Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.74; H, 5.90.

The methoxynaphthylamine acetate (8 g.) was deacetylated by heating with 60 ml. of ethanol and 16 ml. of concentrated hydrochloric acid for 2 hr. on the steam-bath. After evaporation of most of the alcohol and cooling, the crystalline mass was filtered off and washed with 2 *N* hydrochloric acid to yield 7.5 g. of amine hydrochloride melting at 185–190°, which was used for subsequent reactions without further purification.

1-Bromo-7-methoxynaphthalene.—Although treatment of diazotized 2-methoxy-7-naphthylamine with cuprous bromide and copper according to the usual Sandmeyer-Gattermann procedure resulted in a very poor yield of the bromo derivative, the conversion was satisfactorily carried out by application of the Schwechten procedure.[28]

A solution of 5 g. of the amine hydrochloride in 40 ml. of 2 *N* sulfuric acid was cooled to 0° and diazotized with 1.8 g. of sodium nitrite in 9 ml. of water. The clear solution was diluted with 50 ml. of ice-water and a solution of 26 g. of mercuric bromide and 26 g. of potassium bromide in 100 ml. of water was added. After standing for 1 hr. at 0°, the double salt was filtered and dried *in vacuo* at room temperature. It was then mixed with an equal weight of potassium bromide and heated gradually to a temperature of 140° whereupon rapid decomposition of the salt occurred. The entire reaction mixture was sublimed at 150° (1 mm.) to give a white solid which was dissolved in petroleum ether and passed through a Florisil column with the same solvent. A yield of 2.6 g. (46%) of 1-bromo-7-methoxynaphthalene (m.p. 64–67°) was obtained. Recrystallization from ethanol and then petroleum ether gave white prisms, m.p. 68–69°.

Anal. Calcd. for $C_{11}H_9BrO$: C, 55.72; H, 3.83. Found: C, 55.68; H, 3.89.

1-Iodo-7-methoxynaphthalene.—A solution of 10 g. of diazotized 2-methoxy-7-naphthylamine, prepared as above, was slowly added to 14 g. of potassium iodide in 65 ml. of 2 *N* sulfuric acid. The reaction mixture was kept at room temperature for 1 hr., heated on the steam-bath for 15 min., cooled and extracted with ether. The ether extract, after washing with sodium bisulfite solution, dilute alkali and water, was dried over sodium sulfate and evaporated to dryness. The residue was taken up in petroleum ether and, after passage through a Florisil column, 1.1 g. (6.8%) of the iodo derivative was obtained as a white solid, m.p. 74–77°. Several crystallizations from ethanol gave an analytical sample melting at 76–77°.

Anal. Calcd. for $C_{11}H_9IO$: C, 46.83; H, 3.22. Found: C, 46.86; H, 3.19.

2',6'-Dimethoxy-1,2,5,6-dibenz-9,10-anthraquinone (XXXVI).—Addition of the Grignard reagent prepared from either 1-bromo- or 1-iodo-7-methoxynaphthalene to 6-methoxy-1,2-naphthalic anhydride under conditions described above for the preparation of the keto acid XXIIIa gave an amorphous product which we were unable to appreciably purify. Two grams of the crude material was treated with sulfuric acid as described for the preparation of the quinone XXIVa. Elution of the cyclized product from a Florisil column with 1% ethyl acetate in benzene, and crystallization from ethanol and benzene gave 2 mg. of orange needles, m.p. 310–312° alone or mixed with an authentic sample of the dimethyl ether of the 9,10-anthraquinone of the dihydroxy rabbit metabolite, m.p. 310–312°.

Anal. Calcd. for $C_{24}H_{16}O_4$: C, 78.25; H, 4.38. Found: C, 78.11; H, 4.21.

Acknowledgments.—The authors gratefully acknowledge the contribution of Dr. George Wolf who carried out some preliminary experiments, and the capable technical assistance of Mr. Michael Oxman.

MADISON, WISCONSIN

(28) W. E. Bachmann and J. Boutner, THIS JOURNAL, **58**, 2194 (1936).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Terpenoids. XXXII.[1] The Structure of the Cactus Triterpene Treleasegenic Acid. Ring Conformational Alterations in a Pentacyclic Triterpene[2]

BY CARL DJERASSI AND JOHN S. MILLS

RECEIVED SEPTEMBER 30, 1957

Treleasegenic acid, a new triterpene isolated from the cactus *Lemaireocereus treleasei*, has been shown to be 21β,30-dihydroxyoleanolic acid (Ia). The structure proof, proceeding *via* the 30-trityl ether VI, involved multistage interconversions with the methyl esters of the cactus triterpenes machaerinic acid (XVIIa) and queretaroic acid (IXa) and thus led also to a rigorous definition of the stereochemistry. The formation of transient as well as stable lactones between the C-17 carboxyl group and the 21β-hydroxyl function in a D/E *cis* fused pentacyclic triterpene can only be reconciled by conformational alterations (chair to boat) in ring E and probably also ring D. As a consequence, methyl esters of certain ring E substituted oleanolic acids can be saponified with surprising ease.

