VIII is 11-hydroxytaraxerol was demonstrated by acid-catalyzed rearrangement of the corresponding dione IX to 18-*iso*-olean-12-ene-3,11-dione (XI), another example of the taraxerene → oleanene rearrangement.[5,6]



X



XI

In agreement with the conclusion that β-U is a taraxer-14,15-ene are the findings (1) that β-U acetate is converted by excess peracetic acid to a mixture of saturated, epimeric oxides, $C_{32}H_{50}O_4$, and (2) that reaction of β-U acetate with excess osmium tetroxide produces an acetoxy ether diol, $C_{32}H_{52}O_5$ (saturated), which is transformed into an acetoxy ether ketoaldehyde with lead tetraacetate. Clearly there is only one carbon–carbon double bond in β-U and it is trisubstituted.

The nature of the ether oxygen in β-U was established as an 11,12-oxido bridge by the following experiments. Treatment of β-U acetate with lithium aluminum deuteride in dioxane at reflux produced the diol VIII labeled with 1.0 deuterium atom/molecule. Oxidation of the monodeuterated diol (VIII-d_1) produced monodeuterated taraxer-3,11-dione (IX-d_1) which after treatment with sodium methoxide in methanol yielded taraxer-3,11-dione (IX-d_0) which was free of deuterium (above the natural abundance level). This

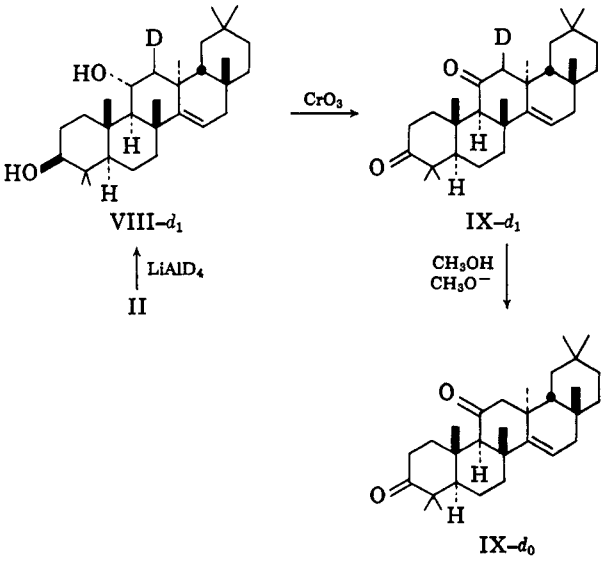
(7) Procedure of K. A. Vesterberg and S. Westerlind, *Ann.*, **428**, 247 (1922).

(8) Kindly provided by Dr. S. Tobinaga.

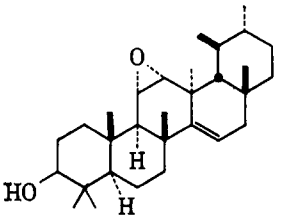
(9) See ref. 5 and 6.

result indicates that the label in the deuterated taraxer-3,11-dione must have been α to the 11-keto function, *i.e.*, either at C-9 or C-12, and hence that β-U is either a 9,11- or an 11,12-epoxide. The 9,11-epoxide formulation was excluded by n.m.r. measurements on the 3-desoxy derivative of β-U (IV) which showed *two* protons in the region to be expected for hydrogen attached to the oxirane ring. The proton resonance patterns appeared at δ 2.79 (1H, doublet; $J_{11,12}$ = 4.5 c.p.s.) and at 3.12 (1H, triplet; $J_{9,11}$ = 5.7 c.p.s., $J_{11,12}$ = 4.5 c.p.s.). The only other proton resonance downfield from the main complex pattern at δ 2.0 to 0.5 was the single olefinic proton quartet centered at δ 5.53. The observed $J_{11,12}$ is in agreement with reported coupling constants observed for the *cis*-oriented hydrogens in several oxirane systems: propylene oxide ($J_{HH_{cis}} \cong$ 4.5 or 2.5 c.p.s.)[10]; styrene oxide ($J_{HH_{cis}} \cong$ 4.0 or 2.6 c.p.s.)[10]; epichlorohydrin ($J_{HH_{cis}}$ = 4.0 c.p.s.)[11]; and a derivative of beyerol[12] (J_{HH} = 3 c.p.s.). The observed $J_{9,11}$ supports the α-orientation of the epoxide function as in II rather than the β-orientation, since the H-9–C-9–C-11–C-11 dihedral angle for the latter is almost exactly 90° (from Dreiding models), for which the expected $J_{9,11}$ value is certainly no more than 1 c.p.s.[13,14] The 9,11α-oxide structure involves a dihedral angle for H-9–C-9–C-11–H-11 of approximately 160°, and a value of $J_{9,11}$ = 5.7 c.p.s., though somewhat lower than expected from theory,[13,14] is not difficult to reconcile with the molecular geometry. Thus, the data lead to the identification of the photooxidation product of β-amyrin, β-U, as 11,12-α-oxidotaraxerol (II). The experiments described above on the use of deuterium tracer to establish the presence of an oxirane unit in β-U can be summarized as shown in Chart I.

CHART I

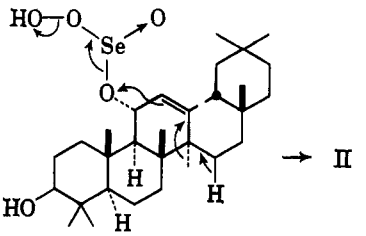


At this point mention should be made of a minor product which accompanies β-U as an impurity when the latter is obtained by photooxidation of a mixture of α- and β-amyrins. This substance, which can be isolated as the acetate by chromatography of crude β-U acetate, and which is designated herein as α-U, is isomeric with β-U and is assigned structure XII, that is, the α-amyrin analog of II, on the basis of data presented in the next section.



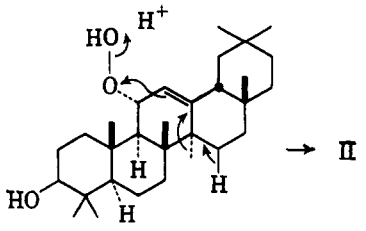
XII

Independent Synthesis of the Photooxidation Products II and XII by Oxidative Rearrangement of β- and α-Amyrin Derivatives.—Once the constitution of the substance β-U was shown to be II, a number of experiments were performed to effect an independent and rational partial synthesis from β-amyrin. The first successful experiment involved the oxidation of olean-12-ene-3β,11α-diol, XIII, readily obtainable in two steps from β-amyrin acetate or benzoate, with a mixture of hydrogen peroxide and selenous acid (equivalent to peroxyselenous acid) in *t*-butyl alcohol–dichloromethane. This process produced II in 50–60% yield; the substance so prepared was *physically and chemically identical* with β-U produced by photooxidation of β-amyrin. The pathway was envisaged *a priori* for the possible formation of II using this reagent is symbolized by XIV. However, this was shown *not* to be the actual mechanism of the formation of II from the 3β,11α-diol XIII from the fact that the reaction of the



XIV

11-epimeric olean-12-ene-3β,11β-diol (XV) with the hydrogen peroxide–selenous acid reagent also afforded II and not the epimeric epoxide; the C-11–O bond clearly is broken during reaction. This suggested an alternative mechanism in which the isomeric diols XIII and XV yield the same C-11,12,13 allylic cation which reacts with the peroxide to form olean-12-en-3β-ol 11α-hydroperoxide (XVI); this in turn undergoes acid-catalyzed O–O fission and carbon rearrangement to give II. As expected from this hypothesis, it was found

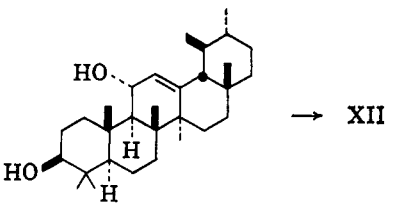


XVI

(10) H. S. Gutowsky, M. Karplus, and D. M. Grant, *J. Chem. Phys.*, **31**, 1278 (1959).
(11) A. Reilly and J. D. Swalen, *ibid.*, **35**, 1522 (1961).
(12) P. R. Jefferies, R. S. Rosich, and D. E. White, *Tetrahedron Letters*, **No. 27**, 1853 (1963).
(13) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
(14) H. Conroy in "Advances in Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1960, p. 311.

that selenous acid merely functions as an acid catalyst and can be replaced by other acids. Thus, the conversion of XIII or XV to the epoxytaraxerol II can also be accomplished using hydrogen peroxide with *p*-toluenesulfonic acid in *t*-butyl alcohol–dichloromethane in *ca.* 60% yield. Further, the reaction of the diacetate of XIII with hydrogen peroxide and acid produces the 3-acetyl derivative of II smoothly.

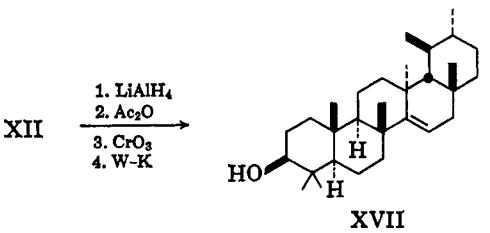
The conversion of the diols XIII and XV to β-U (II) represents an interesting and novel rearrangement. One obvious extention of this reaction is the application to other Δ^{12}-11-hydroxylated pentacyclic triterpenes and, in particular, urs-12-ene-3β,11α-diol, the α-amyrin analog. Indeed, the reaction of hydrogen peroxide and acid with urs-12-ene-3β,11α-diol produces α-U, the α-amyrin counterpart (XII) of β-U (II) in good yield. This product is identical with the compound (designated above as α-U) obtained in small amount



→ XII

together with β-U (II) from the photooxidation of a mixture of α- and β-amyrins.

The constitution of α-U is indicated as XII from independent chemical studies. Reduction of α-U with lithium aluminum hydride at reflux affords a diol by an ether cleavage analogous to that in the β series. This

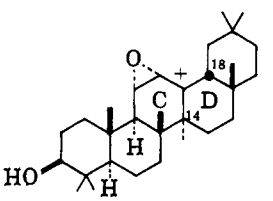


XVII

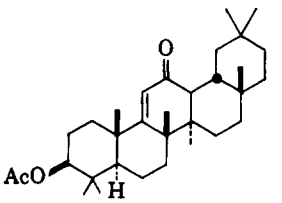
diol was converted *via* the 3-monoacetate and the 3β-acetate 11-ketone (W–K) to a substance, $C_{30}H_{50}O$, with the same melting point as reported for XVII recently prepared by partial synthesis from α-amyrin.[15] In addition the 3β-hydroxy 11-ketone was rearranged by acid treatment to the known 11-keto α-amyrin. The n.m.r. spectrum of α-U acetate indicates a single olefinic proton split by an adjacent methylene group and two protons attached to the oxirane ring as a five-peak overlapping multiplet centered at δ 3.3 in addition to an acetyl peak and a peak at 4.4 due to the 3α-proton. Although there is no conclusive evidence for the orientation of the epoxide function in α-U, it seems probable that the 11,12-oxygen bridge is α as in β-U from the similar independent syntheses of β-U and α-U.

