was distilled at 119–121° (15 mm.) to yield 7.5 g. (42%) of product, $n^{19.5}$D 1.4963.

The picrate was recrystallized from methanol, m.p. 205–207°.[9]

5a,7,8,9,10,10a,11,11a - Octahydroindeno[1,2-*b*]indolizine (XVIII).—A solution of 22.5 g. (0.1 mole) of 1-(2-pyridylmethyl)-2-indanol in 100 ml. of methanol was hydrogenated with 2 g. of Raney nickel at 2000 lbs./in.^{2} and 200° for 24 hr. The product (5 g., 23%) was isolated as described above, b.p. 107–112° (0.3 mm.).

The *hydrochloride* was recrystallized from a mixture of methyl ethyl ketone, ether, and methanol, m.p. 250–251°.

Anal. Calcd. for $C_{15}H_{20}ClN$: C, 72.1; H, 8.1; N, 5.6. Found: C, 72.1; H, 7.7; N, 5.5.

1-Benzylamino-2-indanol.—A solution of 13.2 g. (0.1 mole) of 1,2-epoxyindan and 11.4 ml. (0.1 mole) of benzylamine in 100 ml. of dry benzene was heated under reflux for 22 hr. The solvent was distilled *in vacuo* and the residual material was recrystallized from dilute methanol to give 10 g. (42%) of product, m.p. 100–102°.[6]

The Constituents of *Ecballium elaterium L.* XV.[1,2] The Structures of Elatericin A and Related Cucurbitacins

DAVID LAVIE, YOUVAL SHVO, OTTO RICHARD GOTTLIEB, AND ERWIN GLOTTER

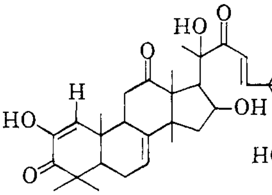
Daniel Sieff Research Institute, The Weizmann Institute of Science, Rehovoth, Israel

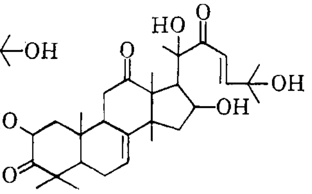
Received July 30, 1962

Elatericin A has been degraded to various compounds. The study of these degradation products labeled the final location of the inert double bond at Δ^5, the hindered carbonyl group at C-11, and a methyl group at C-9 leading to the elucidation of the structure of this substance. Three other cucurbitacins namely, elatericin B, cucurbitacin B, and elaterin, which have been correlated previously with elatericin A, are thereby identified.

In previous papers we[3] dealt with the functions of elatericin A (cucurbitacin D) and certain structures were proposed for this substance and related cucurbitacins; a sequence of experiments was described interrelating 4 of these substances.[4] On the basis of several selenium dehydrogenation experiments done by different investigators[5] as well as by ourselves,[3a,b] and in view of the nature of the side chain which was identified unequivocally during degradation, a "regular" tetracyclic triterpenoid carbon skeleton has been assigned to the cucurbitacins. Subsequently, however, it was found that the proposed structures were incompatible with certain physical and chemical properties. We wish now to describe the detailed sequence of experiments, which induced us to reallocate certain groupings of our previous formulas.

From various considerations, structures Ia and Ib had been proposed[3c] for elatericin B and elatericin A, respectively. The corresponding modified structures now presented[6] are shown in IIa and IIIa and are supported by the following observations.


Ia


Ib

The n.m.r. data for diosphenol systems[7] have indicated that when a proton is present at the γ carbon atom (allylic position) of such α,β-unsaturated α-hydroxy ketone systems, the signal located at the region $\tau \sim 4$ is a spin–spin doublet ($J \sim 2$ c.p.s.). Alternatively, if a hydrogen is not present on the γ carbon atom, a singlet is present in that region. In both cases this signal is attributed to the vinylic hydrogen of the diosphenol system. Since a doublet, centered at $\tau = 4.03$ has been found[7] for a compound formed by the air oxidation of cucurbitacin B,[8] a hydrogen atom has to be present at the γ carbon atom (C-10) of the diosphenol system which was formed during this oxidation (ring A of II). We have confirmed these observations using diosphenol containing cucurbitacins, namely elaterin (IIb), elatericin B (IIa), their acetates, and their dihydro derivatives, for all of them a doublet at the $\tau \sim 4$ region ($J \sim 2$ c.p.s.) has been recorded. It is noteworthy that a model compound, the diosphenol form of 4,4-dimethylcholestane-2,3-dione[9] (no proton at C-10) exhibited a single sharp peak at $\tau = 3.65$, and that dihydroelatericin A[10] (dihydro IIIa) in which the

---

[1] This investigation was supported by a research grant CY-2810 (C3) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] A previous version of this paper was accepted for publication, June, 1960. It was withdrawn in order to avoid unnecessary misinterpretations in the literature. Meanwhile, various communications have been published; however, for the sake of continuity we have kept the numbering of the original version; Part XIV, O. R. Gottlieb and D. Lavie, *Anais assoc. brasil quim.*, **19**, 185 (1960).

[3] (a) D. Lavie and Y. Shvo, *J. Am. Chem. Soc.*, **82**, 966 (1960); (b) D. Lavie and D. Willner, *ibid.*, **82**, 1668 (1960); (c) D. Lavie and Y. Shvo, *Chem. Ind.* (London), 403 (1960).

[4] D. Lavie, Y. Shvo, and D. Willner; P. R. Enslin, J. M. Hugo, and K. B. Norton, *ibid.*, 951 (1959).

[5] P. R. Enslin and D. E. A. Rivett, *J. Chem. Soc.*, 3682 (1956).

[6] D. Lavie, Y. Shvo, O. R. Gottlieb, and E. Glotter, *Tetrahedron Letters*, 615 (1961).

[7] C. R. Noller, A. Melera, and M. Gut; J. N. Shoolery and L. F. Johnson, *ibid.*, No. **15**, 15 (1960).

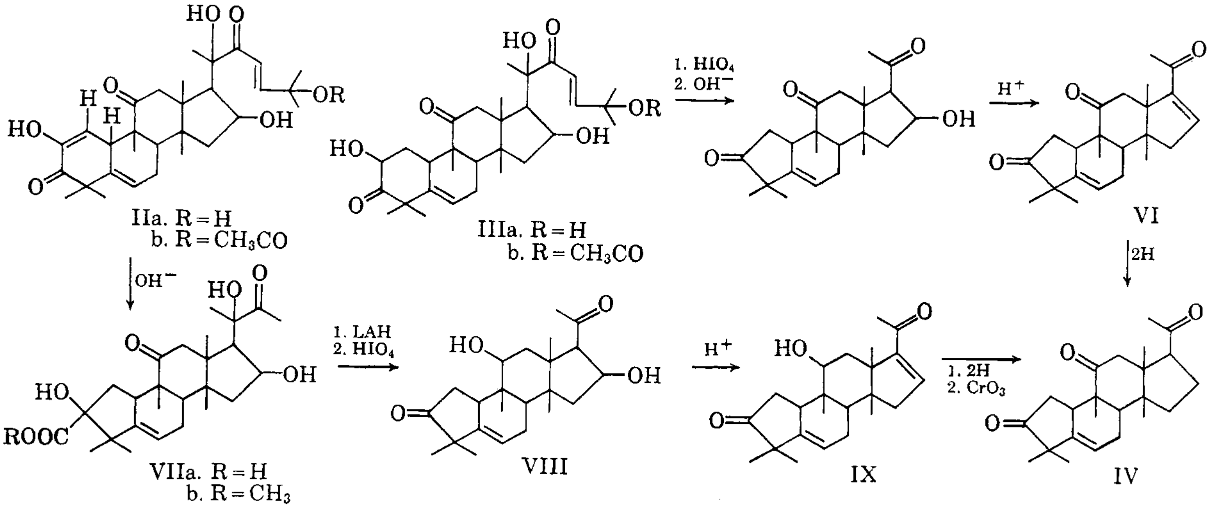
[8] Cucurbitacin B is IIIb; we have previously reported that the base catalysed autoxidation of the α-hydroxy ketone grouping in ring A resulted in the formation of a diosphenol system, *cf.* ref. 9.

[9] G. R. Chaudry, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 2725 (1961).

[10] D. Lavie and Y. Shvo, *J. Am. Chem. Soc.*, **81**, 3058 (1959).

side chain double bond is reduced and which has no unsaturation in ring A, showed no signals in this region of the spectrum. Since it is impossible to accommodate a diosphenol system with an allylic hydrogen in ring A of structure Ia, the methyl groups cannot be distributed in the usual tetracyclic triterpene pattern. One of the methyl groups at C-4 or at C-10 which normally occur there in tetracyclic triterpenes have to be transposed and the structure revised accordingly.[6]

The nature of the carbocyclic skeleton and the distribution of the methyl groups were carefully studied. The selenium dehydrogenation of elatericin A (IIIa) yielded among the various degradation products 1,2,8-trimethylphenanthrene.[3a] This product was also reported from the dehydrogenation of various cucurbitacins[5] and is a well established degradation product for tetracyclic triterpenes. There were earlier descriptions of 1,4-dimethylnaphthalene being obtained by the zinc distillation as well as by selenium dehydrogenation of elaterin.[11] We have attempted unsuccessfully to isolate this derivative from the complicated mixture of the dehydrogenation reactions. However, the only naphthalene derivative which could now be identified is 1,2,5-trimethylnaphthalene. It has been reported that this naphthalene derivative has been obtained in at least two instances, from folienetriol[12a] and from isoeuphol,[12b] both being tetracyclic triterpenes with a methyl group between rings B and C. It is remarkable that no 1,2,8-trimethylphenanthrene was detected in the dehydrogenation mixtures of these substances. The concurrent formation of these two products from elatericin A (IIIa) was unique and implied an unusual distribution of the methyl groups in the tetracyclic skeleton. The formation of the phenanthrene derivative indicated the presence of three methyl groups at the 4, 13 and 14 positions of the steroid skeleton, while the naphthalene derivative pointed toward the presence of a methyl group between rings B and C, assuming that this system was originated from rings A and B. No alternative was deemed acceptable. Corroborative evidences were adduced in support of these assumptions.