The Mexican cactus *Lemaireocereus treleasei* has been shown[3] to be a good source of oleanolic acid and stellatogenin.[4] During a renewed extraction of this cactus in order to accumulate larger amounts of stellatogenin for its eventual conversion[5] to betulinic acid, Dr. Richard Hodges observed the presence of a neutral triterpene. A sufficient quantity of this substance has now been obtained so as to permit its structure elucidation.

Although encountered in the neutral fraction after methanolic hydrochloric acid hydrolysis of the glycosides, it was soon recognized that the substance represented a methyl ester and the probable form in which it occurs in the plant will be discussed below. Saponification with 10% methanolic potassium hydroxide furnished the free parent acid ($C_{30}H_{48}O_5$)—now named treleasegenic acid—and the nature of its functional groups was determined readily by the formation of a methyl ester (Ib), a methyl ester triacetate (Ic) and a triacetoxy acid (Id). Treleasegenic acid is thus a trihydroxy triterpene acid and the ease of acetylation and saponification (of the triacetate) suggested that the hydroxyl

(1) Paper XXXI, C. Djerassi, D. B. Thomas, A. L. Livingston and C. R. Thompson, THIS JOURNAL, **79**, 5292 (1957).

(2) This investigation was supported by the Division of Research Grants (grant No. RG-3863) of the National Institutes of Health, U. S. Public Health Service.

(3) C. Djerassi, A. Bowers, S. Burstein, H. Estrada, J. Grossman, J. Herran, A. J. Lemin, A. Manjarrez and S. C. Pakrashi, THIS JOURNAL, **78**, 2312 (1956).

(4) C. Djerassi, E. Farkas, L. H. Liu and G. H. Thomas, *ibid.*, **77**, 5330 (1955).

(5) C. Djerassi and R. Hodges, *ibid.*, **78**, 3534 (1956).

groups were either primary and/or equatorially oriented secondary alcoholic functions. This was supported further by lithium aluminum hydride reduction to a tetrol (subsequently shown to be IIa) and facile acetylation to a tetraacetate (IIb). Since all of the triterpenes which have been isolated from giant cacti in our laboratories[6] belong either to the β-amyrin or lupeol series, it was first necessary to establish membership of treleasegenic acid in either of these groups. This was done in the customary manner by selenium dioxide oxidation of methyl treleasegenate triacetate (Ic) which led to a $\Delta^{11,13(18)}$-diene (III) with the characteristic[7] triple ultraviolet absorption maxima at 240.5, 249 and 258 mμ. The presence of a 12–13 double bond in a β-amyrin skeleton—already suggested by the course of the selenium dioxide oxidation—was confirmed further by chromium trioxide oxidation of methyl treleasegenate triacetate in hot acetic acid resulting in allylic oxidation and formation of an α,β-unsaturated 11-ketone, whose ultraviolet and infrared spectral properties were fully consistent with structure IV established subsequently for it.

With the gross characterization of treleasegenic acid as a trihydroxy acid of the β-amyrin series completed, attention was turned next to localization of the carboxyl group. Brief treatment of treleasegenic acid triacetate (Id) with bromine in chloroform solution afforded a product which by elemental and infrared spectral analysis[8] was clearly a 5-membered bromolactone. Such a reaction is typical[8] of triterpenes with carboxyl groups at C-17 (*e.g.*, oleanolic acid), although mechanistically and stereochemically a C-8 substituted carboxyl group would react similarly with the initially formed 12α,-13α-bromonium ion. Triterpenes with carboxyl groups at C-8 have so far not been encountered in nature, but their methyl esters would be expected to be even more resistant toward saponification than C-17 methoxycarbonyl derivatives of the methyl oleanolate type. While methyl oleanolate itself is not at all affected by refluxing 10% methanolic potassium hydroxide,[9] it has been shown that this behavior is changed drastically by the presence of a γ-keto group since methyl machaerate (XVIId)[10] is already saponified completely by 5% methanolic alkali. Indeed, even a hydroxyl group beta to the ester function has some influence (see behavior[9] of methyl cochalate[11]) and it has now been observed that a γ-hydroxylated methyl oleanolate derivative —methyl machaerinate (XVIIa)[10]—undergoes ready saponification with 10% methanolic potassium hydroxide as does methyl treleasegenate. Consequently, bromolactone formation and relative ease of saponification are not necessarily incompatible with the presence of a carboxyl group at C-17 and the lability of such esters toward alkali can hardly be used as a criterion for localization since activating groups can alter the picture completely. The steric implications of such activation will be considered below and as will be demonstrated in the sequel, the structure of the bromolactone derived from treleasegenic acid triacetate (Id) should be represented by V.