The syntheses of β-U (II) and α-U (XII) from Δ^{12}-11-ol structures by reaction with acidic solution of hydrogen peroxide, as described immediately above, represent a much more practical preparative method than the photooxidation described in the first part of this paper. Clearly, the two processes are related, and it is reasonable to assume that the photooxidation process involves the conversion of β-amyrin, for example, to the Δ^{12}-11-hydroperoxide by a free-radical process involving oxygen, and subsequent electrophilic attack by the protonated hydroperoxy group on the Δ^{12} olefinic bond with rearrangement of the methyl attached to C-14. It is noteworthy that ethanolic solutions of β-amyrin after long irradiation in the absence of oxygen are unchanged and, further, that no β-U is formed even if the solutions are acidic. Moreover, the irradiation of β-amyrin in the presence of oxygen in neutral ethanol produces a solution which contains peroxide (indicated by the formation of iodine from iodide ion), but which does not deposit β-U until acidified.

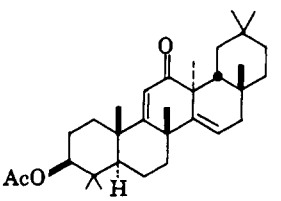
A particularly interesting matter with regard to the above-described mechanism is the question of why the cation XVIII, formed by electrophilic attack of the 11-hydroperoxy group in XVI on the Δ^{12} double bond, rearranges to the less stable taraxerene system. The possibility that the proton attached to C-18 in XVIII might rearrange or be eliminated is not excluded by the over-all thermodynamics for these processes; however, since this proton is equatorial to ring D, it is not well placed either for rearrangement to C-13 or elimination and, hence, these processes ought to be kinetically disfavored. The elimination or rearrangement of the proton attached to C-12 is unlikely from both thermodynamic and kinetic (stereochemical) considerations; this proton is essentially equatorial to ring C. The rearrangement of the 14α-methyl group to C-13 is stereochemically favorable and probably sufficiently favorable kinetically to outstrip the above-mentioned competitive processes. Once the 14 cation is formed, the loss of a proton from C-15 to a basic solvent molecule, a stereochemically favorable process, leads to a negative free-energy change for the formation of the taraxerene system from the cation XVIII. Thus, the



XVIII



XIX



XX

energy of the peroxy function in XVI powers the formation of the cation XVIII, which in this particular case is "boxed in" for stereochemical reasons and forced over to the taraxerene structure by the prevailing kinetics of the system. The peroxy oxygen not only generates the C-13 cation, but it also prevents subsequent rearrangements of the substituents at C-12; it may also effectively decrease the stability of the C-13 cation by virtue of its electron-withdrawing properties.

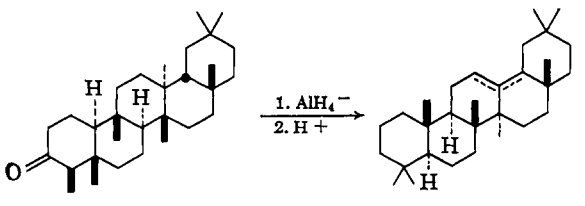
At this point it is appropriate to consider the other known example of methyl migration from C-14 to C-13

(15) F. S. Spring, R. Stevenson, and W. Laird, *J. Chem. Soc.*, 2638 (1961). Unfortunately, a direct comparison of samples was not possible since the Glasgow specimens had been destroyed by fire.

in the olean and ursane series, specifically the reaction of XIX with selenium dioxide or bromine[5,15-18] to produce the rearranged structure XX and the analogous changes in the ursane series. The mechanism of this rearrangement is not known in detail, but it is reasonable to assume that a carbonium ion with charge at C-13 is formed as an intermediate from XIX. The pathways for rearrangement from this cation are limited by the same factors discussed above for the oxidative rearrangement XVI → II, and, as a consequence migration of methyl from C-14 to C-13 emerges as the dominant mode of reaction.

Rearrangements Driven by the Addition of Electrophiles to Olefinic Bonds. The Partial Syntheses of Multiflorenol and 9,11-Dehydromultiflorenol.—In the introductory section mention was made of the possibility of transforming one carbon skeleton to another which is thermodynamically less stable by coupling another chemical process, a process which liberates free energy, to the rearrangement. The formation of 11,12α-oxidotaraxerol (II) from β-amyrin (I), one such event, when analyzed in terms of mechanistic steps and intermediates, illustrates the important prerequisites for the production of relatively less stable arrangements of a carbon framework. (1) The generation of a reactive cation, for example by the addition of an electrophile to a carbon–carbon double bond, should be both efficient and irreversible and should proceed under suitable reaction conditions. (2) The rearrangements to which this cation is subject must be restricted, for example by stereochemical factors or by the group attached during the initial electrophilic attack, so that the most rapid subsequent step is that which leads to the specified rearranged structure. (3) The medium for the reaction must be such that the carbon cation produced by rearrangement is neutralized irreversibly and with a favorable over-all free-energy change from the original cation. Within the bounds of this general formulation lie a large number of specific reagents and structural cases, all proper and interesting subjects for experimentation.

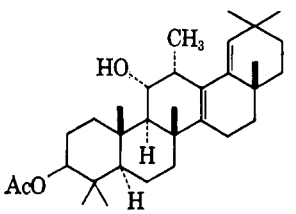
After the completion of the investigations described above we turned our attention to the specific problem of finding a way to convert β-amyrin (I) to friedelin (XXI) or one of the derivatives in that series. Such a synthesis is in the over-all effect a reverse of the exergonic rearrangement which has been found to convert the friedelin series to the β-amyrin (olean) series simply through the agency of acid catalysis.[2b] More importantly, however, the conversion of a β-amyrin derivative to the friedelin series is of interest because of the hypothesis[2b] that friedelin is produced biosynthetically from β-amyrin (or at least the olean-13 cation). It is desirable in this connection to study the nature of the intermediate between β-amyrin and friedelin, and especially the rearrangements of these intermediate structures in the direction of friedelin. The starting material for our experiments was the now readily available taraxerol derivative II.



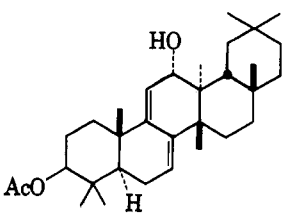
XXI

Δ12 and Δ13,18 mixture

It should be mentioned at the outset that treatment of II, as the 3-acetate, with acid catalyst does not appear to be a satisfactory way of effecting rearrangement in the direction of friedelin. At least part of the difficulty stems from the lability of the 11,12α-epoxide function in the presence of acid. Thus, treatment of the acetate of II with hydrogen bromide–acetic acid in dichloromethane under mild conditions afforded as the main isolable substance a crystalline acetoxyhydroxydiene, $C_{32}H_{50}O$, λ_{max} 240, 248, and 257 mμ (ε 19,000, 21,600, and 15,800, respectively), for which structure XXII is tentatively proposed. The infrared spectrum of this substance indicates the presence of a hydroxyl function and the n.m.r. spectrum shows the presence of a single olefinic proton as a single unsplit peak. The alternative XXIII, a more desirable product, is ruled out by these data and is also disfavored by the resistance



XXII



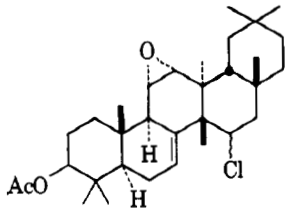
XXIII

of this substance to oxidation by activated manganese dioxide. The formation of XXII and also of the olean derivatives V and VI under more forcing conditions would suggest that there are serious obstacles to the realization of acid-catalyzed rearrangement of II in the direction of friedelin. Consequently alternative approaches are *required*.

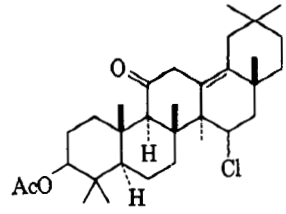
The oxidative rearrangement of II *via* the corresponding 16-hydroperoxy derivative by the process devised above was not investigated in any detail since the 16-keto derivative of II could only be prepared in low yield (sodium dichromate–acetic acid method[2a]) and since the subsequent steps also appeared to be inefficient. Furthermore, it was considered advisable to avoid the introduction of additional oxygen functions because these would add to the task of identifying or correlating reaction products. In view of the ease with which halogen substituents can usually be removed selectively, a study of the reaction of halogens with II seemed worthy of study and was undertaken.

Treatment of II-acetate with solutions of chlorine in acetic acid–methylene chloride afforded a mixture of two isomeric products of composition $C_{32}H_{49}O_3Cl$, corresponding to the replacement of hydrogen in the formula of II-acetate by a chlorine. These chloro compounds, m.p. 193–195° and m.p. 270–272°, have been identified as XXIV and XXV, respectively. The isomer of lower melting point, XXIV, is formed in smaller amount in the presence of sodium acetate relative to isomer of higher melting point, XXV, but the two products are formed in comparable amount in the pres-

(16) O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **28**, 209 (1945).
(17) L. Ruzicka, R. Rüegg, E. Volli, and O. Jeger, *ibid.*, **30**, 140 (1947).
(18) G. G. Allen, J. D. Johnston, and F. S. Spring, *J. Chem. Soc.*, 1546 (1954).

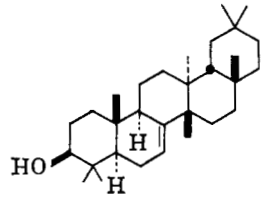


XXIV

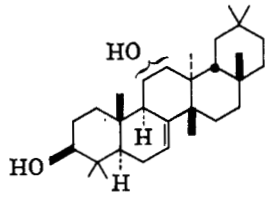


XXV

ence of zinc acetate. The formulation of the lower melting isomer as XXIV implies that this substance is in the multiflorenol (XXVI) series.[19,20] This was established by reduction of XXIV by lithium in ethylenediamine to form a chlorine-free diol XXVII (hydroxyl probably at C-12), followed by acetylation at the 3-hydroxyl, chromic acid oxidation of the remaining free hydroxyl group, and Wolff–Kishner reduction to form synthetic multiflorenol (XXVI), identical in all respects with an authentic sample of natural multiflorenol (kindly provided by Professor F. N. Lahey).



XXVI

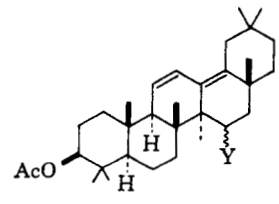


XXVII

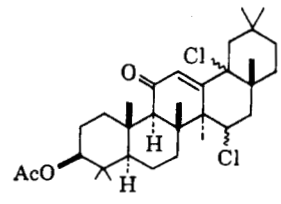
The formula XXIV for the lower melting chloro compound from II is supported by spectroscopic data. The n.m.r. spectrum, for example, reveals the presence of a single olefin proton at δ 5.24 (multiplet), two protons attached to the oxirane ring at 2.52 and 2.83 ($J_{11,12} \cong$ 4.5 c.p.s.), and two protons, downfield from the major complex band, at 4.27 (multiplet assigned to >CH–OAc and >CHCl). The resistance of the 3-acetoxy ketone corresponding to XXVII to isomerization by base to a conjugated enone suggests that the oxygen function on ring C is at C-12, not C-11.

The formation of the multiflorenol derivative XXIV from II by chlorination seems best explained by formation of a chloronium ion from II, migration of methyl from C-8 to C-14, and proton loss from C-7; on this basis the chlorine atom in XXIV is expected to possess the α-orientation, *i.e.*, *trans* to the methyl at C-14.