The experiments outlined below were performed on 16-desoxy-A(2)-norhexanorelatericin A (IV). This product was preferred to substances with the six-membered ring A, due to the absence of the unstable α-hydroxy ketone grouping. Compound IV was prepared by oxidation of elatericin A (IIIa) with two moles of periodic acid, thereby severing the side chain and cleaving ring A. Cyclization to the A(2)-nor ring (V) was effected by heating in sodium carbonate solution, while treating this reaction product with *p*-toluenesulfonic acid in benzene, induced elimination of the hydroxyl group at C-16 yielding VI.[3a] The resulting Δ^{16} has been now hydrogenated over palladium to the triketone IV. Because of the importance of this product, it was felt that further support should be adduced in order to ascertain its structure. It has been therefore prepared by a complete different route, starting from ecballic acid (VIIa). This acid, which has already been described,[13] is obtained by the base treatment of either elaterin (IIb) or elatericin B (IIa); during this reaction, ring A is contracted through a benzilic acid type rearrangement, while the α,β-unsaturated ketone in the side chain suffers hydrolytic splitting.[3b] Esterification of ecballic acid to methyl ecballate

---

[11] Ch. W. Moore, *J. Chem. Soc.*, **97**, 1797 (1910); L. Reichel and K. H. Eisenlohr, *Ann.*, **531**, 287 (1937). A careful comparison of the physical constants of 1,4-dimethylnaphthalene and 1,2,5-trimethylnaphthalene revealed close similarity between the two compounds and their derivatives; it is believed that the compound formerly isolated by these authors might have been the trimethyl derivative. The picrates have been used for identification, and we note for the dimethyl- and trimethylnaphthalenes the respective m.p. 143–144° and 139–142°.

[12] (a) F. G. Fisher and N. Seiler, *Ann.*, **626**, 185 (1959); (b) D. H. R. Barton, J. F. McGhie, M. K. Pradhan, and S. A. Knight, *J. Chem. Soc.*, 876 (1955).

[13] D. Lavie and S. Szinai, *J. Am. Chem. Soc.*, **80**, 707 (1958).

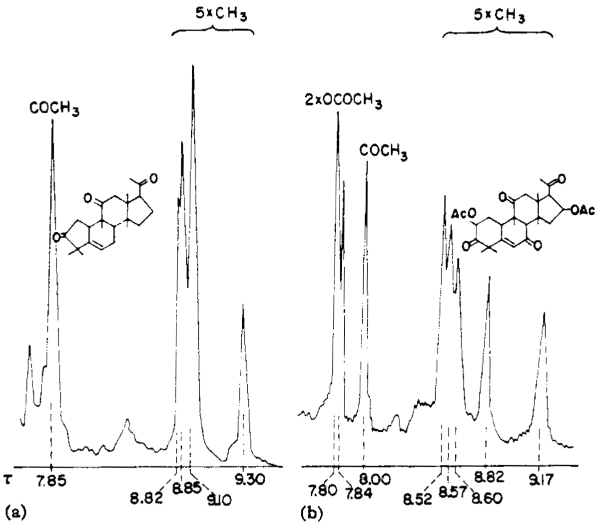
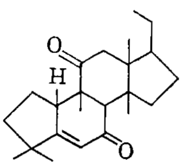


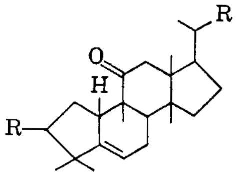
Fig. 1.—N.m.r. spectrum in chloroform-*d* of methyl region: (a) compound IV; (b) compound XIII.

(VIIb),[13] followed by reduction with lithium aluminum hydride, yielded an amorphous product in which all carbonyl groups were reduced, as was indicated by the infrared spectrum. When this amorphous product was treated with periodic acid, substance VIII was formed for which the infrared spectrum indicated the presence of a ketone in a five-membered ring (1742 cm.$^{-1}$) and the expected C-20 methyl ketone (1706 cm.$^{-1}$). Here again upon treatment with *p*-toluenesulfonic acid in boiling benzene, dehydration of the C-16 hydroxyl group took place yielding the Δ^{16} derivative (IX) with the appropriate spectral properties. It is noteworthy that this elimination reaction could be induced with a variety of acid as well as basic reagents. The newly formed double bond was subsequently hydrogenated over palladium and the product was then oxidized with chromium trioxide in acetone. The resulting compound was found identical in all respects with the triketone IV obtained above. The formation of an identical product from such two different reaction sequences confirms the proposed formulation, and specially the structure of the A-nor ring.

The n.m.r. spectra of 16-desoxy-A(2)-norhexanorelatericin A (IV) and of 7-oxohexanorelatericin A-2,16-diacetate (XIII)[14] (Fig. 1), as well as of various other degradation products in which the side chain was removed, showed signals accounting for five methyl groups. An additional strong peak recorded at $\tau = 7.92$ is related to the C-21 methyl ketone formed during the severance of the side chain. In no case could any splitting of these signals be observed, eliminating thereby the possible occurrence of a secondary methyl system ($>CHCH_3$). Five *angular methyl* groups are therefore attached to the carbocyclic skeleton of the cucurbitacins. Inasmuch as one methyl group has already been assigned to C-4 (see above), in order to satisfy the n.m.r. requirement for the absence of a $>CHCH_3$ grouping, an additional methyl has to be attached at C-4, forming thereby a *gem*-dimethyl structure. Indeed, the presence of such a group in the molecule was substantiated by three absorption bands in the infrared spectrum of the monoketone XI at 1384, 1377, and 1367 cm.$^{-1}$. The splitting of the hydrogen deformation bands at 1384 and 1377 are in good agreement with the previously recorded observations for the presence of *gem*-dimethyl groups.[15] The monoketone XI was chosen for this measurement in order to eliminate the absorption of the methyl ketone which masks this region of the spectrum. It was prepared by desulfurisation of the bisthioketal XII. The characterization of the two methyl groups at C-4 and the required presence of a proton adjacent to the diosphenol vinylic proton from n.m.r. data afford only a single arrangement of the diosphenol grouping in ring A with a hydrogen atom at C-10, as shown in II.



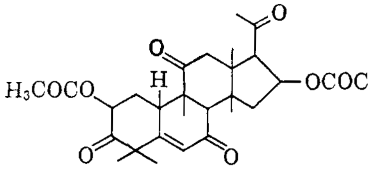
XIa



X. R = $<\begin{smallmatrix}O-CH_2\\ |\\ O-CH_2\end{smallmatrix}$

XI. R = H

XII. R = $<\begin{smallmatrix}S-CH_2\\ |\\ S-CH_2\end{smallmatrix}$



XIII

In view of the above deductions, three tertiary carbon positions are left to be considered for the location of the remaining methyl group excluded from C-10, namely position 5, 8 and 9. In order to establish the position of this methyl group, the n.m.r. spectrum of substance XVb was studied. This product was prepared by ketalization of IV resulting in the formation of the bisethylene ketal, shown in X. The hindered carbonyl group remained unaltered as shown by the infrared spectrum in the carbonyl region of this bisketal which had one sharp band at 1698 cm.$^{-1}$. For further reference, there is in that spectrum, a weak band at 805 cm.$^{-1}$ related to a trisubstituted double bond.[16] It is noteworthy that in the bisethylene ketal (X) the two systems in rings B and C, the double bond and the carbonyl group, could now

---

(14) "Ketone A" in article by W. Schlegel, A. Melera, and C. R. Noller, *J. Org. Chem.*, **26**, 1206 (1961).

(15) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen & Co. Ltd., London, 1958, p. 24.

(16) A. R. H. Cole and D. W. Thornton, *J. Chem. Soc.*, 1332 (1957).

be studied spectroscopically, without interference of the other oxygenated functions of the molecule. This bisketal X was reduced with lithium aluminum hydride, a reagent which reduced the ring C hindered carbonyl to the corresponding alcohol XIV. This alcohol was then submitted to dehydrating conditions forming thereby a new double bond in ring C as shown in XV; subsequent hydrolysis of the ketals yielded XVb. This product possessed a diene in a nonconjugated form, as no maximum of absorption was found in the ultraviolet; however, its infrared spectrum showed a strong new band at 740 cm.$^{-1}$ due to the out of plane hydrogen deformation of the *cis*-disubstituted ethylene.[17] Also present was the band at 805 cm.$^{-1}$, mentioned above, for the C—H at C-6 of the trisubstituted double bond, as well as bands at 1735 and 1708 cm.$^{-1}$ related to the five-membered ring carbonyl and the methyl ketone, respectively.[18] The n.m.r. spectral evidences for XV were instructive, since they offered means to study the nature of the two carbon atoms adjacent to the newly formed ethylenic linkage. A symmetrical AB pattern[19] of lines was observed, forming two doublets centered at τ = 4.72 and 4.00 with equivalent splitting (J_{AB} = 10 c.p.s.) (Fig. 2a). Such a pattern of lines was expected for a system of 2 vinylic protons as at 11 and 12 having no vicinal protons for further splitting of the signals by spin-spin coupling. This observation indicates that *both carbon atoms 9 and 13* are quaternary and support methyl groups. A wide and nonresolved band was also observed in the vinylic hydrogen region at τ = 4.37. This signal is related to the C-6 proton, and it is unresolved because of spin-spin interaction with the two protons at C-7, and with the allylic proton at C-10 (it is noteworthy that the cucurbitacins, as well as compound IV, all exhibit an identical band in this region). In order to indicate the relationship of this unresolved band to the vinylic hydrogen at C-6, the n.m.r. spectrum of substance XVI, obtained by the allylic oxidation of XV, was analyzed. Substance XVI has the following characteristics: ν_{max}^{KBr} 1750 (five-membered ring ketone), 1709 (C-20 carbonyl), 1661 (conjugated carbonyl), 1653 (conjugated double bond), 745 (*cis*-substituted double bond) cm.$^{-1}$; λ_{max} 242 mμ (ϵ 8,720); its n.m.r. spectrum (Fig. 2b) showed again the four line system of the two Δ^{11} protons, while the original unresolved peak appears now as a doublet, τ = 4.04 (J = 2 c.p.s.). The downfield shift of the original signal is pertinent to the deshielding ability of the carbonyl group. The n.m.r. of this

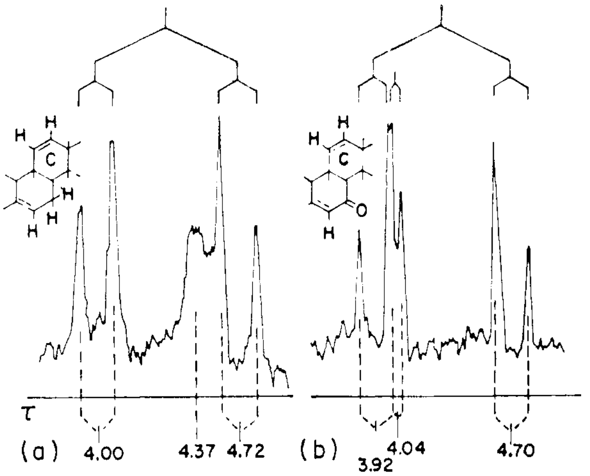


Fig. 2. –N.m.r. spectrum in chloroform-*d* showing the vinylic protons of: (a) compound XV; (b) compound XVI.