In order to attempt a differentiation among the three hydroxyl groups in treleasegenic acid, resort was taken to the tritylation reaction which has served with such success in the structure elucidation of the triterpene tetrol chichipegenin,[12] since only primary hydroxyl groups are etherified under those conditions. In fact, treatment of methyl treleasegenate (Ib) with triphenylmethyl (trityl) chloride in pyridine—dioxane solution led to an oily trityl ether (subsequently shown to be VIa) which was characterized as the diacetate VIb. Oxidation of the trityl ether VIa with chromium trioxide–pyridine gave an oily diketo trityl ether, which was submitted directly to Wolff-Kishner reduction,[13] remethylation with diazomethane and trityl ether cleavage. The resulting monohydroxy methyl ester VIIIa, further characterized as the monoacetate VIIIb, appeared to be the first suitable transformation product of treleasegenic acid which might be related to a known triterpene. There are several reasons for such an assumption.

Our earlier work with cactus triterpenes[6] showed that oxygenation is only to be expected in rings D and E aside from C-3. Assuming the presence in treleasegenic acid of a carboxyl group at C-17 (see formation of bromolactone V) then the most likely position for the primary hydroxyl function would be at C-29 (myrtillogenic acid[9,14]) or C-30 (queretaroic acid (IX)[15]). The simplest approach involved elimination of the C-3 hydroxyl group of methyl queretaroate since this should lead either to the treleasegenic acid degradation product or an isomer thereof. Consequently, methyl queretaroate (IXa)[15] was treated with trityl chloride, the 30-trityl ether IXb was oxidized with chromium trioxide in pyridine solution and the trityl group removed by boiling with acid. The resulting methyl 3-dehydroqueretaroate (Xb) was subjected to Wolff–Kishner reduction (and remethylation) whereupon methyl 3-deoxoqueretaroate (VIIIa) was obtained. This alcohol and its 30-acetate VIIIb proved to be identical in every respect with the corresponding specimens derived from methyl treleasegenate (Ib → VIa → VII → VIII), thus pro-

(6) C. Djerassi, "Cactus Triterpenes" in "Festschrift Arthur Stoll," Birkhäuser, A.G., Basel, 1957, pp. 330–352.

(7) See L. Ruzicka, G. Müller and H. Schellenberg, *Helv. Chim. Acta*, **22**, 767 (1939); D. H. R. Barton and C. J. W. Brooks, *J. Chem. Soc.*, 257 (1951).

(8) For leading references see D. H. R. Barton and P. de Mayo, *ibid.*, 887 (1954).

(9) C. Djerassi and H. G. Monsimer, THIS JOURNAL, **79**, 2901 (1957). See Table I in that paper for comparative rates of saponification of triterpene methyl esters.

(10) C. Djerassi and A. E. Lippman, *ibid.*, **77**, 1825 (1955).

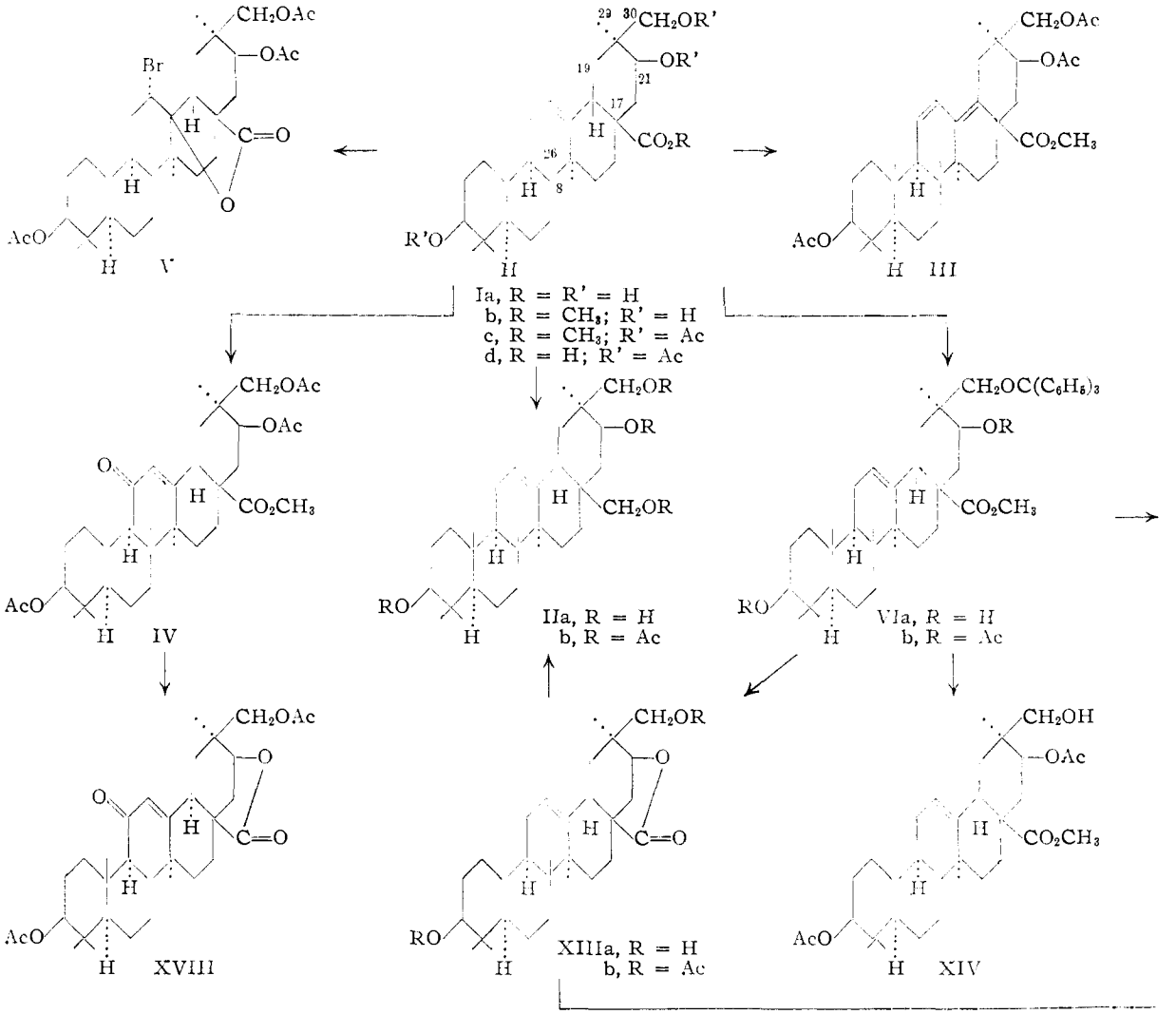
(11) C. Djerassi, G. H. Thomas and H. G. Monsimer, *ibid.*, **77**, 3579 (1955).