The higher melting chlorination product of II is indicated to be XXV by reduction to the 3,11-diol by lithium aluminum hydride, selective acetylation of the 3-hydroxyl and elimination of the 11-hydroxyl to form



XXVIII

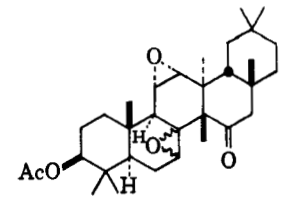


XXIX

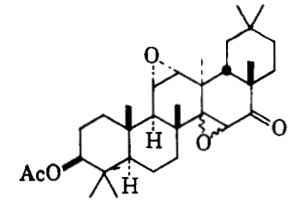
the chlorodiene XXVIII, Y = Cl. The last substance was identified by reductive dechlorination to the known 3β-acetoxyoleana-11,12;13,18-diene XXVIII, Y = H.

The infrared spectrum of the chlorination product of higher melting point exhibits carbonyl absorption due to acetate at 1724 (chloroform) and a shoulder at 1708 cm.$^{-1}$ due to the ketonic function. The ketonic group gives rise to ultraviolet absorption (n → π*) at 297 mμ (ε 61). The n.m.r. spectrum shows, in accord with XXV, the absence of olefinic proton peaks. Chlorination of XXV with *t*-butyl hypochlorite in acetic acid–dichloromethane yields a dichloro ketone [λ_{max} 242 mμ (ε 10,300), n.m.r. peak due to a single proton at δ 5.90 (singlet), and infrared peaks at 1724 and 1672 cm.$^{-1}$ due to acetate and conjugated enone carbonyls] and accordingly structure XXIX is indicated. Treatment of the dichloro ketone XXIX with zinc–acetic acid at 25° results in the regeneration of XXV. Assuming that XXV is formed by methyl rearrangement of a chloronium ion derived from II-acetate, it would appear most likely that the chlorine in XXV is β-oriented. Although there is no convincing evidence at present regarding the factor(s) controlling the relative amounts of the isomers XXIV and XXV which result from the chlorination of II-acetate, the assumption that methyl migration occurs from a chloronium ion (rather than the alternative unbridged, completely classical β-chlorocarbonium ion) leads to the simple hypothesis that the ratio of isomeric products XXIV and XXV is determined principally by the relative rates of formation of the 14,15α- and 14,15β-chloronium ions from II-acetate. It appears from the examination of Dreiding models that steric factors ought not to favor heavily one of these ions over the other, and it is reasonable to expect that both will be formed. Apropos of this is the observation that the reaction of II-acetate with peracids gives a mixture of epimeric 14,15-epoxides.

A different and independent method for the conversion of the epoxytaraxerol II to the multiflorenol series has been discovered. This involves the oxidative rearrangement of II-acetate using chromic acid in the presence of a strong acid as the reagent. These are conditions which in general seem to be less favorable to over-all allylic oxidation to a conjugated enone[1a] and relatively more favorable to the formation of epoxides, glycols, or their further transformation products.[21,22] The product of the oxidation of II-acetate is a dioxidoketo acetate, $C_{32}H_{48}O_5$ (52% yield), which is



XXX



XXXI

formulated as XXX on the basis of chemical and physical data. The infrared spectrum of this substance in $CHCl_3$ reveals acetoxy absorption at 1730 and 1260,

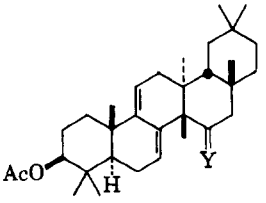
(19) (a) P. Sengupta and H. N. Khastgir, *Tetrahedron*, **19**, 123 (1963); (b) G. Eglinton, R. J. Hamilton, M. Martin-Smith, S. J. Smith, and G. Subramanian, *Tetrahedron Letters*, **No. 34**, 2323 (1964).

(20) Professor F. N. Lahey has informed us (personal communication, Oct. 1960) that he and Dr. M. V. Leeding had some years ago isolated multiflorenol from *Acronychia* baueri and ascertained its constitution independently. These workers have reported the analog of multiflorenol in the ursane series "bauerenol" [*Proc. Chem. Soc.*, 342 (1958)].

(21) W. J. Hickinbottom and G. E. M. Moussa, *J. Chem. Soc.*, 4195 (1957), and previous papers in the series on the oxidation of olefins by chromium(VI), especially W. J. Hickinbottom, D. Peters, and D. G. M. Wood, *ibid.*, 1360 (1955).

(22) H. H. Zeiss and F. R. Zwanzig, *J. Am. Chem. Soc.*, **79**, 1733 (1957), and previous papers in the series.

ketonic absorption at 1705 cm.$^{-1}$, and no hydroxyl or olefinic absorption. The ultraviolet spectrum shows no high intensity absorption above 220 mμ. The n.m.r. spectrum exhibits a band due to the proton at C-3 at δ 4.38, peaks due to the oxirane protons at C-11 and C-12 centered at 2.9, a broad peak due to a single proton at 3.86, and no olefinic proton peaks. The peak at δ 3.85 is assigned to the proton attached to C-7 and the shift downfield from the normal value for oxirane protons (*ca.* δ 3) is explained as due to the deshielding effect of the 15-keto function.[23] The alternative structure XXXI for the oxidation product seems unlikely from the n.m.r. data since the proton at C-15 in XXXI should give rise to a single sharp peak and not a broad one as observed at δ 3.86. Additional evidence in favor of structure XXX for the oxidation product is derived from the transformation of this substance to a known multiflorenol derivative. Treatment of the dioxidoketo acetate with hydrogen iodide in acetic acid gave rise to four products, the major component (34% yield) being an acetoxyketodiene, $C_{32}H_{48}O_3$, λ_{max} 233 mμ (ε 13,500), showing carbonyl absorption in the infrared ($CHCl_3$) at 1728 and 1699 cm.$^{-1}$ and n.m.r. absorption due to two olefinic protons at δ 5.22 and 5.75. This substance was identified as XXXII, Y = O, since it was transferred by Wolff–Kishner reduction and subsequent acetylation to 9,11-dehydromultiflorenyl acetate, XXXII, Y = H_2, which in turn was identified by its characteristic ultraviolet absorption at 232, 238, and 247 mμ (ε 14,100, 15,300, and 9700, respectively) and comparison with an authentic sample (kindly provided by Dr. M. V. Leeding and Professor F. N. Lahey[20]).



XXXII

The synthesis of the diene XXXII, Y = H_2, from II provides a second partial synthesis of the multiflorenol system from β-amyrin. The problem of the conversion of β-amyrin to friedelin now reduces to the realization of the sequence multiflorenol → alnusenol system → friedelin. Studies along these lines are being continued in this laboratory.

Conclusion.—A number of new rearrangements in the pentacyclic triterpene series are described above. These are of interest both in terms of possible application to other carbocyclic systems and with regard to the interconversion of different triterpene skeletons by rearrangement. Although it is clear that much remains to be learned about the rearrangements of triterpenes, a general approach can now be envisaged for the control of carbon rearrangements in such complex systems. Specifically, the above results define a methodology for the generation of a less stable carbon structure from one which is more stable by rearrangement.

(23) (a) Compare the shift of the C-15 proton in desoxytetrahydrolimonin, D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger, *et al.*, *Experientia* **16**, 41 (1960); (b) see also, D. H. Williams, N. S. Bhacca, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2810 (1963).

Experimental[24]

Photooxidation of a Mixture of α- and β-Amyrin to 11α,12α-Oxidotaraxer-14-en-3β-ol (II) in Sunlight.—A solid mixture of α- and β-amyrin (ratio *ca.* 1:2.5) obtained from *Manila elemi* resin[7] was dissolved in warm 95% ethanol, the solution was filtered, and sufficient additional solvent was added to maintain a completely clear solution at 15° (total concentration of solids *ca.* 30 g./l.). A small amount of 12 *N* hydrochloric acid was added to bring wetted pH paper to a color corresponding to pH 2–3 and the solution (in a loosely stoppered Pyrex flask) was exposed to sunlight outdoors. After *ca.* 8 weeks of exposure to summer sunlight (Urbana, Ill.) the appearance of a colorless crystalline precipitate was noted and after *ca.* 12 weeks precipitation appeared to have ceased. The crystals were collected, washed well with 95% ethanol (m.p. 260–265°), and then recrystallized twice from methylene chloride–ethanol to give clear, colorless laths, m.p. 280–285°, in a yield of approximately 10% based on the β-amyrin originally present. The photooxidation required up to 6 months during the cooler months of the year. Material of this melting point, while sufficiently good for use in many reactions, is still not completely pure; further purification was most readily accomplished *via* the acetate. A sample procedure for the purification *via* the acetate is as follows. The crude material (6.82 g.), m.p. 260–265°, was dissolved in methylene chloride (350 ml.) and pyridine (450 ml.) and treated with acetic anhydride (40 ml.); the solution was heated at 70° for 25 min. The solvent was removed under reduced pressure and the resulting solution (*ca.* 150 ml.) was poured into water forming a suspension which was extracted with methylene chloride–ether (1:1). The extracts were washed repeatedly with 3 *N* hydrochloric acid, followed by water, potassium carbonate (6%), and sodium chloride solution, and dried over sodium sulfate. A series of fractional crystallizations from methylene chloride–ethanol gave 3.62 g. of 11α,12α-oxidotaraxer-14-en-3β-yl acetate in several crops exhibiting m.p. >300°. Recrystallization afforded the pure acetate of II, m.p. 310–311°, essentially identical in its infrared spectrum with the material of m.p. 289–295° used routinely in much of our experimental work.

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.42; H, 10.45.

The acetate showed infrared absorption (in $CHCl_3$) at 1725 and 1260 due to acetate and no hydroxyl absorption at 3500–3200 cm.$^{-1}$; a yellow color developed with tetranitromethane.

Saponification of the acetate by heating at reflux (under nitrogen) with a 10% solution of potassium hydroxide (3 equiv.) in ethanol for 8 hr. afforded the hydroxy ether II, m.p. 285–288° after recrystallization from methylene chloride–ethanol.

Anal. Calcd. for $C_{30}H_{48}O$: C, 81.76; H, 10.98. Found: C, 81.60; H, 10.86.

The infrared spectrum of II (in $CHCl_3$) showed hydroxyl absorption in 3500 cm.$^{-1}$ and no absorption in the carbonyl region. A yellow color developed with tetranitromethane. Only olefinic end absorption was noted in the range 200 to 450 mμ.

The combined mother liquors from the crystallization of II-acetate furnished 2.94 g. of amorphous white solid, m.p. <240°, which was carefully chromatographed on 175 g. of Woelm alumina (grade I) packed in petroleum ether containing 30% benzene. Elution was begun and continued with this mixture, using increasing proportions of benzene until pure benzene was reached. Diethyl ether was added to the benzene and the elution was continued; eluting with benzene–ether (98:2) gave 0.496 g. of crystalline material which was crystallized from ethanol to to afford minute laths, m.p. 214–216°. This new substance was found to be identical with a sample of α-U acetate, XII-acetate, synthesized as described below from urs-12-ene-3,11-diol by reaction with acidic hydrogen peroxide followed by acetylation.