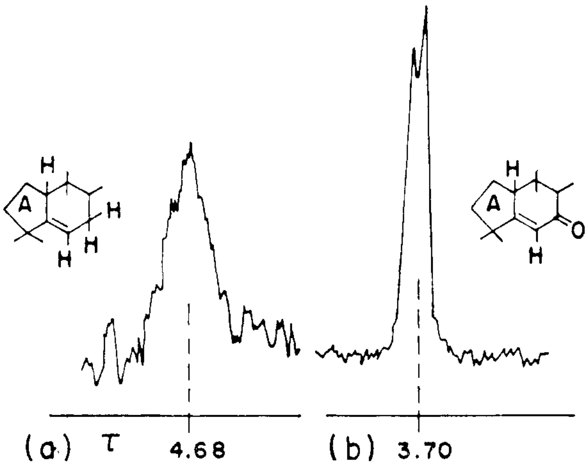
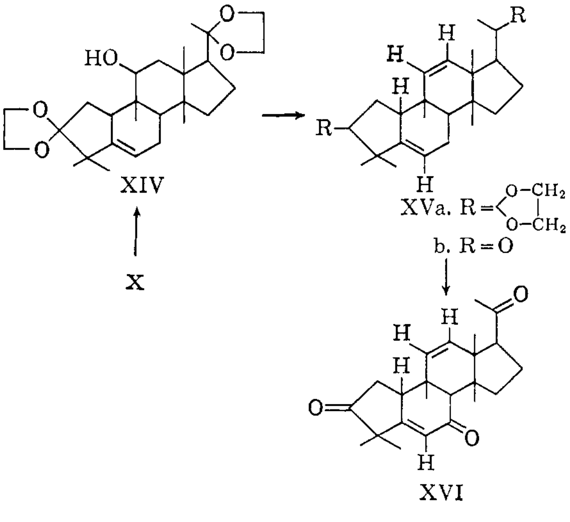


Fig. 3.—N.m.r. spectrum in chloroform-*d* showing the C-6 vinylic proton of: (a) compound XI; (b) compound XIa.



XIV

X

XVa. R = $<\begin{smallmatrix}O-CH_2\\ \vert\\ O-CH_2\end{smallmatrix}$

b. R = O

XVI

---

[17] Ref. 15, p. 48.

[18] Regarding substance XVb, we have previously reported two isomerization reactions leading to a homoannular and a heteroannular diene in rings B and C, from two different reactions (ref. 3c substance V, and D. Lavie, Y. Shvo, and O. R. Gottlieb, *Tetrahedron Letters*, No. **22**, 23 (1960), substance X). These isomerizations which require a free access at the C-9 position cannot be accomodated with the new structure now presented. However, because of the formation of these two substances having the ultraviolet spectra as reported, it is now assumed, that possible skeletal changes might have occurred under the conditions of the reactions reported there. These reactions will be further investigated.

[19] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, New York, N. Y., 1959, p. 89.

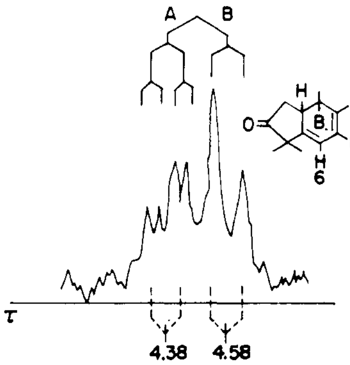


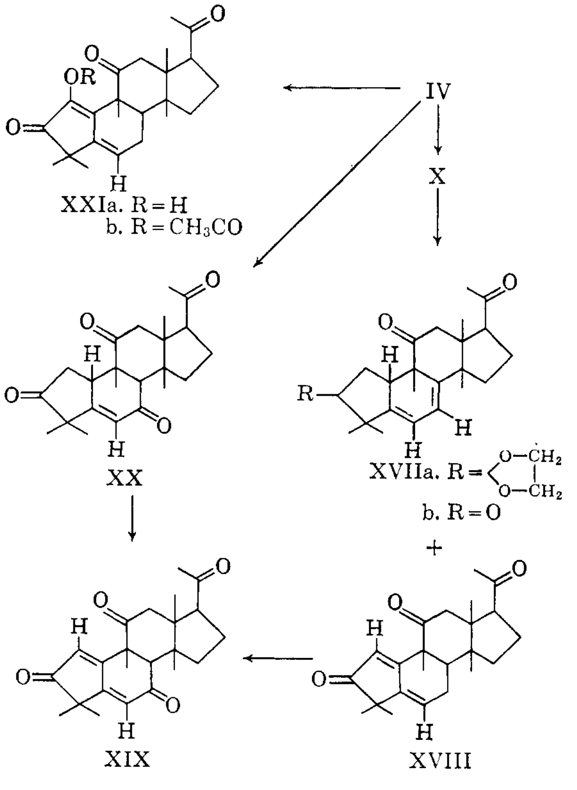
Fig. 4.—N.m.r. spectrum in chloroform-*d*, the *ABX* pattern of the two vinylic protons (C-6 and C-7) in substance XVIIb.

system was further studied without interference of the signals from the Δ^{11} protons. While the monoketone (XI) exhibited a broad and nonresolved band at $\tau = 4.68$ (Fig. 3a), its allylic oxidation product (XIa) gave rise to a neat doublet at $\tau = 3.70$ ($J = 2$ c.p.s.) (Fig. 3b). The introduction of the oxygen at C-7 eliminated the spin–spin coupling of the original two C-7 protons with the vinylic hydrogen which now couples its spin only with a single allylic hydrogen present at C-10, leading therefore to the expected doublet. This observation indicates an assignment of the original inert double bond in ring B at Δ^5.

In order to ascertain the location of the inert double bond in our system, N-bromosuccinimide reacted with the bisketal X to induce allylic bromination; during the reaction, evolution of hydrobromic acid took place. The crystalline product gave a brown color with tetranitromethane and its ultraviolet spectrum showed a maximum at 275 mμ (ϵ 7,800). Such a maximum corresponds to a homoannular diene system. Among the various possible alternatives for its location in rings B and C, the infrared spectrum of the product pointed toward the $\Delta^{5,7}$ position only. A strong band recorded at 820 cm.$^{-1}$ is due to the bending vibrations of the two C—H groups at C-6 and C-7 of the two trisubstituted double bonds[20a] (XVIIa). No absorptions were recorded at about 700 cm.$^{-1}$ for a *cis*-disubstituted ethylene.[20b] In order to study the n.m.r. of this system the compound XVIIa was hydrolysed to triketone XVIIb. The n.m.r. spectrum of this compound (Fig. 4) indicated an *ABX* system,[21] the *AB* lines being centered at $\tau = 4.58$ and 4.38 ($J_{AB} = 4$ c.p.s., $J_{AX} = 2$ c.p.s., $J_{BX} = 0$) and are attributed to the two vicinal vinylic protons. Since only one of these doublets was further split by about 2 c.p.s. (J_{AX}), the *X* part of the system constitutes the only allylic proton which flanks this diene system, as indicated by the magnitude of the coupling constant. This allylic proton may now be identified with the hydrogen atom previously demonstrated to exist at the C-10 position of formula (IIa). Consequently, C-9 (as well as C-13) appears to be quaternary and occupied by a *methyl group*, and therefore only structure XVII can represent this diene.

In connection with the reaction with N-bromosuccinimide, it is noteworthy that because of prevailing acidic conditions resulting from the emanating hydrobromic acid, hydrolysis of one ketal occurred. That only one of the ketals was hydrolysed was indicated by the analytical data of the reaction product, while the infrared spectrum indicated that it was the C-20 ketal which was attacked. Furthermore a comparison of the areas enclosed by the band at 1700 cm.$^{-1}$ of the reaction product XVIIa and by the band at 1698 cm.$^{-1}$ of the starting material (*X*), both having the same concentration in chloroform solution, indicated a ratio of two to one, respectively. Two carbonyl groups are therefore superimposed in the band at 1700 cm.$^{-1}$ of the reaction product (XVIIa); they are the hindered carbonyl and the C-20 ketone.

Careful chromatography of the N-bromosuccinimide reaction mixture yielded a second product which accompanies the homoannular diene XVII in rather minor quantities. Structure XVIII, which corresponds to the alternative allylic bromination, namely the C-10 position, followed by dehydrobromination was assigned to this product. Its infrared spectrum in the carbonyl region showed one strong band at 1707 cm.$^{-1}$ related to the three carbonyls present in the molecule. This lowering of the five-membered ring ketone absorption band,



---

(20) (a) Ref. 15, p. 51; (b) ref. 15, p. 48.