(12) A. Sandoval, A. Manjarrez, P. R. Leeming, G. H. Thomas and C. Djerassi, *ibid.*, **79**, 4468 (1957).

(13) The stability of the trityl ether grouping under the conditions of the Huang-Minlon modification of the Wolff–Kishner reduction already has been demonstrated in ref. 12.

(14) Oxygenation at C-29 rather than C-30 was assumed (ref. 9) because methyl myrtillogenate was saponified with 5, 7 or 10% methanolic potassium hydroxide in double the yield observed with methyl deoxoglycyrrhetate (oxygenated at C-30). However, we have been informed recently by Dr. J. W. W. Morgan of British Celanese, Ltd., that F. E. King and J. W. W. Morgan (*Proc. Chem. Soc.*, 228 (1957)) have observed that a triterpene 29-oic acid methyl ester can be saponified with 1% methanolic alkali, which would suggest that myrtillogenic acid has an axial (C-30) rather than an equatorial (C-29) carboxyl group.

(15) C. Djerassi, J. A. Henry, A. J. Lemin, T. Rios and G. H. Thomas, THIS JOURNAL, **78**, 3783 (1956).



viding unambiguous proof that treleasegenic acid possesses an intact β-amyrin system with a carboxyl group at C-17 and a hydroxyl group at C-30.[16]

The remaining unknown features of treleasegenic acid are the locations of its two secondary hydroxyl groups. By analogy to all other triterpenes encountered among the *Cactaceae*[6] one of them could be expected to be attached at C-3 (β). The surprising ease of saponification of methyl treleasegenate—paralleling that of methyl machaerinate (XVIIa)—suggested activation by a γ-hydroxyl group[17] and this would leave only positions 15β, 19β and 21β open for consideration. The first possibility is excluded since a 15β-hydroxyl function cannot be acetylated[18] under standard conditions and experiments were undertaken to differentiate between the other two alternatives.