Irradiation of β-Amyrin in the Presence of Oxygen.—A concentrated ethanolic solution of pure β-amyrin[7] was placed in a cylindrical crystallizing dish, covered with a Pyrex plate, and

(24) Elemental analyses were performed by Mr. J. Nemeth and associates; Urbana, Ill., by A. Bernhardt, Mülheim (Ruhr), Germany, and by the Scandinavian Microanalytical Laboratories, Herlev, Denmark. Deuterium analyses were done by Mr. Nemeth. Melting points are corrected. Most of the n.m.r. spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as internal standard. Infrared data were obtained using Perkin-Elmer Model 21 and Infracord instruments, and ultraviolet data were obtained from a Cary Model 14 spectrometer, in ethanol as solvent unless otherwise indicated.

irradiated with a Hanovia Model 7420, 325-w. ultraviolet lamp from above at a distance of *ca.* 40 cm. From time to time additional solvent was added to maintain the original volume. In some experiments the solution of β-amyrin was acidified with hydrochloric acid from the start of irradiation and in other experiments the acid was added after 10–14 days of irradiation. Usually after about 2 weeks a considerable precipitate of dense colorless laths formed or, in those runs to which no acid had been added, the precipitate resulted soon after the addition of acid in the 10–14-day period. After 18–21 days no further precipitation was noted. The crystals were removed by filtration, washed well with ethanol, and recrystallized from methylene chloride–ethanol to afford II, m.p. 282–286°, in an average yield of 15%. This product was chemically and spectroscopically identical with the product II obtained from the mixture of α- and β-amyrin as described above and the mixture melting point was undepressed.

11α,12α-Oxidotaraxer-14-en-3-one (III).—The oxidotaraxerol II (100 mg.) was added to a suspension obtained from 45 mg. of chromic anhydride and 5 ml. of ice-cold pyridine and the reaction mixture was stirred at 25° for 23 hr. The reaction mixture was diluted with water and the solid which separated was filtered and dissolved in ether. The ethereal solution was washed with water and dilute hydrochloric acid solution and evaporated. The residue was crystallized from methylene chloride–ethanol to yield 89 mg. (89%) of III, m.p. 240–243°. Three recrystallizations and sublimation raised the melting point to 251–254°; infrared absorption (chloroform) 1700 cm.$^{-1}$, yellow coloration with tetranitromethane.

Anal. Calcd. for $C_{30}H_{46}O_2$: C, 82.13; H, 10.57. Found: C, 81.77; H, 10.48.

The **2,4-dinitrophenylhydrazone** was prepared from a solution of 30 mg. of III in 25 ml. of boiling ethanol and a solution of 150 mg. of 2,4-dinitrophenylhydrazine in water containing a few drops of sulfuric acid. Boiling was continued for 15 min. and the solution was cooled. The orange plates which separated were filtered and recrystallized four times from methylene chloride–ethanol to give 32.5 mg. of the 2,4-dinitrophenylhydrazone: m.p. 253–254°, no carbonyl absorption in the infrared.

Anal. Calcd. for $C_{36}H_{50}N_4O_5$: N, 8.91. Found: N, 8.88.

11α,12α-Oxidotaraxer-14-ene (IV) by Wolff–Kishner Reduction of III.—A suspension of 100 mg. of III in 15 ml. of dry ethanol containing 500 mg. of sodium and 2 ml. of hydrazine hydrate (80%) was heated at 170° in a sealed tube for 15 hr. The mixture was dissolved in ether and the ether solution was washed thoroughly with water and then evaporated. Crystallization of the residue from methylene chloride–ethanol gave 65 mg. of IV: m.p. 252–255°, no carbonyl or hydroxyl absorption in the infrared, yellow coloration with tetranitromethane. An analytical sample was prepared by further recrystallization and a sublimation.

Anal. Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.62; H, 11.33.

As indicated in the earlier discussion, the n.m.r. spectrum of IV[25] shows a single olefinic proton (quartet centered at δ 5.53) and two oxirane protons as a doublet at 2.79 and a triplet at 3.12.

Reaction of II-Acetate with Hydrogen Iodide.—To a suspension of II-acetate (100 mg.) in 6 ml. of acetic acid and 6 ml. of acetic anhydride under nitrogen was added dropwise 2 ml. of 50% aqueous hydriodic acid with cooling. After 1 hr. at 25° the reaction mixture was concentrated under reduced pressure and diluted with water to give a colorless solid. Recrystallization several times from chloroform–ethanol afforded colorless crystals: m.p. 227–228°; ultraviolet absorption at 242, 251, and 261 mμ (ε 26,000, 30,000, and 19,000, respectively); spectroscopically identical with an authentic sample of 3β-acetoxyoleana-11,12;13,18-diene (V).[26] A mixture melting point with the authentic specimen was undepressed.

The reaction of II-acetate with hydrogen iodide to give V could be used as an analytical method to detect the presence of II by taking advantage of the intense ultraviolet absorption of V. Using this assay on an acetylated mixture of α- and β-amyrins from *Manila elemi*[7] it was ascertained that no appreciable amount of the oxidation product II was present originally in the amyrin mixture used in the photooxidation reaction described above.

Reaction of II-Acetate with Hydrogen Bromide to Form VI.—A solution of 75 mg. of II-acetate in 3 ml. of methylene chloride was treated with 5 ml. of a saturated solution of anhydrous hydrogen bromide in acetic acid at 25° for 4 hr. The reaction solution was diluted with 2:1 ether–methylene chloride and the solution was washed successively with water, dilute sodium hydroxide, and saturated brine. Evaporation and two recrystallizations from methylene chloride–methanol gave 37 mg. of VI as colorless prisms: m.p. 221–222°, ultraviolet absorption 282 mμ (ε 8600).

Anal. Calcd. for $C_{32}H_{49}BrO_2$: C, 70.44; H, 9.05; Br, 14.65. Found: C, 70.60; H, 9.21; Br, 14.61.

The n.m.r. spectrum of the acetoxybromodiene VI showed a sharp peak due to acetoxy at δ 2.05, a broad peak due to the proton at C-3 at 4.6, and a sharp peak due to a single olefinic proton at 5.8.

Conversion to VI to VII.—A solution of 17 mg. of the acetoxybromodiene VI in 10 ml. of purified dioxane was heated at reflux under nitrogen with 100 mg. of lithium hydride for 72 hr. The excess hydride was decomposed with water and the product was isolated in the usual way with recrystallization from methanol as colorless crystals (10 mg.): m.p. 217–218°, λ_{max} 281 mμ (ε 9600), identical with an authentic specimen[27] of 3β-acetoxyoleana-9,11;12,13-diene (VII) spectroscopically and in melting point and mixture melting point.

Taraxer-14-ene-3β,11α-diol (VIII). **A.**—To a solution of 11α,-12α-oxidotaraxer-14-en-3β-yl acetate (II-acetate, 232 mg.) in 50 ml. of dry dioxane at room temperature was added approximately 500 mg. of lithium aluminum hydride. The mixture was refluxed for 117 hr., cooled, diluted with 800 ml. of water, acidified, and extracted with ether–methylene chloride (4:1). The extracts were combined, washed with potassium bicarbonate (6%), water, and saturated salt solutions, and dried over anhydrous sodium sulfate. Removal of the solvent and crystallization of the residue from ethanol yielded 197 mg. of taraxer-14-ene-3β,11α-diol (VIII) as colorless needles, m.p. 258–262°. One recrystallization from chloroform–ethanol gave 167 mg. of needles, m.p. 261–264°.

B.—A solution of 250 mg. of II in 100 ml. of anhydrous ethylenediamine[28] at 100° was treated with 2.0 g. of lithium in portions to maintain a blue color, and then the solution was heated at reflux for 0.5 hr.

The mixture was then cooled and poured into ether–methylene chloride–water (4:1:5) and the ether solution was washed with water, 1.2 *N* hydrochloric acid, water, dilute potassium carbonate, and water, dried over sodium sulfate, and evaporated to dryness. The resulting solid was crystallized from methylene chloride–ethanol giving 179 mg. (71.5%) of VIII, m.p. 247–257°. A portion of this sample was crystallized three times from methylene chloride–ethanol and then sublimed giving pure VIII, m.p. 260–264°. This product was identical with that obtained by procedure A above.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.80; H, 11.54.

The **diacetate** of VIII was obtained by reaction with excess acetic anhydride–pyridine at 40° for 24 hr.: m.p. 254–260°, infrared bands at 1730 and 1245 cm.$^{-1}$ and no hydroxyl absorption in carbon tetrachloride.

Anal. Calcd. for $C_{34}H_{54}O_4$: C, 77.52; H, 10.33. Found: C, 77.25; H, 10.36.

The **di-*p*-nitrobenzoate** was prepared from 25 mg. of VIII and *p*-nitrobenzoyl chloride (500 mg.) in 7.5 ml. of dry pyridine heated at 75–80° for 25 hr. After work-up 46 mg. (68.5%) of crude di-*p*-nitrobenzoate was obtained. The material was crystallized three times from methylene chloride–ethanol giving 18 mg. of pure compound VIII-di-*p*-nitrobenzoate: m.p. 294–295°; infrared bands at 1712, 1607, 1529, 1350, 1280, 1118, and 1103 cm.$^{-1}$ in chloroform.

Anal. Calcd. for $C_{44}H_{56}N_2O_8$: C, 71.32; H, 7.62; N, 3.78. Found: C, 70.47; H, 7.63; N, 4.05, 3.96.

Oxidation of VIII to the Dione IX.—The diol VIII (30 mg.) was added to a solution of 60 mg. of chromium trioxide in 10 ml. of pyridine and the solution was allowed to stand for 13 hr. at room temperature. Isopropyl alcohol was then added; the solu-

(25) See A. G. Hortmann, Ph.D. Thesis, Harvard University, 1964, for a reproduction of the complete spectrum.

(26) For preparation from β-amyrin, see L. Ruzicka, G. Muller, and H. Schellenberg, *Helv. Chim. Acta*, **22**, 767 (1939).

(27) C. W. Picard and F. S. Spring, *J. Chem. Soc.*, 1198 (1940).

(28) L. Reggel, R. A. Friedel, and I. Wender, *J. Org. Chem.*, **22**, 891 (1957).

tion was allowed to stand for 45 min. and then was evaporated to dryness. The resulting solid was dissolved in ether and water and the ether solution was washed with water, 1.2 *N* hydrochloric acid, water, dilute potassium carbonate, and water, and evaporated to dryness giving 26.3 mg. (88%) of crude dione IX. This solid was recrystallized twice from ethanol–water and then sublimed to give 12 mg. (40.3%) of purified dione IX: m.p. 233–236°, infrared bands at 1704 cm.$^{-1}$ (very strong) and no hydroxyl absorption in carbon tetrachloride.

Anal. Calcd. for $C_{30}H_{46}O_2$: C, 82.13; H, 10.56. Found: C, 81.91; H, 10.66.

Conversion of the Dione IX to Taraxer-14-ene (X).—To a solution of 850 mg. of sodium in 100 ml. of dry triethylene glycol was added 44 mg. of dione IX and 5 ml. of freshly distilled hydrazine. The reactants were heated under nitrogen to 120° for 14 hr. Hydrazine and water were then distilled off until the temperature of the solution reached 200° and the solution was maintained at this temperature for 24 hr. After cooling, the solution was poured into water and ether and the product was isolated in the usual way. The resulting oily solid was crystallized from ethanol–water giving 18.5 mg. (50%) of crude taraxer-14-ene. This material was sublimed and then chromatographed to give pure product, m.p. 238–241°, mixture melting point undepressed with an authentic sample[8] of taraxer-14-ene, m.p. 238–241°.