(21) Ref. 19, p. 90.

which is present in IV (1742 cm.$^{-1}$), clearly indicates that it is the five-membered ring carbonyl which underwent conjugation. Its ultraviolet spectrum $\lambda_{\max}$ 289 mμ (ϵ 9,000) is consistent with the calculated value. This structure was further supported by oxidation of XVIII with chromium trioxide in acetic acid yielding a yellow crystalline substance, $C_{23}H_{28}O_4$, m.p. 176–178°, $\lambda_{\max}$ 282 mμ (ϵ 18,700); $\nu_{\max}$ 1717, 1709, 1666, and 1569 cm.$^{-1}$ to which formula XIX is ascribed. Its n.m.r. spectrum showed two doublets at low field centered at $\tau = 3.79$ and 3.92 ($J = 1$ c.p.s.) which are related to the two vinylic protons which couple their spins, presumably through the conjugated system (Fig. 5). Such an allylic oxidation of the nuclear trisubstituted double bond has been encountered in this series of compounds.[22] The same yellow substance has been obtained by a quite different route. The triketone IV was oxidized with chromium trioxide resulting in the formation of an α,β-unsaturated ketone in ring B of structure XX: $\nu_{\max}$ 1665 cm.$^{-1}$ and $\lambda_{\max}$ 242 mμ (ϵ 8,800). When this substance (XX) was treated with sodium methoxide in methanolic solution at room temperature, oxidation took place yielding the same yellow crystalline substance XIX, identified by all its properties. This reaction, which is rather surprising, can be explained by analogy to the recently investigated base-catalyzed autoxidation of 1,4-diketones to enediones.[23] The system in rings A and B of XX which upon treatment with base yields the dienedione (XIX), is actually a 2-ene-1,6-diketone and bears a vinylogous relationship to the 1,4-diketone referred above. It may be assumed therefore that these two reactions proceed by similar mechanisms.

A second oxidation reaction which defined the environment of the ketone group in the A(2)-nor ring was done when compound IV was autoxidized in benzene solution containing *tert*-butyl alcohol saturated with potassium *tert*-butoxide.[24] Introduction of an oxygen atom at C-1 resulted in formation of a diosphenol chromophore in the amorphous reaction product XXIa as was shown by its spectroscopic and chemical properties. Upon acetylation at room temperature, a crystalline substance was obtained which was well characterized (XXIb): $\nu_{\max}$ 1773 (enol acetate), 1706 cm.$^{-1}$ and $\lambda_{\max}$ 291 mμ (ϵ 10,900); the n.m.r. spectrum of this substance showed for the C_6-vinylic proton, a quartet of lines as expected from the interaction of the two vicinal hydrogen atoms at C-7. It is noteworthy that the monoketone (XI), when treated under the same reaction conditions, was recovered unchanged indicating the unreactive nature of the ring C carbonyl. Since no band was recorded for a ketone in a saturated five-membered ring, it can be deduced that oxidation took place at the C-1 position, this leading to the formation of the diosphenol system.

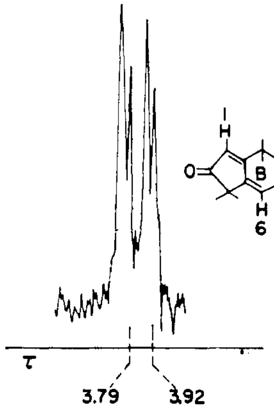


Fig. 5.—N.m.r. spectrum in chloroform-*d* indicating the coupling of the two vinylic protons C-1 and C-6 in compound XIX.

A sequence of experiments described earlier involved the hydroxylation with osmium tetroxide of the nuclear double bond in ring B. The triketone IV was used for this reaction, which lasted one week and resulted in the formation of a 1,2-glycol system. That one only of the hydroxyl groups is secondary (XXIIa) was shown by acetylation of the glycol to a monoacetate (XXIIb), the infrared spectrum of which showed a band at 3450 cm.$^{-1}$ for the tertiary hydroxyl. Furthermore, the secondary hydroxyl group was oxidized with chromium trioxide to a ketone, the oxidation product being a hydroxy tetraketone (XXIII). When heated to reflux in benzene with *p*-toluenesulfonic acid, XXIII underwent dehydration. Instead of the expected unsaturated tetraketone XXIV, the spectroscopic evidences of the yellow reaction product pointed towards the presence of its enolic isomer XXVa: $\lambda_{\max}$ 335 mμ (ϵ 10,300), and 405 mμ (ϵ 3,100), $\lambda_{\max}^{1\%\ \mathrm{KOH}}$ 405 mμ (ϵ 21,700), $\nu_{\max}$ 3500, 1750 (weak), 1700, and 1660 cm.$^{-1}$. The product was easily soluble in sodium carbonate, and upon acetylation yielded a monoacetate, which was identified as the enol acetate XXVb. The maximum of absorption in the ultraviolet: $\lambda_{\max}$ 290 mμ (ϵ 25,800), compared to the main maximum of the starting material in neutral solution (335 mμ), was shifted to shorter wave lengths by 45 mμ. Such a hypsochromic shift is characteristic for the conversion of the enols to their esters.[25] This enol acetate (XXVb) could also be characterized in the infrared by a new band at 1765 cm.$^{-1}$ which corresponds to such a system. To accommodate the requirements of the new chromophore and its chemical behavior, we propose therefore for the yellow reaction product the structure shown in XXVa. This system is the enol form of the

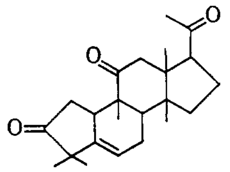
---

[22] P. R. Enslin, J. M. Hugo, K. B. Norton, and D. E. A. Rivett, *J. Chem. Soc.*, 4779 (1960).

[23] W. G. Dauben, G. A. Boswell, and W. Templeton, *J. Org. Chem.*, **25**, 1853 (1960).

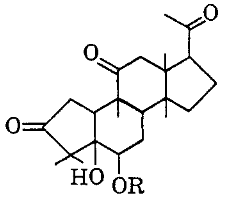
[24] R. Hanna and G. Ourisson, *Bull. soc. chim. France*, 1945 (1961).

[25] L. Dorfman, *Chem. Revs.*, **53**, 79 (1953).



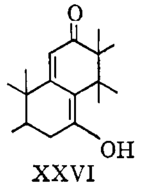
IV

→

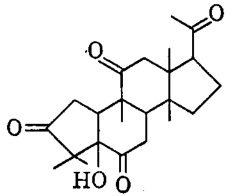


XXIIa. R = H
b. R = CH_3CO

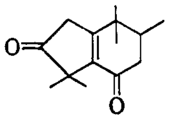
↓



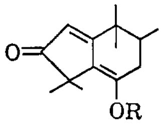
XXVI



XXIII



XXIV

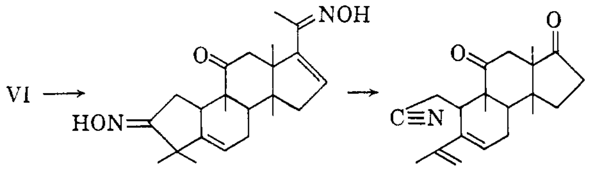


XXVa. R = H
b. R = CH_3CO

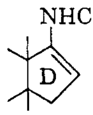
ene-1,5-diketone XXIV. A similar system having a similar ultraviolet spectrum, has been described previously in rings A and B of steroids.[26]

A different structure (XXVI) previously has been proposed by us for this reaction product, from which formulations I were then deduced.[3c] This structure was consistent with the observation of the infrared band at 1750 cm.$^{-1}$ which was believed then to be indicative of a nonconjugated five-membered ring ketone in the molecule. However, careful comparisons of the absorption intensities of the different bands indicated that this band is in fact of a much weaker intensity than would be expected for a carbonyl group. This was also true for the intensity of the band at 1660 cm.$^{-1}$ which is now related to the α,β-unsaturated carbonyl at C-6 (XXIV). The spectrum of the reaction product was measured in chloroform, and apparently, the solution must contain a mixture of the two tautomeric forms XXIV and XXVa. Indeed when this product was acetylated, XXVb was obtained in pure form, its infrared spectrum showed the following major bands: 1765 (enol acetate), 1707 (strong), 1557 cm.$^{-1}$. No absorption band for a saturated five-membered ring ketone was observed, nor were indications present for an α,β-unsaturated carbonyl in a six-membered ring (XXIV). The n.m.r. spectrum of XXVb showed a single line at $\tau = 4.45$ for the vinylic proton situated at C-1.

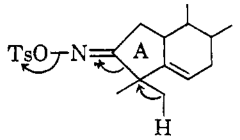
Summing up, the various reactions and spectral evidences require the presence of a hydrogen atom at C-10 instead of the usual methyl group situated there. In these reactions the ring B double bond was conjugated directly with the ketone of the A(2)-nor ring. It can be deduced therefore that it is situated at Δ^5 while free access should be retained for conjugation between rings A and B through carbon atom 10.



XXVII XXIX



XXVIIIa



XXVIIIb

An experiment which established the relationship between the double bond in ring B and the *gem*-dimethyl in ring A is described in the following sequence. Substance VI, Δ^{16}-desoxy-A(2)-norhexanorelatericin A, was treated with hydroxylamine hydrochloride in order to form the 3,20-bisoxime shown in XXVII. This was a crystalline substance with *one* sharp band in the infrared at 1692 cm.$^{-1}$, while in the ultraviolet spectrum a band at 239 mμ (ϵ 13,000) was recorded for the conjugated oxime system attached to ring D. This bisoxime was then treated with *p*-toluenesulfonyl chloride in order to induce a Beckmann rearrangement. From the conjugated oxime attached at C-20 the expected eneamine was formed (XXVIIIa) which through subsequent hydrolysis at room temperature resulted in the C-17 ketone[27] shown in XXIX. It was expected that at the same time the oxime at C-2 would rearrange, forming thereby a lactam structure in a six-membered ring. However, the resulting reaction product, although in low yield, was different. Structure XXIX derived from the abnormal Beckmann rearrangement[28] of the oxime *p*-toluenesulfonate (XXVIIIb) was assigned to the product on the basis of the following evidences: ν_{max}^{KBr} 2243 (nitrile), 1740 (C-17 ketone), 1705 (C-11 ketone), 1652, 1620 (both for double bonds), 900 ($>C = CH_2$) and 837 (C_6—H) cm.$^{-1}$; furthermore, a single band was recorded in this spectrum at 1379 cm.$^{-1}$ for the methyl groups. Had a *gem*-dimethyl group been present, this band would have been split as described above. The maximum of absorption at 229 mμ (ϵ 9,000) is related to the conjugated diene system, and ultimately the analytical data accounted for one nitrogen atom only in the molecule. Certain selected signals of the n.m.r. spectra of compound XXIX, which are

---

(26) R. H. Lenhard and S. Bernstein, *J. Am. Chem. Soc.*, **78**, 989 (1956).