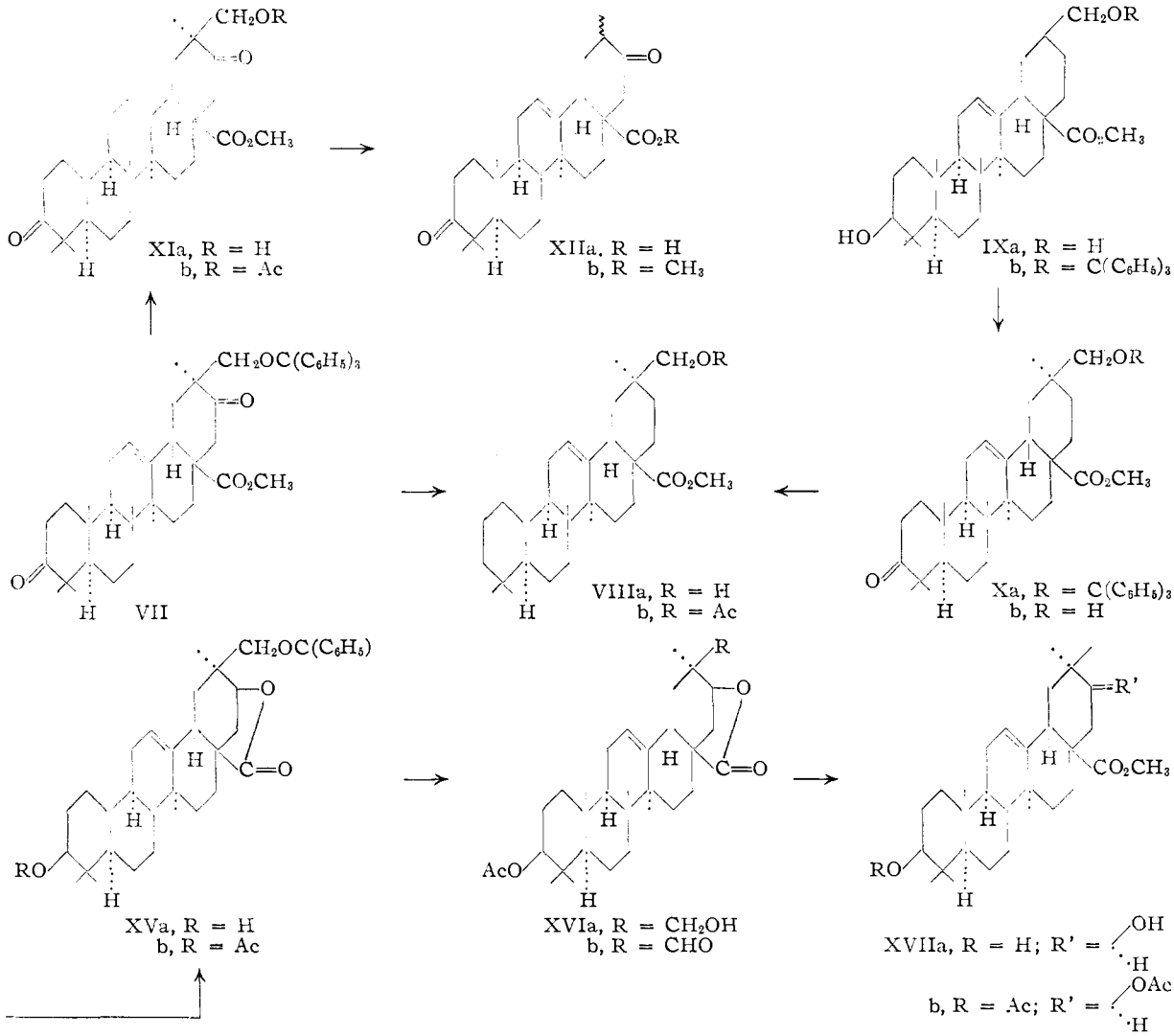
If the secondary hydroxyl group is indeed located at C-19 or C-21, then the chromium trioxide oxidation product (subsequently shown to be VII) of methyl treleasegenate 30-trityl ether (VIa) should be a derivative of an α-(hydroxymethyl) ketone, amenable to reverse aldolization[8] by either acid or base. In fact, acid detritylation of such compounds[19] usually is accompanied by loss of formaldehyde, the intermediate hydroxymethyl ketone not being isolated. It was surprising, therefore, to observe that the relatively drastic treatment (refluxing 5% sulfuric acid in dioxane–water) to which the oxidized trityl ether VII was subjected resulted only in detritylation without loss of formaldehyde. This was demonstrated by the analytical composition of the crystalline hydroxy ketone XIa and by the formation of a 30-monoacetate XIb. However, further treatment of this substance with 10% methanolic alkali followed by methylation with diazomethane yielded an oily methyl ester (probably

(16) This point has been established rigorously since queretaroic acid has been interrelated (ref. 15) with glycyrrhetic acid and its structure and stereochemistry is known (see J. M. Beaton and F. S. Spring, *J. Chem. Soc.*, 3126 (1955)).

(17) The 30-hydroxyl function does not affect the rate of hydrolysis to any extent as shown by complete recovery of methyl queretaroate (IXa) after refluxing with 10% methanolic potassium hydroxide.

(18) C. Djerassi, C. H. Robinson and D. B. Thomas, THIS JOURNAL, **78**, 5685 (1956). Furthermore, the hydroxy acid would be expected to lactonize spontaneously as was found to be the case with dumortierigenin.

(19) See C. Djerassi, W. Rittel, A. L. Nussbaum, F. W. Donovan and J. Herran, *ibid.*, **76**, 6410 (1954).