Taraxer-14-ene-3β,11α-diol-12β-*d* (VIII-d_1).—Using the procedure described above, a solution of II (500 mg.) and lithium aluminum deuteride (356 mg.) in dry dioxane (41 ml.) was refluxed for 10 days under a nitrogen atmosphere and anhydrous conditions. The product was isolated as above and recrystallized twice from ethanol to give taraxer-14-ene-3β,11α-diol-12β-*d* as needles: m.p. 258–260°; yield, 402 mg. (80%). The infrared spectrum of the product was superimposable on that of undeuterated VIII obtained as described above.

Taraxer-14-ene-3,11-dione-12β-*d* (IX-d_1).—A solution of taraxer-14-ene-3β,11α-diol-12β-*d* (262 mg.) and chromium trioxide (540 mg.) in 80 ml. of pyridine was allowed to stand for 10.5 hr. at 26° followed by 14 hr. at 5°. The excess chromic acid–pyridine complex was decomposed with 3 ml. of 2-propanol. The solvent was removed and the residue was triturated with ether–methylene chloride (4:1). The resulting solution was washed three times with water, dried, treated with charcoal, filtered, and evaporated. The residue was crystallized twice from ethanol yielding 125 mg. of taraxer-14-ene-3,11-dione-12β-d_1: m.p. 227–231°, ν_{max}^{Nujol} 1705 cm.$^{-1}$. The infrared spectrum of the product was superimposable on that of undeuterated dione IX.

Two further recrystallizations from methanol yielded an analytical sample, m.p. 230–232°. Deuterium analysis revealed the presence of 2.34 relative atom % deuterium, corresponding to 1.08 atoms of excess deuterium/molecule of IX.

Treatment of Taraxer-14-ene-3,11-dione-12β-*d* (IX-d_1) with Sodium Methoxide in Methanol.—To 55 ml. of absolute methanol in which *ca.* 1 g. of sodium had been previously dissolved was added 60 mg. of taraxer-14-ene-3,11-dione-12β-*d*. The solution was refluxed for 6.5 hr., the solvent was removed, and the residue was shaken with ether–methylene chloride (4:1) and water. The organic layer was washed with potassium bicarbonate solution (6%), water, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a residue which upon successive crystallizations from ethanol and methanol yielded 50 mg. (83%) of taraxer-14-ene-3,11-dione (IX), m.p. 227–231°. Three additional crystallizations from methanol yielded an analytical sample, m.p. 228–231°. The infrared spectrum of IX was superimposable on that of the deuterated starting material.

Deuterium analysis revealed the presence of 0.08 ± 0.05 relative atom % deuterium, corresponding to 0.04 ± 0.03 atoms of excess deuterium/molecule.

Olean-12-ene-3,11-dione.—A solution of olean-12-en-11-on-3β-ol[27] (293 mg.) and chromic acid (300 mg.) in 25 ml. of pyridine was stirred continuously for 24 hr., and 2 ml. of 2-propanol was added to decompose the excess chromic acid–pyridine complex. The solvent was evaporated *in vacuo* and the residue was triturated with ether–methylene chloride (4:1). The resulting solution was washed successively with water, hydrochloric acid (3 *N*), water, potassium bicarbonate solution (6%), and saturated sodium chloride solution, dried over anhydrous sodium sulfate, and filtered through alumina. Removal of the solvent and crystallization from methanol gave 216 mg. (74%) of *cis*-D/E ring-fused olean-12-ene-3,11-dione as thin plates, m.p. 228–231°. Several recrystallizations and two sublimations yielded a final product of m.p. 229–231° (lit.[27] m.p. 235°), ν_{max}^{Nujol} 1700 and 1655 cm.$^{-1}$, λ_{max}^{EtOH} 251 mμ (ϵ 12,800), lit.[27] λ_{max} 251 mμ (ϵ 10,500).

18-Isoolean-12-ene-3,11-dione (XI). A. By Acid-Catalyzed Isomerization of Olean-12-ene-3,11-dione.—To a 15-ml. capacity glass bomb tube containing 32 mg. of olean-12-ene-3,11-dione[27] was added 5 ml. of a glacial acetic acid solution containing 3% by weight of dry hydrogen chloride gas. The tube was sealed (to prevent reduction of the hydrogen chloride concentration), heated for 1 hr. at 90°, and cooled. The reaction mixture was evaporated to dryness and the resulting residue was dissolved in methylene chloride, heated with charcoal, filtered, and crystallized from methanol yielding 25 mg. (78%) of *trans*-D/E ring-fused 18-isoolean-12-ene-3,11-dione (XI) as flat plates: m.p. 275–277°, ν_{max}^{Nujol} 1705 and 1660 cm.$^{-1}$, λ_{max}^{EtOH} 246 mμ (ϵ 11,800). Two additional recrystallizations from methanol yielded an analytical sample, m.p. 275–277°.

Anal. Calcd. for $C_{30}H_{46}O_2$: C, 82.13; H, 10.56. Found: C, 82.40; H, 10.60.

B. By Acid-Catalyzed Isomerization of Taraxer-14-ene-3,11-dione (IX).—To a 30-ml. bomb tube containing 55 mg. of taraxer-14-ene-3,11-dione (IX) was added 14 ml. of glacial acetic acid solution containing 3% by weight of dry hydrogen chloride gas. The tube was sealed and allowed to stand at room temperature for 25 hr. The sealed tube was then heated at 88° for 1 hr., cooled, and reopened. The reaction mixture was treated as described in part A yielding 39 mg. of XI as flat plates, m.p. 275–277°; the melting point was undepressed on admixture of the product with a sample from part A. The infrared spectrum was superimposable on that of a sample of XI obtained by method A. The ultraviolet spectrum exhibited λ_{max}^{EtOH} 246 mμ (ϵ 11,600).

Epoxidation of II-Acetate.—To 3 ml. of a solution of peracetic acid (0.3 *M*) in chloroform was added 24 mg. of II-acetate. The solution was stored at 5° for 2 weeks and the product was isolated by dilution with ether, washing, and concentration. The crystalline solid product gave no color with tetranitromethane and showed acetoxy absorption but no other carbonyl and no hydroxyl absorption in the infrared. It appeared to be a mixture of isomers judging from the melting point range 220–228° after recrystallization from methanol–water. Further recrystallization afforded colorless crystals, m.p. 228–231°, which were sublimed for analysis.

Anal. Calcd. for $C_{32}H_{50}O_4$: C, 77.06; H, 10.11. Found: C, 77.01; H, 9.91.

Sequential Oxidation of II-Acetate by Osmium Tetroxide and Lead Tetraacetate.—A solution of II-acetate (200 mg.), osmium tetroxide (1 g.), dry ether (30 ml.), and dry pyridine (30 ml.) was placed in a sealed tube and heated at 100° for 24 hr. After opening, the contents of the tube were transferred to a flask using chloroform as a transfer solvent, hydrogen sulfide was bubbled into the mixture for 20 min., and the mixture was allowed to stand at room temperature for 24 hr. The mixture was filtered and the filtrate was evaporated to dryness. The resulting solid was dissolved in chloroform and filtered twice through Florisil columns. The chloroform solution was evaporated to dryness and the resulting solid was recrystallized from ethanol–water yielding 187 mg. (87.5%) of taraxerane-3,14,15-triol 3-monoacetate, m.p. 235.5–240°. The triol monoacetate was crystallized once from ethanol–water and twice from methylene chloride–hexane to give an analytical specimen: m.p. 236–239°; infrared bands at 3420, 3300, 1728, and 1250 cm.$^{-1}$ (Nujol mull).

Anal. Calcd. for $C_{32}H_{52}O_5$: C, 74.37; H, 10.14. Found: C, 74.47; H, 10.31.

To a solution of 50.5 mg. of the above acetoxydiol in 100 ml. of glacial acetic acid was added 2.41 g. of lead tetraacetate. The solution was stirred and heated to 60 ± 5° for 18 hr. and then evaporated to dryness. The resulting white solid was dissolved in 4:1 ether–methylene chloride and poured into water. The ether solution was then washed with water, dilute potassium bicarbonate, and water, dried over sodium sulfate, and evaporated to dryness yielding 42.5 mg. (84.5%) of crude solid. This crude solid was sublimed at 205° (0.1 mm.) to a yellow glass: infrared bands at 2720, 1730 (very strong and broad), 1700, 1665 (weak), and 1240 cm.$^{-1}$ in carbon tetrachloride.

Conversion of β-Amyrin Benzoate to 11α,12α-Oxidotaraxer-14-en-3β-ol (II) and the Acetate. A.—Sodium dichromate (100 g.) in 3 l. of glacial acetic acid at 70° was added to 100 g. of β-amyrin

benzoate (recrystallized from ethyl acetate) in 700 ml. of boiling benzene (80–90°) during 5 hr. The solution was stirred for 19 hr. more at 80–85°. To this solution 400 ml. of 95% ethanol was added and the reaction mixture was concentrated to one-third its volume *in vacuo*. The concentrate was poured into ice–water and the insoluble solid was collected by filtration, dissolved in benzene, and washed with water. The benzene solution was dried over sodium sulfate, filtered, concentrated, and then treated with 95% ethanol to give, after recrystallization, 75 g. of pure 3β-benzoyloxyolean-12-en-11-one, m.p. 264–265°.

A solution of this 11-keto benzoate (100 g.) in 800 ml. of dry benzene and 300 ml. of dry ether was added with stirring to a mixture of 50 g. of lithium aluminum hydride and 2500 ml. of refluxing ether (stirred previously for 2 hr. under reflux) during 3 hr. After stirring for 6 hr. at reflux, the solution was stirred for 12 hr. at room temperature. To destroy excess hydride a minimum volume of water was added dropwise at room temperature. The precipitate was removed by decantation and washed with ether, and the combined ethereal solution was washed with 10% aqueous sodium hydroxide solution and then water. After drying with anhydrous sodium sulfate, the ethereal phase was evaporated giving 81 g. of olean-12-ene-3,11-diol. This product was sufficiently pure for the next step.

To the 60 g. of olean-12-ene-3,11-diol in 3400 ml. of methylene chloride was added 1260 ml. of oxidizing solution which was prepared from 60 ml. of 30% hydrogen peroxide in 1200 ml. of *t*-butyl alcohol containing 36 g. of *p*-toluenesulfonic acid at room temperature. The solution was stirred slowly for 24 hr. and then poured into water. The mixture was extracted with methylene chloride and the methylene chloride solution was washed with water, aqueous sodium bicarbonate solution, and then again with water. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure furnishing 57 g. of crude product. The crude product was acetylated by dissolving it in 3 l. of pyridine at 40° and adding to this solution with stirring, 2000 ml. of acetic anhydride. The solution was maintained at 40° with stirring for 18 hr. The crystals which deposited from the solution were collected and washed with 95% ethanol giving 33 g. of II-acetate, m.p. 293–303°, undepressed upon admixture with a sample obtained from the direct photooxidation of β-amyrin and subsequent acetylation as described above. The infrared and n.m.r. spectra of samples prepared by the two methods were identical.

The pyridine solution from which the acetate of II was obtained furnished an additional 9 g. of pure product after concentration to one-third volume, filtration of the solid which precipitated, and recrystallization from methylene chloride–acetone; total yield was 42 g. (60% based on the 11-ketobenzoate).