(27) G. Rosenkranz, O. Mancera, and F. Sondheimer, *J. Org. Chem.*, **21**, 520 (1956).

(28) G. H. Whitham, *J. Chem. Soc.*, 2016 (1960), and ref. 11 cited therein.

shown in Fig. 6, support the proposed structure. The wide and unresolved band at $\tau = 4.13$ is related to the C_6—H while the 5.10 and 5.30 signals are due to the two C-30 terminal methylenic protons. The peaks related to the various methyl groups are also shown, they account for four methyl groups only, in contradistinction to the five peaks of the previously described degradation products. Furthermore, the location of the peak $\tau = 8.04$ corresponds to the vinylic methyl group of C-4.

In the triterpene literature, such a Beckmann rearrangement of a 3-ketoxime, and the formation of an unsaturated nitrile has been reported in the β-amyrin series, as well as for a 2,2-disubstituted cyclic ketone.[28] In our experiment the formation of the conjugated diene supported once more the location of the double bond, while the resulting methyl vinyl system is best explained as originating from a *gem*-dimethyl group at carbon atom 4, as postulated from our previous observations.

The carbonyl group of ring C remained to be located. We have previously favored the C-11 position on spectroscopic grounds.[3a,b] However, various chemical developments described later induced us to consider the C-12 position for this carbonyl group[3c] (*cf.* I). In view of the present description, two positions were left for consideration namely C-11 or C-12. The spectroscopic evidences are today the only data available for the assignment of this group; they require its location at C-11. The ultraviolet spectrum of Δ^{16}-desoxy-A-(2)-norhexanorelatericin A (VI) has been reported[3a] as λ_{max} 240 mμ (ϵ 8,500). A review of the literature[29] indicates that in steroids while Δ^{16}-11,20-diketone systems have a maximum of absorption at 240 mμ, Δ^{16}-12,20-diketones absorb at 230 mμ. The hypsochromic shift brought about by the ketone at C-12 has been explained as being due to the increased energy of excitation required for the favored S-*trans* configuration of the α,β-unsaturated carbonyl function wherein the two carbon–oxygen dipoles in the excited states are then directly opposed.[29] No such interaction occurs if the ketone is at C-11. Furthermore the infrared band attributed to the α,β-unsaturated carbonyl group at C-20 of VI is at 1666 cm.$^{-1}$, while this group in steroids in which the ring C carbonyl is located at C-12 has been found to be in the 1670–1680 region, and is therefore influenced by the interaction between these groups. It is deduced therefore from the above spectral data that the ketone in ring C is at C-11.

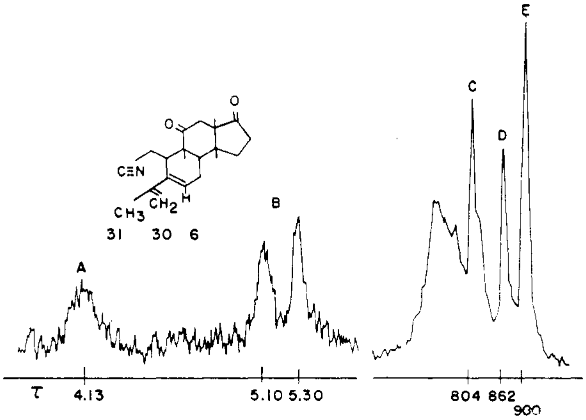
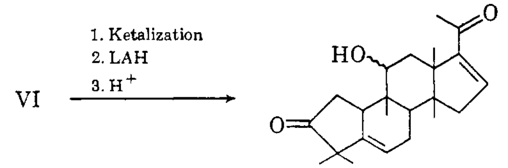


Fig. 6.—N.m.r. spectrum of compound XXIX in chloroform-*d*: *A*, C-6 proton; *B*, C-30 methylene protons; *C*, C-31 methyl protons; *D* and *E* are for 3 methyl groups. The two spectra are not on the same scale.

Additional support in favor of the C-11 position was obtained by studying the epimeric hydroxy compounds XXX. They were obtained by reducing with lithium aluminum hydride the bis-3,20-ethylene ketal of VI, thereby converting the ketone in ring C to the corresponding hydroxyl group. Following the hydrolysis of the ketals, the two epimeric alcohols of XXX were isolated from the reaction mixture by chromatography. The infrared spectrum of each substance in dilute carbon tetrachloride solution showed one band only at 3640 cm.$^{-1}$ for a free hydroxyl group. The capacity of a hydroxyl group at C-12, when equatorial, to form a hydrogen bond with an α,β-unsaturated C-20 carbonyl group has been studied on the 12-methyl hemiketals derived from pregnene derivatives.[30] The influence of such intramolecular bonding has been found to result in an absorption band at 3340 cm.$^{-1}$ which does not concur by any means to the observed absorption of the presently investigated hydroxyl derivatives. When the hydroxyl group is situated at C-11, no hydrogen bonding should occur. Further support for the absence of hydrogen bonding was derived from the fact that the absorption band in the infrared of the C-20 α,β-unsaturated ketone in both epimers have the same location (1666 cm.$^{-1}$). We conclude therefore that no hydrogen bonding of the hydroxyl group occurs in either epimer and that the location of the hydroxyl group is therefore at C-11.



XXX

In view of these observations and this evidence we propose to revise the structures of elatericin B and elaterin to IIa and IIb, respectively. Consequently elatericin A and cucurbitacin B, which have been previously correlated to these substances have now structures IIIa and IIIb. The stereochemistry of the cucurbitacins will be presented in the following paper; the formulas as written here are without stereochemical implications.

---

[29] G. P. Mueller, R. E. Stobaugh, and R. S. Winniford, *J. Am. Chem. Soc.*, **75**, 4888 (1953).

[30] M. E. Wall and S. Serota, *Tetrahedron*, **10**, 238 (1960).

Experimental

Melting points were taken on a Kofler hot-stage microscope and are corrected. Optical rotations have been measured in chloroform solution. Ultraviolet absorption spectra were done on a Unicam model S.P. 700 recording spectrophotometer in methanol solution. Infrared spectra were recorded on a Perkin–Elmer Infracord Model 137 spectrophotometer equipped with sodium chloride prism. Unless otherwise stated all spectra were determined in chloroform solution of about 5–10% concentration. N.m.r. spectra were recorded on a Varian high resolution n.m.r. spectrometer, Model V-4300-B operating at 60 Mc. The spectra were determined in deuterated chloroform solutions of about 5–10% concentration and containing tetramethylsilane as internal standard. Calibration was done by sideband technique. The line positions given are τ values. In the chromatographies, activated alumina refers to Alcoa F-20.

16-Desoxy-A(2)-nor-hexanor-elatericin A (IV).—Δ^{16}-Desoxy-A(2)-norhexanorelatericin A[3a] (VI) (480 mg.), in ethanol (60 ml.), was hydrogenated over 5% palladium-on charcoal. The absorption stopped when 35 ml. of hydrogen was absorbed (calculated 32 ml.). The catalyst was filtered and the solvent evaporated to dryness. The solid residue was crystallized from ether–hexane; 300 mg., m.p. 177–179°. This product was dissolved in benzene, and chromatographed on activated alumina (25 g.); the column was developed with benzene (250 ml.), ether–benzene 1:9 (250 ml.), and ether–benzene 1:3. A crystalline product emerged with the last solvent mixture. It was crystallized from ether, m.p. 179–181°, $[\alpha]_D + 95°$ (c 1.54); no maximum of absorption in the ultraviolet; ν_{max} 1704 (overlapping of C-11 and C-20 ketones), 1742 (five-membered ring ketone) cm.$^{-1}$; yellow coloration with tetranitromethane; n.m.r. 9.30, 9.10, 9.10, 8.85, 8.82 (5 methyls), 7.85 (methyl ketone), 4.43 (C_6—H, broad).

Anal. Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.43; H, 9.00.

Preparation of Diketone VIII from Methyl Ecballate (VIIb).—A solution of methyl ecballate[13] (VIIb) (4.8 g.) in dry tetrahydrofuran (300 ml.) was added during 1 hr. to a suspension of lithium aluminum hydride (10 g.) in tetrahydrofuran (250 ml.). The mixture was boiled for 40 hr. with stirring, and then decomposed by adding ethyl acetate and a saturated aqueous solution of sodium sulfate. Inorganic salts were removed by filtration, washed with ethyl acetate, and the combined filtrate was dried over sodium sulfate. Evaporation of the solvent to dryness yielded an amorphous powder (4.2 g.) which did not show any carbonyl stretching absorption in the infrared spectrum.

This substance (4.2 g.) in dioxane (200 ml.) was added to periodic acid (8 g.) in water (120 ml.) and left overnight at room temperature. Excess periodic acid was destroyed with ethylene glycol (2 ml.), and the resulting mixture was concentrated under reduced pressure to about half of its original volume, then diluted with water (150 ml.), and extracted with chloroform (3 × 70 ml.). After drying over sodium sulfate, and evaporation of the solvent, an oil (3 g.) was obtained which failed to crystallized, and was identified as VII ν_{max} 1742 (five-membered ring ketone), 1706 (C-20 ketone), cm.$^{-1}$.

Dehydration of VIII to IX.—A solution of VIII (1.5 g.) and *p*-toluenesulfonic acid (100 mg.) in dry benzene (200 ml.) was heated under reflux during 2 hr. using a water collector for the azeotrope. The solution was then washed with water, dried over sodium sulfate, and evaporated to dryness yielding an amorphous powder (1.1 g.) which was identified as IX; ν_{max} 1744 (five-membered ring ketone), 1660 (C-20 ketone), 1590 (C-16 double bond) cm.$^{-1}$.