XIIb), which in contrast to the high melting starting material (XIa) did not exhibit a hydroxyl band in the infrared. This reaction sequence suggested tentatively that a reverse aldol condensation had taken place and that a keto group (and hence a hydroxyl group in treleasegenic acid itself) was indeed present on a carbon atom adjacent to C-20. Of the two possibilities (C-19 or C-21), C-19 could now be excluded since boiling with either acid or base would have caused migration of the 12–13 double bond to a position of conjugation (13–18),[20] which was not indicated by the spectral data, thus leaving C-21 as the only likely position. The tentative inference that the two secondary hydroxyl groups of treleasegenic acid are located at C-3 and C-21—the former on biogenetic grounds[6] and the latter because of the above described reaction sequence—had to be subjected to a firm experimental test involving correlation with a triterpene of known constitution containing those two structural features. If our structural hypothesis were indeed correct, then the obvious candidate for such an interrelation would be methyl machaerinate (XVIIa)[10] (methyl 21β-hydroxyoleanolate) and this should be obtainable by selective removal of the 30-hydroxyl function of methyl treleasegenate (Ib).

Preferential manipulation of the primary C-30 hydroxyl group appeared most promising *via* the trityl ether diacetate VIb, it being hoped that detritylation could be accomplished without loss of the acetate functions. In actual fact, when the reaction was carried out with 5% sulfuric acid in water–dioxane—precisely the conditions employed successfully in the detritylation of the diketo trityl ether methyl ester VII—there was obtained a high melting (m.p. 300–303°) product of the empirical formula $C_{30}H_{46}O_4$. The analysis already demonstrated that the loss of the trityl ether function was accompanied by disappearance of the acetate and methyl ester groupings and the infrared spectrum afforded strong indication of the presence of a 5-membered lactone ring. That this substance was indeed a dihydroxy lactone (subsequently shown to be XIIIa) was confirmed by acetylation to a crys-

(20) A pertinent example can be found in the siaresinolic acid series—P. Bilham, G. A. R. Kon and W. C. J. Ross, *J. Chem. Soc.*, 540 (1942), and L. Ruzicka, A. Grob, R. Egli and O. Jeger, *Helv. Chim. Acta*, **26**, 1218 (1943).

talline diacetoxy lactone XIIIb. The absence of any rearrangements was established by lithium aluminum hydride reduction of the lactone and acetylation to the tetrol tetraacetate IIb, already obtained earlier from methyl treleasegenate triacetate (Ic), as well as by transformation to methyl treleasegenate triacetate (Ic) by successive treatments with alkali, diazomethane and finally acetic anhydride.

The identical acid treatment did not result in loss of the ester function and lactonization when the secondary hydroxyl groups were oxidized (see VII → XIa). It was clear, therefore, that one of these hydroxyl groups was implicated and this was confirmed when the lactone XIIIa was obtained in good yield by heating methyl treleasegenate (Ib) with 5% sulfuric acid. Since theoretically lactonization could also have proceeded through an intermediate olefin (15–16 or 21–22 double bonds), model experiments were carried out with methyl cochalate, cochalic acid, echinocystic acid, methyl Δ^{15}-oleanolate, dumortierigenin, methyl *epi*-machaerinate (XVIIc) and methyl machaerinate (XVIIa). In all cases, the starting material was recovered except for methyl machaerinate (XVIIa) where infrared analysis of the total reaction product showed the presence of appreciable amounts of lactone. This not only suggested that the secondary hydroxyl group of treleasegenic acid involved in lactone formation is located at C-21, but it also afforded excellent evidence for the β-orientation of the C-21 hydroxyl group in machaerinic acid[10,21] since its epimer XVIIc showed no trace of lactone by infrared examination.

In an attempt to accomplish detritylation of the diacetoxy trityl ether VIb without loss of the acetate functions, the acid cleavage was conducted with hydrogen chloride in chloroform solution and there was isolated indeed the required diacetoxy 30-ol XIV accompanied by the diacetoxy lactone XIIIb. The latter apparently was produced by ester exchange and lactonization and in view of the unsatisfactory yield of XIV, the following alternate approach involving repeated trityl ether formation was employed.

Since in the dihydroxy lactone XIIIa—produced from the trityl ether VIa or more directly from methyl treleasegenate (Ib)—one of the alcoholic groups is already protected as the lactone, the latter was again tritylated at C-30 and acetylated to yield the acetoxy lactone 30-trityl ether XVb. Treatment with hydrogen chloride–chloroform now resulted only in loss of the trityl group and thus offered an intermediate (XVIa) in which all functional groups except the C-30 alcohol were protected. Chromium trioxide oxidation furnished the corresponding aldehyde-lactone acetate XVIb and Wolff-Kishner reduction followed by methylation (of the hydroxy acid formed by alkaline opening of the lactone) gave methyl machaerinate (XVIIa), further characterized as the 3β,21β-diacetate XVIIb.

The above described interconversions of treleasegenic acid with queretaroic acid and machaerinic acid provide rigorous proof for the structure and stereochemistry of this novel cactus triterpene acid which can now be given the systematic name 21β,30-dihydroxyoleanolic acid. It is noteworthy that this structure falls beautifully within the earlier mentioned pattern[6] for cactus triterpenes, according to which oxygenation is observed only in rings D and E aside from C-3. Treleasegenic acid is the third naturally occurring triterpene for which oxygenation at C-21 has been established, the other two[10] being machaeric (XVIId) and machaerinic (XVIIa) acids.