This product afforded by treatment with hydrogen bromide the acetoxybromodiene VI, identical with material obtained as described above; with lithium aluminum hydride the same diol (VIII) was obtained as from samples of II obtained by the photooxidation process.

An analysis was performed on the II-acetate prepared by this method.

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.75; H, 10.51.

B.—Another experiment was conducted as follows. A solution of 2 g. of 3β-benzoyloxyolean-12-en-11-one in 50 ml. of benzene and 50 ml. of ether was added during 30 min. with stirring to a slurry of 2 g. of powdered lithium aluminum hydride in 100 ml. of anhydrous ether. After an additional 2 hr. of stirring, the mixture was left overnight and the excess hydride was decomposed with ethanol. Sodium hydroxide (10% in water) was then added, the layers were separated, and the organic layer was washed with water. The solvents were removed *in vacuo* and the residue was recrystallized from methylene chloride–methanol to give olean-12-ene-3β,11β-diol, m.p. 180–181°.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.38; H, 11.38. Found: C, 81.47; H, 11.31.

This diol had been prepared previously but had not been purified or analyzed.[18]

The 3β,11β-diol (250 mg.) was oxidized as described above with hydrogen peroxide–*p*-toulenesulfonic acid in methylene chloride–acetone to give 145 mg. of pure 11α,12α-oxidotaraxer-14-en-3β-ol, m.p. 284–285° after recrystallization from methylene chloride–ethanol.

The 3β,11β-diol (250 mg.) was also converted to II by treatment in 15 ml. of methylene chloride with a solution of 150 mg. of selenous acid and 0.25 ml. of 30% hydrogen peroxide in 5 ml. of *t*-butyl alcohol at 25° for 7 hr. The product (m.p. 282–285°) was identical with II prepared by the other methods described above.

Anal. Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 81.48; H, 10.88.

C.—Treatment of olean-12-ene-3β,11α-diol, m.p. 238–239° (prepared by reduction of 3β-benzoyloxyolean-12-en-11-one with sodium in isoamyl alcohol[27]), with hydrogen peroxide with either *p*-toluenesulfonic acid or selenous acid as catalyst also gave II, m.p. 284–285°.

D.—Acetylation of olean-12-ene-3β,11β-diol by excess acetic anhydride–pyridine at 25° for 18 hr. gave the diacetate, m.p. 222°.

Anal. Calcd. for $C_{34}H_{54}O_4$: C, 77.52; H, 10.33. Found: C, 77.52; H, 10.21.

This 3β,11β-diacetate, when treated with 30% hydrogen peroxide in methylene chloride–*t*-butyl alcohol in the presence of selenous acid, gave II-acetate, m.p. 293–303°.

Conversion of α-Amyrin to XII.—To 10 g. of α-amyrin benzoate (m.p. 192–193°) was added 10 g. of sodium dichromate in 200 ml. of acetic acid. The mixture was heated at 100° for 6.5 hr. (The α-amyrin benzoate dissolved only after 2-hr. heating.) Ethanol (50 ml.) was then added in portions, the solution was cooled, and 200 ml. of water was added. The precipitate which formed was collected and washed three times with water and two times with methanol. There was obtained 9.5 g. of crude product, m.p. 255–258°. This was dissolved in 40 ml. of chloroform, filtered, and diluted with 250 ml. of methanol to give 7.8 g. of 3β-benzoyloxyurs-12-en-11-one, m.p. 265–267°.

Reduction of this product with lithium aluminum hydride as described in the preceding section afforded an oily mixture of urs-12-ene-3β,11α-diol and urs-12-ene-3β,11β-diol.

The oily diol (1.05 g.) was dissolved in 90 ml. of methylene chloride and a solution of 900 mg. of selenous acid and 1.5 ml. of 30% hydrogen peroxide in 30 ml. of *t*-butyl alcohol was added. After 14 hr. at 25° the solid product was isolated in the usual manner. Two recrystallizations from ethyl acetate afforded pure XII, m.p. 249–250°.

Anal. Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 81.61; H, 10.74.

Acetylation of XII with excess acetic anhydride–pyridine gave the 3-acetate, m.p. 214–216°, undepressed upon admixture with II-acetate obtained from photooxidation of a mixture of α- and β-amyrin.

The acetate of XII was also prepared in 60% yield by acetylation of the urs-12-ene-3,11-diol mixture and subsequent reaction with hydrogen peroxide–*p*-toluenesulfonic acid in methylene chloride–*t*-butyl alcohol (21 hr. at 25°), m.p. 215°.

11,12-Oxidoisours-14-en-3-one.—A solution of 300 mg. of XII in 30 ml. of pyridine was mixed with a solution of 350 mg. of chromic acid in 50 ml. of pyridine and kept at room temperature for 43 hr. Excess chromic acid was reduced by 5 ml. of 2-propanol, and the solvent was evaporated under reduced pressure. The residue was extracted with dichloromethane–ether, and the solution was washed with 10% hydrochloric acid and aqueous sodium bicarbonate solution. Evaporation of the solvent and addition of methanol yielded 213 mg. of a product melting at 193–194°. Crystallization of this product from acetone–methanol gave needles, m.p. 195–196°.

Anal. Calcd. for $C_{30}H_{46}O_2$: C, 82.13; H, 10.57. Found: C, 82.18; H, 10.38.

3,11-Dihydroxyisours-14-ene.—A mixture of 500 mg. of XII and 1 g. of lithium aluminum hydride in 100 ml. of dry dioxane was refluxed under nitrogen with stirring for 135 hr. The solution was cooled, the excess hydride was decomposed by acetone, and ether and 10% aqueous sodium hydroxide solution was added. The organic layer was separated and washed three times with water and the solvent was evaporated. Addition of petroleum ether to the residue yielded 420 mg. of a product melting at 225–226°. Crystallization from acetone gave the diol, m.p. 226–227° (needles).

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.48; H, 11.38. Found: C, 81.44; H, 11.37.

3β-Hydroxyisours-14-en-11-one.—A solution of 500 mg. of 3,11-dihydroxyisours-14-ene in 25 ml. of pyridine was mixed with a solution of 500 mg. of chromic acid in 75 ml. of pyridine and kept at room temperature for 24 hr., after which 10 ml. of 2-propanol was added. The solvent was evaporated under reduced pressure, the residue was extracted with dichloromethane–ether, and the solution was washed with 10% hydrochloric

acid and aqueous sodium bicarbonate. Evaporation of the solvent left a solid which was recrystallized from acetone to yield 125 mg. of a product, m.p. 197–198°. The infrared spectrum showed carbonyl (1710 cm.$^{-1}$) and hydroxyl absorption.

Anal. Calcd. for $C_{30}H_{48}O_2$: C, 81.75; H, 10.99. Found: C, 81.68; H, 10.74.

Acid-Catalyzed Isomerization of 3β-Hydroxyisours-14-en-11-one to 3β-Hydroxyurs-12-en-11-one.—A solution of 90 mg. of the keto alcohol in 20 ml. of acetic acid saturated with hydrogen chloride was kept at room temperature for 32 hr., then heated on the steam bath for 1 hr. with a stream of hydrogen chloride being passed through the solution. The solvent was then evaporated under reduced pressure and the residue was crystallized from methanol to give 20 mg. of the Δ^{12}-11 ketone: m.p. 276–278°; infrared bands at 1740 (s), 1670 (s), and 1650 cm.$^{-1}$ (w); λ_{max}^{EtOH} 250 mμ (ε 12,000).

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.72; H, 10.12.

Conversion of 3β,11-Dihydroxyisours-14-ene to 3β-Acetoxyisours-14-ene (XVII).—To 400 mg. of 3β,11-dihydroxyisours-14-ene (from XII and lithium aluminum hydride) in 20 ml. of pyridine at −20° was added 20 ml. of cold acetic anhydride. After 18 hr. at −20° the excess acetic anhydride was decomposed by the addition of 20 ml. of methanol. The resulting solution was concentrated under reduced pressure, poured into water, and extracted with methylene chloride. The methylene chloride was washed with water and evaporated *in vacuo*. Recrystallization of this solid (387 mg.) from acetone and then methanol furnished crystals of 3-monoacetate: m.p. 252–254°; $\lambda_{max}^{CHCl_3}$ 1258 and 1721 (acetate), 3690 cm.$^{-1}$ (alcohol).

Anal. Calcd. for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.59; H, 10.87.

A mixture of 100 mg. of chromium trioxide and 1.5 ml. of pyridine was added to 100 mg. of the above monoacetate and the mixture was stored at room temperature for 24 hr. The suspension was poured into water and extracted with ether–methylene chloride (4:1); the organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. The product was then chromatographed on 5 g. of neutral alumina (Woelm grade III). Benzene–hexane (1:1) eluted 20 mg. of crystals: m.p. 232–235°; infrared absorption ($CHCl_3$) at 1258 and 1724 (acetate), 1698 cm.$^{-1}$ (saturated carbonyl).

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.71; H, 10.45.

To 45 mg. of the above 3β-acetoxy-11-ketone in a glass tube (7 mm. diam.) was added 0.5 ml. of hydrazine and 40 mg. of sodium metal dissolved in 2 ml. of diethylene glycol. The air was replaced by nitrogen, the tube was sealed, and the contents were heated to 185–195° for 24 hr. The resulting mixture was cooled, poured into water, and extracted with ether–methylene chloride (4:1). The organic layer was evaporated *in vacuo* and 3 ml. of acetic anhydride was added to the residue in 3 ml. of pyridine. After standing at room temperature overnight, the solution was treated with water and extracted with methylene chloride. The methylene chloride was washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness *in vacuo*. The product in hexane was chromatographed on 3 g. of neutral Woelm alumina (grade III); hexane eluted a crystalline material which was rechromatographed on 10 g. of neutral Woelm alumina (grade III) with chloroform–methanol (6:1). The eluted product was chromatographed again in a column containing 5 g. of neutral Woelm alumina (grade III). Hexane eluted a crystalline material which after recrystallization from ethanol furnished isours-14-en-3β-yl acetate, m.p. 214–216°.[15]

Anal. Calcd. for $C_{32}H_{52}O_2$: C, 81.99; H, 11.18. Found: C, 82.10; H, 11.29.

Treatment of II-Acetate with Hydrogen Bromide under Mild Conditions. XXII.—A solution of 500 mg. of II-acetate in 100 ml. of methylene chloride and 100 ml. of glacial acetic acid was heated at reflux and 240 mg. of hydrogen bromide gas in 4 ml. of glacial acetic acid was added. The solution was stirred for 7 min. at reflux temperature and then poured into ice–water and extracted with methylene chloride. The organic layer was washed with water and then evaporated *in vacuo*. The residue was recrystallized from methanol and the crystalline mixture (158 mg.) was chromatographed on Florisil using benzene–petroleum ether (1:1) as solvent. The fractions containing crystalline material in quantity were combined and recrystallized from methanol to give 113 mg. of pure product regarded tentatively as XXII: m.p. 250–253°, negative Beilstein test for halogen; infrared absorption (in $CHCl_3$) at 1715 and 1260 (acetate), 3435–3285 cm.$^{-1}$ (hydroxyl); ultraviolet absorption 240, 248, and 257 mμ (ε 19,000, 21,600, and 15,800, respectively). The n.m.r. spectrum showed peaks expected for the 3β-acetoxy group and also a single unsplit peak downfield at δ 5.28 (1H) due to an olefinic proton; one of the methyl groups appeared split into a doublet (J = 6.8 c.p.s.) centered at δ 1.15. A broad multiplet appeared at δ 4.5 due to two protons, presumably those attached to C-3 and C-11.