Conversion of IX to IV.—Hydrogenation of the above crude product was performed in ethanol (150 ml.) using palladium on charcoal as catalyst. Absorption of hydrogen ceased after consumption of 80 ml.; the catalyst was filtered and the solvent evaporated leaving a white powder (0.9 g.). A chloroform solution of the reduced substance was percolated through a column of activated alumina (40 g.) yielding a semicrystalline product (0.55 g.); ν_{max} 1742 (five-membered ring ketone), 1700 (C-20 carbonyl) cm.$^{-1}$.

The above substance was then oxidized (0.5 g.) in acetone solution (50 ml.), in an ice bath with chromium trioxide (27 g. chromium trioxide in 100 ml. of a 35% aqueous solution of sulfuric acid) until a brown coloration persisted. Excess oxidant was then decomposed with methanol, the solvent removed under reduced pressure, and water (100 ml) added to the residue. The product was extracted with chloroform (100 ml.), washed, dried over sodium sulfate, and the solvent evaporated to dryness. Crystallization of the residue from acetone–ether yielded 0.25 g., m.p. 177–179°, $[\alpha]_D$ +93° (*c* 1.5). Mixed m.p. with a sample of substance IV described above was not depressed, and the infrared spectra of both samples were superimposable throughout the whole range.

Preparation of Bisthioketal (XII).—A mixture of compound IV (400 mg.) and 1,2-ethanedithiol (0.4 ml.), was cooled in an ice bath, and boron trifluoride etherate complex (0.25 ml.) was added. After 15 min., the product which separated was suspended in hexane, cooled, and filtered (375 mg.). Crystallizations from acetone–ether yielded needles, m.p. 195–196°, $[\alpha]_D + 41°$ (*c* 1.69); ν_{max} 1692 (hindered carbonyl) cm.$^{-1}$.

Anal. Calcd. for $C_{27}H_{40}OS_4$: C, 63.76; H, 7.93. Found: C, 63.95; H, 7.80.

Monoketone (XI) from Bisthioketal (XII).—The bisthioketal (XII) (200 mg.) in dioxane (40 ml.) solution containing Raney nickel (2 g.) was heated to reflux for 24 hr. with stirring. After removal of the catalyst, and evaporation of the solvent, the residue was dissolved in pentane and chromatographed on activated alumina (30 g.). The column was eluted successively with mixtures of benzene–pentane, 1:19 and 1:3. A crystalline product (84 mg.) emerged with the last solvents mixture. Crystallizations from methanol yielded needles, m.p. 110–112° $[\alpha]_D$ + 127° (*c* 0.94); ν_{max} 1692 (hindered carbonyl), 1384, 1377, 1367 (methyls and *gem*-dimethyl), 815 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{36}O$: C, 84.08; H, 11.05. Found: C, 84.09; H, 10.85.

Allylic Oxidation of Monoketone (XI) to XIa.—To a solution of XI (615 mg.) in acetic acid (30 ml.) at 50° there was added during 1 hr. a solution of chromium trioxide (3.3 ml.) (2.0 g. of chromium trioxide in 18 ml. of acetic acid and 2 ml. of water). The reaction mixture was kept for 2.5 hr. at the above temperature, excess oxidant was then decomposed with methanol. The substance which separated upon addition of water (100 ml.) was extracted with chloroform (120 ml.). The organic layer was washed with aqueous sodium bicarbonate, dried over sodium sulfate, and evaporated to dryness. The residue was dissolved in benzene–hexane 1:1, percolated through activated alumina (50 g.), then crystallized from benzene–hexane, m.p. 225–227°, λ_{max} 246 mμ (ϵ 10,500); ν_{max} 1700 and 1650 cm.$^{-1}$; n.m.r. 3.70 (doublet, $J = 2$ c.p.s.).

Anal. Calcd. for $C_{23}H_{32}O_2$: C, 80.65; H, 10.01. Found: C, 80.66; H, 9.99.

3,20-Bisethylene Ketal of IV (X).—A mixture of IV (250 mg.), ethylene glycol (2 ml.), and *p*-toluenesulfonic acid (30 mg.) in benzene solution (30 ml.), was heated overnight under reflux using a water collector for the azeotrope. The solution was shaken with a saturated solution of sodium carbonate (10 ml.) and washed with water (5 × 25 ml.). The organic layer was dried over sodium sulfate and evaporated to dryness under reduced pressure. The oily residue was twice crystallized from acetone–hexane, yield 180 mg., m.p. 165–167°, $[\alpha]_D + 90°$ (*c* 1.81); ν_{max} 1698 (C-11 ketone) cm.$^{-1}$.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.94; H, 9.07. Found: C, 72.74; H, 8.88.

Hydrolysis of the bisethylene ketal regenerated substance IV. A mixture of the bisketal X (130 mg.) and *p*-toluenesulfonic acid (18 mg.) in acetone (4 ml.), was left overnight at room temperature. The solution was neutralized with aqueous sodium bicarbonate and diluted with water (100 ml.). The solid which separated was collected by filtration; it crystallized from ether (65 mg.), and was identified as IV, m.p. 179–181°, $[\alpha]_D$ +95° (*c* 2.08); the infrared spectrum of the hydrolysis product and of IV were superimposable throughout the whole range.

Lithium Aluminum Hydride Reduction of Bisethylene Ketal (X) to XIV.—To a suspension of lithium aluminum hydride (700 mg.) in tetrahydrofuran (35 ml.), a solution of the bisethylene ketal (X) (350 mg.) in tetrahydrofuran (35 ml.) was added The mixture was heated under reflux with stirring for 24 hr., then decomposed by adding ethyl acetate, and a saturated aqueous solution of sodium sulfate. The solution was filtered from the insoluble salts, dried over sodium sulfate, and evaporated to dryness. The infrared spectrum of the residue exhibited an absorption band at 3450 cm.$^{-1}$ for a hydroxyl group, but no absorption was recorded in the carbonyl region. This amorphous product, which was identified as XIV, was used in the next dehydration experiment without any further purification.

Dehydration of XIV to XVa.—To a solution of XIV (590 mg.) in dry pyridine (6 ml.) freshly distilled phosphorus oxychloride (0.6 ml.) was added and the tightly sealed mixture was stored at room temperature for 72 hr. The mixture was then decomposed with ice, and the solid material collected and washed well with water (430 mg.). Repeated crystallizations from methanol and from acetone yielded a product, m.p. 167.5–169°, $[\alpha]_D$ −4.7° (*c* 1.06); ν_{max}^{KBr} 805 and 740 cm.$^{-1}$; no maximum of absorption in the ultraviolet, yellow coloration with tetranitromethane.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41. Found: C, 75.67; H, 9.37.

Hydrolysis of XVa to XVb.—Crude XVa (626 mg.) (above reaction) was dissolved in dry acetone (8 ml.) containing *p*-toluenesulfonic acid (36 mg.) and kept 12 hr. at room temperature. Chloroform (100 ml.) was added, the mixture was washed several times with water and dryed over sodium sulfate. Subsequent evaporation of the solvent left a residue which was dissolved in benzene–pentane 1:1 and chromatographed on activated alumina (30 g.). Elution with the above solvents mixture gave traces of oil, while with a mixture of benzene–pentane 3:1 a substance emerged which crystallized from methanol as leaflets, m.p. 152–154°. $[\alpha]_D$ +12° (*c* 0.93). The product gave a yellow coloration with tetranitromethane; ν_{max}^{KBr} 1735 (five-membered ring ketone) 1708 (C-20 ketone), 805 (C_6—H) and 740 (strong, *cis* double bond) cm.$^{-1}$; n.m.r., 9.17, 9.08, 9.00, 8.95, 8.83 (5 methyls), 7.80 (methyl ketone), 4.72 (doublet, J = 10 c.p.s.), 4.37 (broad C_6—H), 4.00 (doublet, J = 10 c.p.s.).

Anal. Calcd. for $C_{23}H_{32}O_2$: C, 81.13; H, 9.47. Found: C, 81.22; H, 9.35.

Allylic Oxidation of XVb to XVI.—To a solution of XVb (110 mg.) in acetic acid (5 ml.) at 50° (bath temperature) there was added dropwise, with stirring, during 0.5 hr. a solution of chromium trioxide (2.15 ml.) (100 mg. of chromium trioxide in acetic acid, 9 ml., and water, 1 ml.). Stirring was continued for 1 hr. at 50° when the brown color disappeared and an additional portion of the oxidant (0.5 ml.) was added; heating was continued for 1 hr. Excess chromium trioxide was then destroyed with methanol. Upon addition of water (50 ml.) a solid separated which was extracted with chloroform (70 ml.), then successively washed with water and dilute aqueous sodium bicarbonate solution. The organic solution was dried over sodium sulfate and evaporated to dryness leaving an oily residue (110 mg.) which was purified by chromatography on alumina (30 g.). Development of the column with benzene eluted traces of oil while a mixture of ether–benzene 1:9, yielded the starting material; this was followed by a second crystalline product (50 mg.), crystallized from acetone–hexane, m.p. 207–209°, λ_{max} 242 mμ (ϵ 8,720); ν_{max}^{KBr} 1750 (five-membered ring ketone), 1709 (C-20 carbonyl), 1661 (conjugated carbonyl), 1653, 745 cm.$^{-1}$; n.m.r. 9.12, 8.98, 8.92, 8.80, 8.80 (5 methyls), 7.85 (methyl ketone), 4.70 (doublet, J = 10 c.p.s.) 4.04 (doublet, J = 2 c.p.s.) and 3.92 (doublet, J = 10 c.p.s.).

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.83; H, 8.49.