One stereochemical point merits additional comment. The formation of a lactone between a 28-oic acid and a 21-hydroxyl group is sterically impossible in a D/E *cis* fused pentacyclic triterpene with the conventional all-chair conformation. Conformational rigidity among triterpenes is generally accepted[22] although cases are known[23,24] of the terminal A ring existing in a boat form due to special circumstances. It should be noted that lactone formation in the case of treleasegenic acid would require as a minimum a change of the E ring from a chair to a boat form, but inspection of models would suggest that most likely ring D would also have to undergo a transformation to a quasi-boat. Such conformational transformations among non-terminal rings are unexpected, but apparently are rather facile if the proper driving force exists. This conformational distortion, permitting lactone formation, also explains why the methyl esters of machaeric, machaerinic and treleasegenic acids are saponified with relative ease since 5-membered cyclic intermediates[10] are possible, thus permitting intramolecular assistance by a 21-ketone or 21β-alcohol.[25]

It will be recalled that treleasegenic acid was isolated from the cactus in the form of its methyl ester. Since a prior step in the isolation procedure involved hydrolysis of the glycosides with methanolic hydrochloric acid, it can be considered almost certain that the methyl ester is formed during the processing of the cactus extract. While methylation of the free acid is the most obvious explanation, it is also conceivable that treleasegenic acid might occur in the cactus as a glycoside of the lactone XIIIa, which formed the methyl ester upon refluxing with methanolic hydrochloric acid. That such an alternative cannot be rejected is demonstrated by the experimental conversion of the lactone with methanolic hydrochloric acid to methyl treleasegenate

(21) The earlier (ref. 10) assignment of the β-orientation was based only on a molecular rotation argument

(22) D. H. R. Barton, A. J. Head and P. J. May, *J. Chem. Soc.*, 935 (1957).

(23) H. R. Arthur, A. R. H. Cole, K. J. L. Thieberg and D. E. White, *Chemistry & Industry*, 926 (1956).

(24) D. H. R. Barton, D. A. Lewis and J. F. McGhie, *J. Chem. Soc.*, 2907 (1957).

(25) The β-orientation of the 21-hydroxyl group is further supported by the observation that when methyl 11-oxotreleasegenate triacetate (IV) is heated with 10% methanolic potassium hydroxide and then acidified, methylated (diazomethane) and acetylated, another lactone diacetate is formed. This spontaneous lactonization under conditions where the hydroxy acid is stable in the 11-deoxo series (and hence should lead to the methyl ester after exposure to diazomethane) can be ascribed to isomerization at C-18 (for leading references see J. Simonsen and W. C. J. Ross, "The Terpenes," Vol. IV, p. 192, Cambridge University Press, Cambridge, Eng., 1957), the axial 21β-alcohol in a D/E *trans* system now being situated perfectly for lactonization to yield ultimately XVIII. The ease of lactonization of such a system in its ring D counterpart already has been demonstrated in the dumortierigenin series (ref. 18).

(Ib). It should also be remembered that triterpenoid lactones are fairly common[6] among the *Cactaceae* and that the lactone stellatogenin is the main triterpenoid component of *Lemaireocereus treleasei*.

Experimental[26]

Isolation of Treleasegenic Acid.—The dry alcoholic extract (632 g.)[3] of *L. treleasei* was digested with ether for 2 days, the solution decanted, the residue ground up and again digested with ether. The insoluble saponins (576 g.) were hydrolyzed by heating under reflux for 3 hr. with 5.5 l. of methanol and 1.1 l. of concd. hydrochloric acid. On cooling, 22 g. of crystalline material separated which was collected and recrystallized once from methanol–chloroform to yield stellatogenin of m.p. 316–318°. The sapogenins were isolated from the filtrate by dilution with water and extraction with ether and were then divided in the customary manner[6] into neutral and acidic components. The neutral fraction (125 g.) was acetylated with acetic anhydride–pyridine overnight at room temperature and the crude acetates (132 g.) were chromatographed in benzene solution on 2.5 kg. of alumina. A total of 29 g. (consisting of slightly impure stellatogenin acetate) was insoluble in benzene and was not put on the column. The early benzene eluates yielded high melting material, which crystallized as needles (2.0 g.) melting above 350° from methanol–chloroform and these were identified as oxyallobetulin acetate by infrared comparison with an authentic sample.

Further elution with benzene gave **methyl treleasegenate triacetate** (Ic) crystallizing as needles (13.8 g.) from methanol, m.p. 235–239°. The analytical sample exhibited m.p. 244–245°, $[\alpha]_D$ +88°, $\lambda_{max}^{CHCl_3}$ 5.76 μ (broad).