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.74; H, 10.45.

The above product was unchanged after treatment with (a) acetic anhydride–pyridine at 25° for 24 hr., (b) activated manganese dioxide in chloroform at 25° for 24 hr., and (c) dichlorodicyano-*p*-benzoquinone in benzene at 25° for 11 hr. and at 40° for 2 hr.

3β-Acetoxy-11α,12α-oxidotaraxer-14-en-16-one by Dichromate Oxidation of II-Acetate.—To a solution of 400 mg. of sodium dichromate dihydrate, 80 mg. of sodium acetate, and 100 mg. of manganous sulfate monohydrate in 35 mg. of glacial acetic acid was added 96 mg. of II-acetate and the solution was heated on a steam bath for 10 hr. Ethanol was then added to decompose the excess dichromate. Water was added and, after cooling, the resulting solid was filtered, washed with water, and dried yielding 74 mg. of crude solid. This solid was chromatographed on 1.9 g. of Florisil and the product (33.8 mg., 35.3%, m.p. 291–295°) eluted by pure benzene was crystallized twice from ethanol–water and then sublimed yielding pure 16-ketone: m.p. 303–309°; λ_{max} 242 mμ (ε 11,000); infrared bands at 1725, 1682, 1620 (weak), and 1253 cm.$^{-1}$ in Nujol and 1725, 1668, 1612 (weak), and 1255 cm.$^{-1}$ in chloroform.

Anal. Calcd. for $C_{32}H_{48}O_4$: C, 77.37; H, 9.74. Found: C, 77.13; H, 9.62.

3β-Acetoxy-11α,12α-oxido-15ξ-chloromultiflor-7-ene (XXIV).—To a solution of 1 g. of 11α,12α-oxidotaraxer-14-en-3β-yl acetate in 200 ml. of methylene chloride and 200 ml. of acetic acid was added 2.5 g. of zinc acetate and this was stirred at room temperature for 1 hr. After the suspension was cooled at 0° in an ice–water bath, 160 mg. of chlorine dissolved in 100 ml. of glacial acetic acid was slowly added dropwise with stirring over 1.5 hr. at 0°. Stirring was continued for 3.5 hr. at 0°. The suspension poured into 200 ml. of water and the solution was extracted with methylene chloride. The methylene chloride was washed seven times with water, dried with anhydrous sodium sulfate, and then evaporated *in vacuo* at room temperature. The product was dissolved with *ca.* 200 ml. of hot acetone, concentrated on a steam bath to *ca.* 70 ml., and cooled to give 180.7 mg. of fine needles of 11α,12α-oxidoolean-15ξ-chloro-13(18)-en-3β-yl acetate (XXV). The mother liquor was evaporated under reduced pressure; the residue was washed with 10 ml. of cold methanol and collected by suction filtration. The white solid was recrystallized from acetone to give 307.8 mg. of a mixture (1:4) of 11α,12α-oxidoolean-15ξ-chloro-13(18)-en-3β-yl acetate (XXV) and XXIV. Fraction crystallization from acetone afforded ultimately 286 mg. of XXIV (26.8%) as prisms: m.p. 193–195° dec.; infrared absorption at 1035, 1258, and 1724 cm.$^{-1}$; ultraviolet end absorption at 206 mμ (ε 3700). The n.m.r. spectrum showed peaks at δ 5.24 (1H, multiplet), 4.27 (2 H, multiplet), 2.83 (1H), and 2.52 (1 H), assigned, respectively, to protons attached at carbons 7, 3 and 15, and 11 and 12 with $J_{11,12}$ = 4.5 c.p.s.

Anal. Calcd. for $C_{32}H_{49}ClO_3$: C, 74.31; H, 9.55; Cl, 6.90. Found: C, 74.29; H, 9.46; Cl, 6.78.

3β-Acetoxymultiflor-7-en-12α-ol (XXVII-Acetate).—A solution of 500 mg. of 11α,12α-oxidomultifloran-15ξ-chloro-7-en-3β-yl acetate (XXIV) in 6 ml. of hot dioxane was added at once to a stirred blue solution prepared from 200 ml. of dry ethylenediamine and 100 mg. of lithium metal at 70° under nitrogen. The blue color was maintained for 15 min. at 70° by adding lithium in 100-mg. portions. After 15 min. the colorless solution was poured into a mixture of ice and 10 g. of sodium chloride in a 1-l. separatory funnel and extracted with methylene chloride–ether (1:5). The organic layer was washed successively with water, 3% hydrochloric acid, saturated aqueous sodium bicarbonate solution, and water, dried with anhydrous sodium sulfate, and evaporated *in vacuo*. This reaction was carried out twice and 995 mg. of product XXVII was obtained. A solution of 995 mg. of this diol in 100 ml. of pyridine was maintained at −20°, and then 100 mg. of cold acetic anhydride was added at

−20°. After standing for 18 hr. at −20°, the excess acetic anhydride was decomposed by the addition of 100 ml. of 95% ethanol. The solution was concentrated to *ca.* 100 ml. *in vacuo* and then poured into water and extracted with methylene chloride. The methylene chloride was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The product was dissolved in *n*-hexane and benzene (1:1) and then transferred to a column of 50 g. of Florisil (100–200 mesh) with *n*-hexane and benzene. This solvent eluted impure material. Elution with 650 ml. of benzene gave 298 mg. of solid material, which gave 58 mg. of multiflor-7-en-12α-ol-3β-yl acetate after recrystallization from methanol. Continued elution of the column with 1250 ml. of benzene produced an additional 235 mg. of multiflor-7-en-12α-ol-3β-yl acetate. With chloroform and then methanol, there was eluted 322 mg. of a mixture of multiflor-7-en-12α-ol-3β-yl acetate and starting material (multiflor-7-ene-12α,3β-diol). The yield of multiflor-7-en-12α-ol-3β-yl acetate was 293 mg. (31%).

A sample, recrystallized once from methanol for analysis, gave m.p. 210–213°. The infrared spectrum in chloroform showed hydroxyl stretching absorption at 3759 and acetate absorption at 1259 and 1733 cm.$^{-1}$. The n.m.r. spectrum exhibited peaks at δ 3.64 (1H, multiplet, H-12), 4.49 (1H, triplet, H-3), and 5.43 (1H, multiplet, H-7) and also the main group of peaks at higher field.

Anal. Calcd. for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.31; H, 10.85.

3β-Acetoxymultiflor-7-en-12-one.—A mixture of 100 mg. of chromium trioxide and 1.8 ml. of pyridine was added at room temperature to 100 mg. of multiflor-7-en-12α-ol-3β-yl acetate in 3.3 ml. of pyridine and the reactants were stored at 25° overnight. The resulting solution was poured into water, extracted with methylene chloride, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. A solution of the residue in chloroform was passed through 1 g. of Florisil (100–200 mesh). Elution with 50 ml. of chloroform gave 80 mg. of crystals. Recrystallization from methanol gave 60 mg. of crystalline 12-ketone, m.p. 242–245°.

A sample sublimed for analysis, m.p. 245–247°, exhibited saturated carbonyl absorption at 1701 and acetate absorption 1258 and 1727 cm.$^{-1}$ in the infrared spectrum (chloroform).

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.57; H, 10.55.

The n.m.r. spectrum showed peaks at δ 4.50 (1H, triplet, H-3) and 5.55 (1 H, multiplet, H-7) in addition to the major absorption upfield.

Multiflorenol (XXVI).—To 30 mg. of multiflor-7-en-12-on-3β-yl acetate in a 7-mm.-diam. glass tube was added successively 0.3 ml. of dry hydrazine and 0.06 g. of sodium metal in 3 ml. of diethylene glycol. The air was replaced by nitrogen and the glass tube was sealed and heated at 185–192° for 24 hr. The reaction mixture was cooled, poured into ice–water, and extracted with ether–benzene (1:1). The organic layer was washed with water, dried with anhydrous sodium sulfate, and evaporated *in vacuo* to give 22.5 mg. of residue. The product was dissolved in a little ligroin–benzene (1:1) and then chromatographed on a column of 3 g. of Florisil (100–200 mesh); the first fraction with ligroin–benzene (1:1, 25 ml.) contained oily material. The following 75 ml. of ligroin–benzene (1:1) eluted 7.8 mg. of multiflorenol.

The product was recrystallized once from methanol giving the pure product, m.p. 190–191°, weight 3 mg., identical by infrared spectrum and mixture melting point (190–191°) with an authentic sample[20] of multiflorenol, m.p. 190–191°. The behavior of the two specimens on a thin layer plate of alumina with chloroform was identical.

3β-Acetoxy-15-chlorooolean-13(18)-en-11-one (XXV).—A solution of 500 mg. of 11α,12α-oxidotaraxer-14-en-3β-yl acetate in 100 ml. of methylene chloride was combined with 200 mg. of sodium acetate in 100 ml. of acetic acid and 30 ml. of water. The solution, cooled to 0° and vigorously stirred, was treated dropwise with 80 mg. of chlorine in 25 ml. of acetic acid over 1 hr. After stirring for 4 hr. in an ice–water bath, the solution was poured into ice–water and the mixture was extracted with methylene chloride. The methylene chloride was washed several times with 100 ml. of water, dried with anhydrous sodium sulfate, and evaporated *in vacuo* at room temperature. Recrystallization of the residue once from acetone furnished 242.7 mg. (44.5%) of XXV as needles, m.p. 267–270° dec. A sample recrystallized twice from acetone gave needles, m.p. 270–272° dec. The infrared spectrum in chloroform showed broad carbonyl absorption centered at 1719 and C–O stretching absorption at 1256 cm.$^{-1}$ (acetate). The ultraviolet spectrum showed λ_{max} 207 mμ (ε 8300) in cyclohexane and λ_{max} 297 mμ (ε 61).

Anal. Calcd. for $C_{32}H_{49}ClO_3$: C, 74.31; H, 9.55; Cl, 6.86. Found: C, 74.31; H, 9.58; Cl, 6.78.

The n.m.r. spectrum showed the absence of olefinic protons (no peaks downfield from δ 5); peaks were noted at δ 4.5 (2H, multiplet H-3, H-15) and at 3.0, 3.3, and 3.6 in addition to the major proton absorption upfield.