Bromination of the Bisethylene Ketal (X).—A solution of the bisethylene ketal X (530 mg.) in carbon tetrachloride (60 ml.) was heated on a flood lamp, and N-bromosuccinimide (300 mg.) was added. The mixture was heated to reflux for 20 min., during this time evolution of hydrobromic acid occurred. The cooled reaction mixture was filtered and treated with 15 ml. of a 10% solution of sodium bicarbonate, then washed with water (5 × 25 ml.). The organic layer was dried over sodium sulfate and subsequently evaporated leaving an oily residue (510 mg.). This residue was dissolved in 4 ml. of benzene and chromatographed on a column packed with activated alumina (40 g.). Elution with benzene yielded traces of oil, while with a solvent mixture of ether–benzene, 1:9, a crystalline product emerged. It was recrystallized twice from hexane, (200 mg.), m.p. 155–156°, $[\alpha]_D$ −151° (*c* 1.31); λ_{max} 275 mμ (ϵ 7,800); ν_{max}^{KBr} 1692 (overlapping of C-11 and C-20 ketones), 1650, 1600, and 820 cm.$^{-1}$. The infrared spectrum of this reaction product was also recorded in chloroform solution, and the area enclosed by the band at 1700 cm.$^{-1}$ was compared with the area enclosed by the band at 1698 cm.$^{-1}$ of the bisethylene ketal (X), using the same solvent and the same concentration. A ratio of two to one, respectively, was found for these two measurements. The reaction product is identified as the **diene XVIIa**; it gives a dark brown coloration with tetranitromethane.

Anal. Calcd. for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.20; H, 8.70.

In a second experiment, the crude product which was obtained from the bromination of the bisketal (X) (830 mg.) was hydrolyzed in a solution of acetone (60 ml.) containing *p*-toluenesulfonic acid (90 mg.). This mixture was kept at room temperature for 12 hr. The solvent was evaporated to dryness under reduced pressure and the residue dissolved in chloroform. The organic layer was washed with a dilute aqueous solution of sodium bicarbonate, dried over sodium sulfate, and evaporated to dryness. The residue gave a brown coloration with tetranitromethane, λ_{max} 278 mμ; ν_{max} 1741, 1705 cm.$^{-1}$. This crude product was dissolved in benzene and purified by chromatography on activated alumina (90 g.). The chromatogram was eluted with benzene (400 ml.), ether–benzene 1:9 (300 ml.), and ether–benzene 1:3 (550 ml.) which all yielded only traces of oil. With a solvent mixture of ether–benzene 2:3, a crystalline substance was obtained (220 mg.), while with ether–benzene, 3:2, another crystalline product emerged (140 mg.). The first crystalline product (220 mg.) which was identified as **XVIIb** crystallized from hexane, needles m.p. 174–175° $[\alpha]_D$ −147° (*c* 1.07) λ_{max} 275 mμ (ϵ 5,500); ν_{max} 1744 (five-membered ring ketone), 1706 (C-20, and hindered carbonyls), 1662, 1610 (conjugated double bonds), 820 (strong) cm.$^{-1}$; n.m.r. 8.92, 8.88, 8.85, 8.82, 8.75 (5 methyls) 7.88 (methyl ketone), 4.58 (doublet, J = 4 c.p.s.) 4.38 (doublet, J = 4 c.p.s.).

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 78.00; H, 8.56.

The second crystalline fraction (140 mg.) was found to consist of a mixture of XVIIb and XVIII. Rechromatography of a solution of this mixture in benzene on activated alumina (15 g.) followed by elution with ether–benzene, 1:3, yielded a series of crystalline fractions. Examination of the infrared spectra of these various fractions showed variations in the intensity of the absorption band at 1742 cm.$^{-1}$ of the five-membered ring ketone. The fractions having weak bands at this location were combined (30 mg.) and crystallized several times from hexane. Only a small quantity of pure product could be obtained; it was identified as **XVIII**, λ_{max} 289 mμ (ϵ 9,000), ν_{max} 1707 (broad, overlapping of conjugated five-membered ring carbonyl, C-20 and C-11 carbonyls) and 1560 cm.$^{-1}$.

Allylic Oxidation of XVIII to Form XIX.—To a solution of compound XVIII (100 mg., containing a small quantity of XVIIb as impurity) in acetic acid (15 ml.), a solution of chromium trioxide (1.5 ml.) (2 g. of chromium trioxide in 18 ml. of acetic acid and 2 ml. of water) was added dropwise at 55° (bath temperature) during 1 hr. The reaction mixture was kept at this temperature for an additional hour, then the excess oxidant was decomposed with methanol. Water (80 ml.) was added and the mixture was extracted with chloroform. The organic layer was washed with a dilute solution of sodium bicarbonate dried over sodium sulfate and evaporated to dryness under reduced pressure. The oil (80 mg.) was dissolved in benzene and chromatographed on activated alumina (15 g.). The chromatogram was eluted with benzene and ether–benzene 1:9 without yielding any substances; with ether–benzene, 1:3, a crystalline product (38 mg.) was obtained. Crystallizations from ether gave faint yellow colored needles, m.p. 176–178°, λ_{max} 282 mμ (ϵ 18,700); ν_{max} 1717, 1709, 1666, 1569 cm.$^{-1}$; n.m.r. 9.16, 9.01, 8.73, 8.73, 8.50 (5 methyls) 7.86 (methyl ketone) 3.92 (doublet, J = 1 c.p.s.) 3.79 (doublet, J = 1 c.p.s.).

Anal. Calcd. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66. Found: C, 74.87; H, 7.84.

Allylic Oxidation of Triketone IV to XX.—To a solution of IV (2.2 g.) in glacial acetic acid (28 ml.) heated to 50° (bath temperature) under a stream of nitrogen and with continuous stirring, an oxidative solution (6.6 ml.) (9.49 g. of chromium trioxide in 30 ml. of 90% acetic acid) was added during a period of 5 hr. The reaction mixture was stirred for three additional hours at the same temperature and overnight at room temperature. Excess oxidant was then decomposed with methanol. The product which separated upon addition of water (400 ml.) was collected and water washed (1.31 g.). Upon standing, an additional crop (480 mg.) was obtained from the mother liquor. Several crystallizations of the main crop from acetone–hexane yielded fine needles (660 mg.) m.p. 278–280°, $[\alpha]_D$ +92.5° (c 0.96); 242 mμ (ϵ 8,800); ν_{max} 1753 (five-membered ring ketone), 1710 (C-11 and C-20 ketones) and 1665 (conjugated ketone) cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16. Found: C, 74.53; H, 7.88.

Formation of XIX from XX (Sodium Methoxide Reaction).—To a stirred suspension of XX (200 mg.) in methanol (20 ml.) cooled to 4°, a methanolic solution (10 ml.) of 0.1 N sodium methoxide was added during a period of 10 min. Stirring was continued for 2 hr. at 4° and 2 hr. at room temperature, resulting in an homogenous yellow solution. This solution was acidified with dilute hydrochloric acid, followed by addition of water (100 ml.). The precipitated substance was collected by filtration, dissolved in benzene, and chromatographed on activated alumina (25 g.). The chromatogram was developed successively with benzene-ether mixtures of 1:19; 1:9 and 1:4. Pale yellow crystals (50 mg.) emerged with the last solvent mixture; they were crystallized from acetone-hexane and then from ether, m.p. 179–181°; λ_{max} 282 mμ (ϵ 18,700); ν_{max} 1717, 1709, 1666 and 1569 cm.$^{-1}$.

A mixed melting point with the substance which was obtained above by the oxidation of XVIII was not depressed. The spectral properties of both samples were found identical.

Oxidation of IV with Potassium *tert*-butoxide to XXI.—A solution of IV (1.0 g.), in benzene (80 ml.) and *tert*-butyl alcohol saturated with potassium *tert*-butoxide (15 ml.) was stirred overnight at room temperature. The resulting reaction mixture was extracted with water until its reaction was neutral. The combined extracts were acidified with aqueous dilute hydrochloric acid, and extracted with chloroform. The organic layer was dried over sodium sulfate and evaporated yielding an amorphous residue (0.62 g.). The product, which could not be induced to crystallize gave an intense dark coloration with ferric chloride and was identified as XXIa λ_{max} 244 (infl.) and 313 mμ; (ϵ 3,280 and 5,000), $\lambda_{max}^{1\%\ KOH}$ 225 (infl.), 256 (infl.) and 356 mμ (ϵ 6,100, 2,780 and 4,800); ν_{max} 1709 (broad), 1630 and 1598 cm.$^{-1}$.

The crude product (XXIa) (0.5 g.) was acetylated overnight with pyridine (4 ml.) and acetic anhydride (4 ml.). The reaction mixture was poured on ice and the solid collected. Dissolved in benzene, it was chromatographed on acid washed alumina (Merck) (50 g.). Elution of the chromatogram with benzene yielded an oil, while with ether–benzene 1:5, a crystalline substance emerged (160 mg.). Several crystallizations from acetone–ether yielded a product which was sublimed at 180–210°, m.p. 232–234°, ν_{max} 1773, 1182 (enol acetate), 1706 (intense), 1610 cm.$^{-1}$; λ_{max} 291 mμ (ϵ 10,900); n.m.r. 9.30, 9.05, 8.82, 8.82, 8.57 (5 methyls), 7.70, 7.76 (both for methyl ketone and methyl acetate), and 3.7 (a quartet of lines centered at this value, C_6—H).

Anal. Calcd. for $C_{25}H_{32}O_5$: C, 72.79; H, 7.82. Found: C, 73.10; H, 7.87.

Reaction of the Triketone IV with Osmium Tetroxide (XXIIa).—Osmium tetroxide (0.5 g.) was added to a solution of the triketone IV (540 mg.) in pyridine (15 ml.). The mixture was kept at room temperature for 1 week; thereafter, the pyridine was distilled *in vacuo*. To the residue, ethanol (30 ml.), water (30 ml.), and sodium sulfite (2 g.), were added and the resulting mixture was heated under reflux for 3.5 hr., then filtered while hot. The cake was washed with hot acetone and the combined filtrates were concentrated under reduced pressure to a small volume. The product, was extracted with ethyl acetate (3 × 80 ml.), and the solution was dried over sodium sulfate. By evaporation of the solvent to a small volume, the product crystallized (225 mg.), m.p. 285–290°. Two recrystallizations from boiling ethanol yielded needles, m.p. 291–294°, $[\alpha]_D$ + 55° in pyridine (c 0.87), ν_{max} 3450 (hydroxyl), 1738 and 1702 cm.$^{-1}$. No coloration with tetranitromethane.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.79; H, 8.72.

The monoacetate (XXIIb) was prepared by acetylating XXIIa (295 mg.) overnight at room temperature in a mixture of pyridine (4 ml.) and acetic anhydride (4 ml.). The reaction mixture was poured on ice, and the resulting amorphous solid was collected by filtration. It was recrystallized three times from acetone–hexane, as needles, m.p. 254–255°, $[\alpha]_D$ +49° (c 0.95), ν_{max} 3450 (hydroxyl), 1738 (overlapping of five-membered ring ketone and of acetate), 1700, and 1250 (acetate) cm.$^{-1}$.

Anal. Calcd. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39; CH_3CO, 10.0. Found: C, 69.44; H, 8.37; CH_3CO, 11.7.

Oxidation of XXIIa to the Hydroxytetraketone XXIII.—To an ice-cold solution of XXIIa (150 mg.) in acetone (50 ml.; previously distilled over potassium permanganate) a solution of chromium trioxide (27 g. of chromium trioxide in 100 ml. of 35% aqueous solution of sulfuric acid) was added. During addition of the oxidizing solution, the reaction mixture was stirred under a stream of nitrogen in an ice cooled flask. When 0.2 ml. of the oxidizing solution was consumed (*ca.* 0.5 hr.), the brown-red color persisted. The solution was allowed to reach room temperature, and any excess oxidant was reduced with methanol. The solution was then diluted with water, and the crystalline product which separated was collected, 135 mg. Two crystallizations from ethanol yielded needles, m.p. 235–244° dec., ν_{max}^{KBr} 3450, 1742, 1710, and 1692 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.08; H, 8.49.

Dehydration of XXIII.—A solution of XXIII (250 mg.) and *p*-toluenesulfonic acid (50 mg.) in dry benzene (75 ml.) was refluxed for 1 hr. using a water collector for the azeotrope. After cooling, the mixture was extracted with a saturated solution of sodium carbonate (4 × 15 ml. portions); the basic aqueous extract was washed once with benzene, and acidified with dilute hydrochloric acid. The mixture was left for 24 hr. at room temperature and the solid material was collected by filtration, 125 mg. Crystallization from ethanol–water yielded yellow crystals, m.p. 200° dec., λ_{max} 335 mμ (ϵ 10,300 and 405 mμ (ϵ 3,100); $\lambda_{max}^{KOH\ 1\%}$ 405 mμ (ϵ 21,700); ν_{max} 3500, 1750 (weak, five-membered ring ketone) 1700, 1660, 1605, and 1540 cm.$^{-1}$. The product which was found to be composed of a mixture and XXIV and of XXVa did not crystallize from organic solvents and gave consistently low analytical results.

The monoacetate **XXVb** was prepared by acetylation of XXVa (100 mg.) overnight at room temperature, in a solution of pyridine (2 ml.) and acetic anhydride (2 ml.). The reaction mixture was decomposed with ice, and the solid material (80 mg.) recrystallized twice from acetone–hexane, m.p. 173–175°, $[\alpha]_D + 366°$ (c 0.68), λ_{max} 290 mμ (ϵ 25,800); ν_{max} 1765 (enol acetate), 1707 (strong), and 1557 (conjugated double bonds) cm.$^{-1}$; n.m.r. 9.28, 8.90, 8.82, 8.82, 8.55 (5 methyls), 7.92, 7.76 (both for methyl ketone and methyl acetate) and 4.45 (C_1—H).

Anal. Calcd. for $C_{25}H_{32}O_5$: C, 72.79; H, 7.82; CH_3CO, 10.43. Found: C, 72.67; H, 7.83; CH_3CO, 10.14.

Beckmann Rearrangement of Bisoxime (XXVII) to XXIX.—The bisoxime (XXVII) was prepared by heating during 35 min. a solution of the triketone VI (900 mg.) in absolute ethanol (5 ml.) containing pyridine (2.6 ml.) and hydroxylamine hydrochloride (600 mg.). Water was added to turbidity, the mixture was cooled in an ice bath, and the crystalline product which separated was filtered and washed with water (810 mg.), λ_{max} 239 mμ (ϵ 13,000), ν_{max} 1692 cm.$^{-1}$. This substance was used in the following experiment without any further purification.

The bisoxime was subjected to Beckmann rearrangement by dissolving (800 mg.) in pyridine (2.5 ml.) cooling to 5°, and adding *p*-toluenesulfonyl chloride (1.8 g.). The mixture was kept under nitrogen while stirring at room temperature for 12 hr. The dark reaction mixture was poured onto ice, dilute sulfuric acid (5 ml.) was added, and the resulting solution was left for 24 hr. at room temperature. The product was extracted with chloroform (150 ml.) which was washed successively with dilute hydrochloric acid (3 × 20 ml.), sodium bicarbonate solution (2 × 20 ml.), and water (3 × 20 ml.). Drying and subsequent evaporation of the chloroform solution yielded an oil (200 mg.), which was dissolved in benzene, and chromatographed on acid-washed alumina (Merck). The following solvents were passed through the column: benzene, ether, and benzene–chloroform 9:1 and 3:2. With the last solvent mixture a crystalline substance (97 mg.) was obtained which crystallized from acetone–ether, m.p. 171–173°, λ_{max} 229 mμ (ϵ 9,000); ν_{max} 2243 (nitrile), 1740 (C-17 ketone), 1705 (hindered carbonyl), 1652, 1620, 1379, 900, 837 cm.$^{-1}$; n.m.r. 9.00, 9.00, 8.62 (3 methyls) 8.04 (methyl on double bond), 5.30, 5.10 (terminal methylene), 4.13 (broad, C_6—H).

Anal. Calcd. for $C_{21}H_{27}O_2N$: N, 4.30. Found: N, 4.90.

Formation of XXX from VI.—The bisketal of VI was prepared in the usual manner: ν_{max} 1695 (C-11 carbonyl) cm.$^{-1}$. No maximum of absorption was recorded in the ultraviolet spectrum. The above crude bisketal (1.05 g.) was reduced with lithium aluminum hydride (1 g.) in dry tetrahydrofuran (150 ml). The mixture was heated under reflux for 24 hr. After the usual work-up there was obtained an amorphous product (1 g.) which showed no absorption in the carbonyl stretching region of the infrared spectrum.

Hydrolysis of the ketals was done by dissolving the above substance (1 g.) in dry acetone (100 ml.) containing *p*-toluenesulfonic acid (120 mg.). The usual processing of the reaction mixture yielded an oil (830 mg.) which was dissolved in benzene and chromatographed on acid washed alumina (Merck) (70 g.). The column was passed with the following solvents mixture: ether–benzene 1:9, 1:3, and 2:3. The last solvents mixture eluted an amorphous product (300 mg.) which could not be induced to crystallize. It was identified as the axial isomer of XXX λ_{max} 240 mμ (ϵ 8,000); ν_{max} 3640 (free hydroxyl, measured in dilute carbon tetrachloride solution), 1745, and 1666 cm.$^{-1}$. The chromatogram was further developed with ether, followed by chloroform–benzene mixtures 1:9, 1:2, and 3:1. A second amorphous product (250 mg.) was obtained with the last solvents mixture, and was identified as the equatorial isomer of XXX. This substance also could not be induced to crystallize, λ_{max} 240 mμ (ϵ 8,100), ν_{max} 3640 (free hydroxyl, measured in dilute carbon tetrachloride solution), 1744, and 1665 cm.$^{-1}$.

Dehydrogenation of Elatericin A.—Elatericin A was treated with lithium aluminum hydride until all the carbonyl groups were reduced as indicated by the infrared spectrum of the reaction product. This crude product was then acetylated in the usual way at room temperature. The crude acetate (12 g.) was subjected to dehydrogenation with selenium powder (24 g.) as previously described.[3a] The reaction mixture was then exhaustively extracted with ether (Soxhlet). The ethereal extract was washed with aqueous sodium hydroxide (10%) and water, and dried over sodium sulfate. Evaporation of the solvent left an oily residue which was fractionated *in vacuo*. The following fractions were collected: I, 50 mg., b.p. 50–90° (1.5 mm.); II, 180 mg., 90–140° (1.0 mm.); III, 650 mg., 140–230° (1.0 mm.); IV, 80 mg. 230–300° (1.0–0.5 mm). Fraction I did not exhibit any absorption in the ultraviolet and was discarded, while fractions II and III were combined. They were chromatographed on activated alumina, the column being developed with pentane. Sixty fractions of 25 ml. each were collected. Fractions 1–20 were combined and rechromatographed. The fractions from the latter chromatography exhibiting strong absorption at λ_{max} 232 mμ were recombined and distilled *in vacuo* (1.0–1.5 mm.). Three fractions were obtained at the following ranges: (i) 70–105°; (ii) 105–120°; (iii) 120–145°. The second fraction had the following ultraviolet absorption maxima in isoöctane solution: λ_{max} in mμ (ϵ) 228 (38,200); 232 (55,500); 279 (3,190); 288 (3,470); 309 (694); 324 (347), and 329 (43). This pattern is specific for **1,2,5-trimethylnaphthalene**[31] and identifies this substance notwithstanding the fact that no crystalline adduct with 1,3,5-trinitrobenzene or picric acid could be obtained.

Fractions 25–37 from the main chromatography, which all showed strong absorption maxima in the ultraviolet at λ_{max} 269 mμ were combined and evaporated to dryness. A solid residue (190 mg.) was obtained, crystallized twice from absolute ethanol, and sublimed *in vacuo* at 130° (1 mm.) yielding white crystals, m.p. 144–146° of **1,2,8-trimethylphenanthrene** (lit. 144–145°); **1,3,5-trinitrobenzene adduct**, yellow crystals m.p. 174–178°, mixed m.p. with an authentic sample of this adduct gave no depression.

Fraction IV (80 mg.) was chromatographed on activated alumina using pentane as eluent and the middle fractions recombined and evaporated, leaving an oily residue having the following ultraviolet absorption maxima: λ_{max} 233, 272, 288, 305, and 321 mμ. No definite compound could be identified from this fraction.

Acknowledgment.—Thanks are due to Mrs. R. Tugenhaft for valuable assistance, and to the microanalytical laboratory of our Institute. One of the authors (O. R. G.) acknowledges support from the Conselho Nacional de Pesquisas, Brasil.

---

(31) E. Heilbronner, U. Fröhlicher, and Pl. A. Plattner, *Helv. Chim. Acta*, **32**, 2479 (1949).