3β-Acetoxy-15-chlorooolean-13(18)-en-11β- and -11α-ol.—A solution of 2 g. of XXV in 100 ml. of dry benzene and 100 ml. of absolute ether was added to a stirred mixture of 5 g. of lithium aluminum hydride and 600 ml. of anhydrous ether (prestirred for 1.5 hr. under reflux) at reflux. The mixture was refluxed for 6 hr. with stirring and then stirred for 30 min. at room temperature. The excess lithium aluminum hydride was destroyed by dropwise addition of water. The precipitate was removed by decantation and washed with methylene chloride. The combined organic solution was washed several times with water, dried with anhydrous sodium sulfate, and evaporated to give 1.63 g. of crude product. This was acetylated by treatment with 60 ml. of pyridine at 0° and 60 ml. of acetic anhydride at 0°. After standing 24 hr. at 2–5° the solution was poured into ice–water and extracted with methylene chloride. The methylene chloride was washed successively with water, 3% hydrochloric acid, saturated aqueous sodium bicarbonate, and water. The organic layer was dried with anhydrous sodium sulfate and the methylene chloride was evaporated to give 1.43 g. of residue. This product was dissolved in a minimum volume of hot acetone and then cooled to room temperature for 5 min. to give needles (301 mg.), m.p. 197–199° dec. The mother liquor was concentrated to produce prisms (551 mg.), m.p. 216–219° dec. The material which crystallized as needles was recrystallized for analysis from acetone: m.p. 197–199° dec., infrared absorption at 1724 and 1255 (acetate) and 3704 and 1095 cm.$^{-1}$ (11-hydroxyl).

Anal. Calcd. for $C_{32}H_{51}ClO_3$: C, 74.03; H, 9.90; Cl, 6.83. Found: C, 74.24; H, 9.78.

Recrystallization of the prisms from acetone gave pure isomeric alcohol, m.p. 216–219° dec., with infrared absorption due to acetate (1723 and 1253 cm.$^{-1}$) and hydroxyl (3731 and 1096 cm.$^{-1}$).

Anal. Calcd. for $C_{32}H_{51}ClO_3$: C, 74.03; H, 9.90; Cl, 6.83. Found: C, 74.12; H, 9.93.

3β-Acetoxy-15-chlorooleana-11,13(18)-diene (XXVIII, Y = Cl).—A mixture of epimeric 11-alcohols (100 mg.) in 10 ml. of dry pyridine was treated with 0.08 ml. of thionyl chloride at 0° with stirring. After 30 min. the resulting solution was poured into ice–water and extracted with methylene chloride. The methylene chloride was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. Recrystallization of the product from methanol furnished 44 mg. of prisms, m.p. 163–166°. A sample recrystallized once from acetone had m.p. 166–167°. Infrared absorption was noted at 1253 and 1724 cm.$^{-1}$ (acetate). The ultraviolet spectrum of this compound exhibited the characteristic 11,13(18)-diene absorption in 95% ethanol: 241, 248, and 258 mμ. This product gave a positive Beilstein halogen test.

Anal. Calcd. for $C_{22}H_{49}ClO_2$: C, 76.66; H, 9.86; Cl, 7.07. Found: C, 76.60; H, 9.88; Cl, 7.12.

Conversion of the Chlorodiene XXVII, Y = Cl, to 3β-Acetoxyoleana-11,13(18)-diene (XXVIII, Y = H).—A solution of 20 mg. of 15ξ-chlorooleana-11,13(18)-dien-3β-yl acetate in 10 ml. of 95% ethanol was heated on the steam bath with stirring with 1 g. of zinc–copper couple for 6 hr. The zinc–copper couple was prepared by shaking 100 mg. of zinc powder with 200 ml. of 1% aqueous copper sulfate, followed by washing with water and then ethanol, and was kept in ethanol. The zinc–copper couple was separated using Hyflo–Supercel by suction and washed with methylene chloride. The organic solutions were combined, poured into water, and then extracted with methylene chloride. The methylene chloride was washed with water and evaporated *in vacuo*. The product, which gave a negative Beilstein test for halogen, was dissolved in petroleum ether and chromatographed on a column of 5 g. of Florisil (100–200 mesh). Elution with petroleum ether–benzene (4:1) gave 12.6 mg. of a crystalline compound which showed strong diene absorption in the ultraviolet spectrum at 243, 251, and 260 mμ. One recrystallization from methanol furnished oleana-11,13(18)-dien-3β-yl ace-

tate, 225–227°, either alone or mixed with authentic oleana-11,13(18)-dien-3β-yl acetate. The infrared spectrum and ultraviolet spectrum [λ_{max} 243, 251, and 260 mμ (ε 26,400, 29,800, and 19,000 respectively)] were identical with those of the authentic sample.

Chlorination of XXV to give the Dichloro Ketone XXIX.—A solution of 200 mg. of XXV in 12 ml. of methylene chloride and 28 ml. of acetic acid was maintained at 0° and 100 mg. of *t*-butyl hypochlorite in 1 ml. of carbon tetrachloride was added. After 24 hr. at 0°, the solution was poured into ice–water and extracted with methylene chloride. The organic layer was washed several times with water, dried over anhydrous sodium sulfate, and evaporated *in vacuo* at room temperature. One recrystallization from acetone afforded 140 mg. of plates (66%), m.p. 270–272° dec.

A small sample was recrystallized twice from acetone and gave a pure product, m.p. 270–272° dec. The infrared spectrum in chloroform showed α,β-unsaturated carbonyl absorption at 1672 and acetate absorption at 1255 and 1724 cm.$^{-1}$. Absorption due to the α,β-unsaturated carbonyl appeared at 242 mμ (ε 10,300) (cyclohexane) in the ultraviolet spectrum. This dichloro compound gave a positive Beilsein test and showed n.m.r. peaks consistent with XXIX at δ 4.51 (2H, multiplet, H-3 and H-15) and 5.90 (1H, singlet, due to the olefinic proton at C-12).

Anal. Calcd. for $C_{32}H_{48}Cl_2O_3$: C, 69.67; H, 8.77; Cl, 12.86. Found: C, 69.78; H, 8.75; Cl, 12.94.

The dichloride XXIX (50 mg.) was dechlorinated by treatment with zinc powder in acetic acid–benzene to give the monochloro ketone XXV, identical in all respects with the specimens prepared as described above, m.p. 270–272° dec.

3β-Acetoxy-7,8;11α,12α-dioxidomultifloran-15-one (XXX).—To a stirred mixture of glacial acetic acid (600 ml.) and concentrated sulfuric acid (1.7 ml.) was added 0.875 g. of chromium trioxide in 3.6 ml. of water followed by 0.534 g. of 11α,12α-oxidotaraxer-14-en-3β-yl acetate (II-acetate) dissolved in 20 ml. of methylene chloride. After 50-min. stirring at 26° 2-propanol was added to the solution. The resulting green reaction mixture was poured into water and extracted with ether. The ether extracts were washed thoroughly with water, sodium bicarbonate (5%), and saturated sodium chloride solutions. Two recrystallizations of the product gave 7ξ,8ξ;11α,12α-dioxidomultifloran-15-on-3β-yl acetate (XXX) as needles: m.p. 344–348°; yield 0.296 g. (52%); $\nu_{max}^{CHCl_3}$ 1730, 1705, and 1260 cm.$^{-1}$; ν_{max}^{Nujol} 1725 (sh), 1715, 1680, and 1255 cm.$^{-1}$. The purified product exhibited no high intensity ultraviolet absorption above 220 mμ. The n.m.r. spectrum of the product in deuteriochloroform exhibited resonance patterns at δ 2.73 (2H), 2.91 (2H), 3.86 (1H), and 4.38 (1H).

Anal. Calcd. for $C_{32}H_{48}O_5$: C, 74.95; H, 9.43. Found: C, 74.96; H, 9.43.

3β-Acetoxymultiflora-7,9(11)-dien-15-one (XXXII, Y = O).—A solution of 5 g. of XXX in a mixture of chloroform (25 ml.) and glacial acetic acid (25 ml.) was added to a solution of hydrogen iodide in acetic acid–acetic anhydride (prepared by dissolving 60 ml. of aqueous hydriodic acid and adding this solution dropwise under nitrogen to 300 ml. of acetic anhydride with vigorous stirring. The temperature was maintained at 5–10° during the addition). The resulting solution, after addition of the above solution of XXX under nitrogen, was deep red in color; stirring was continued at room temperature for 22 hr. At the end of this time, the reaction mixture was poured onto 1 kg. of ice, adjusted carefully to pH 5 with 40% aqueous sodium hydroxide solution (400 ml.), and decolorized with sodium bisulfite solution. Extraction with ether–methylene chloride followed by the usual work-up gave a green residue which was dissolved in 40 ml. of methylene chloride and absorbed on a column of Florisil (320 g., 100–200 mesh, packed in petroleum ether). Elution with petroleum ether containing 4% diethyl ether gave, after crystallization from ethanol, 1.67 g. (34%) of crude multiflora-7,9(11)-dien-15-on-3β-yl acetate (XXXII, Y = O) as heavy prisms, m.p. 270–274°. Several recrystallizations from ethanol gave 1.13 g. of pure product exhibiting m.p. 274°; $\nu_{max}^{CHCl_3}$ 1728, 1699, and 1255 cm.$^{-1}$; ν_{max}^{Nujol} 1720, 1690, and 1250 cm.$^{-1}$; ν_{max}^{KBr} 1730, 1698, and 1250 cm.$^{-1}$; λ_{max}^{EtOH} 233 mμ (ε 13,500). The n.m.r. spectrum (60 Mc.) in deuteriochloroform exhibited characteristic peaks at 2.06 (3 H, singlet; acetate-CH_3) 4.50 (1H, multiplet; 3α-H), 5.22 (1H, multiplet; H-11), and 5.75 (1H, multiplet; H-7) p.p.m. downfield from tetramethylsilane as an internal standard.

Anal. Calcd. for $C_{32}H_{48}O_3$: C, 79.95; H, 10.06. Found: C, 79.78; H, 9.83.

Further elution of the column with petroleum ether containing diethyl ether in amounts varying from 4 to 10% gave three other minor products which are described in detail in the thesis of A.G.H.[25]

3β-Acetoxymultiflora-7,9(11)-diene (XXXII, Y = H_2).—A solution of multiflora-7,9(11)-dien-15-on-3β-yl acetate (XXXII, Y = O; 92 mg.) in diethyl ether (10 ml.) and ethanol (20 ml.) was added to a mixture of 42 ml. of diethylene glycol and 10 ml. of water containing 2.9 g. of potassium hydroxide. The mixture was heated, allowing the lower boiling solvents to escape. When the temperature of the solution had reached 140°, hydrazine (3.5 ml., 95%) was added. The flask was fitted with a condenser, and the resulting solution was refluxed for 1.25 hr. The condenser was removed and the boiling was continued until the temperature of the vapor directly above the solution had reached 192°. Refluxing was continued for 14 hr. The cooled reaction mixture was poured into water and worked up in the usual fashion. The crude product was crystallized from ethanol–water, dried, and acetylated with acetic anhydride–pyridine (9 hr., room temperature). The usual work-up procedure followed by several recrystallizations from ethanol gave multiflora-7,9(11)-dien-3β-yl acetate (XXXII, Y = H_2) as minute prisms: m.p. 227–228°; yield, 39 mg. (41%). An analytical sample, m.p. 227–228°, exhibited λ_{max}^{EtOH} 232, 238, and 247 mμ (ε 14,100, 15,300, and 9700, respectively) and ν_{max}^{Nujol} 1733 (s) and 1257 (s) cm.$^{-1}$.

Anal. Calcd. for $C_{32}H_{50}O_2$: C, 82.34; H, 10.80. Found: C, 81.69; H, 10.88.

A sample of XXXII, Y = H_2 (m.p. 228.5–229.8°), was later shown to exhibit m.p. 223–225° when admixed with a compound (m.p. 211–219.5°) obtained by selenium dioxide oxidation of multiflorenyl acetate and having essentially the same ultraviolet absorption as cited above.

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