Anal. Calcd. for $C_{37}H_{56}O_8$: C, 70.67; H, 8.98; O, 20.36; methoxyl, 4.93. Found: C, 71.03; H, 9.03; O, 20.03; methoxyl, 4.88.

Saponification of the methyl ester triacetate was accomplished by boiling for 4 hr. with 10% methanolic potassium hydroxide. Dilution with water gave a clear solution from which the potassium salt separated rapidly. Acidification with hydrochloric acid and filtration afforded **treleasegenic acid** (Ia), m.p. 270–280° after recrystallization from dilute methanol. Further recrystallization raised the m.p. to 280–290° but no sharper m.p. could be realized; λ_{max}^{Nujol} 2.85, 3.06 and 5.83 μ.

Anal. Calcd. for $C_{30}H_{48}O_5$: C, 73.73; H, 9.90. Found: C, 73.43; H, 9.63.

Methyl treleasegenate (Ib) was produced when a methanol suspension of the acid was treated with ethereal diazomethane. Crystallization from aqueous methanol and from chloroform gave needles, m.p. 216–220°, while recrystallization from nitromethane led to a m.p. of 222–225°, $[\alpha]_D$ +77° (pyridine). The analytical results showed that samples from either chloroform or nitromethane were solvated and it proved impossible to secure satisfactory figures.

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03; methoxyl, 6.17. Found: (a) dried at 80° *in vacuo:* C, 67.43; H, 9.15; (b) dried at 100°: C, 70.24; H, 9.51; (c) dried at 140°: C, 72.89; H, 9.65; methoxyl, 6.15; (d) sublimed at 230°: C, 72.86; H, 10.43.

Acetylation of treleasegenic acid (Ia) with acetic anhydride–pyridine and crystallization of the product from methanol gave **treleasegenic acid triacetate** (Id), m.p. 270–275°, $[\alpha]_D$ +87°.

Anal. Calcd. for $C_{36}H_{54}O_8$: C, 70.33; H, 8.85. Found: C, 70.14; H, 8.97.

Δ^{12}-Oleanene-3β,21β,28,30-tetrol (IIa).—Methyl treleasegenate triacetate (Ic) (250 mg.) in 50 cc. of ether was heated under reflux for 20 hr. with 1 g. of lithium aluminum hydride. The excess reagent was decomposed with ethyl acetate followed by addition of a saturated aqueous solution of sodium sulfate. After drying with anhydrous sodium sulfate, the precipitate was filtered and the filtrate was evaporated to dryness and recrystallized from methanol to yield the tetrol IIa, m.p. 319–323° (sublimation starting at 300°), $[\alpha]_D$ +74° (pyridine).

Anal. Calcd. for $C_{30}H_{50}O_4$: C, 75.90; H, 10.62; O, 13.48. Found: C, 75.37; H, 10.78; O, 13.74.

Acetylation in the customary manner and recrystallization from aqueous methanol furnished the tetraacetate IIb, m.p. 150–156° (not improved by two further recrystallizations), $[\alpha]_D$ +75°.

Anal. Calcd. for $C_{38}H_{58}O_8$: C, 70.99; H, 9.09; O, 19.91. Found: C, 70.80; H, 9.03; O, 19.89.

Selenium Dioxide Oxidation of Methyl Treleasegenate Triacetate (Ic).—The methyl ester triacetate Ic (150 mg.) in 15 cc. of acetic acid was heated under reflux with 150 mg. of selenium dioxide for 2 hr. The product, isolated in the usual manner with ether, was filtered through 5 g. of alumina in benzene solution and crystallized from ethanol and ethanol–ethyl acetate to give needles (48 mg.), m.p. 322–324°, $[\alpha]_D$ −37°; λ_{max}^{EtOH} 240.5, 249 and 258 mμ; log ϵ 4.35, 4.37 and 4.18.

Anal. Calcd. for $C_{37}H_{54}O_8$: C, 70.90; H, 8.68. Found: C, 70.70; H, 8.67.

Methyl 11-Oxotreleasegenate Triacetate (IV).—A refluxing solution of 300 mg. of the triacetate methyl ester Ic in 20 cc. of acetic acid was treated dropwise over a period of 1 hr. with 150 mg. of chromium trioxide dissolved in 10 cc. of acetic acid. After heating for a further 30 min., water was added, the precipitate was collected and recrystallized from methanol to yield 195 mg. of colorless needles, m.p. 277–278°, $[\alpha]_D$ +90°; λ_{max}^{EtOH} 247 mμ, log ϵ 4.11; $\lambda_{max}^{CHCl_3}$ 5.76, 6.00 and 8.0 μ.

Anal. Calcd. for $C_{37}H_{54}O_9$: C, 69.13; H, 8.47; O, 22.40. Found: C, 68.72; H, 8.65; O, 22.95.

A sample of this substance was heated under reflux for 3 hr. with 10% methanolic potassium hydroxide, diluted with water, acidified and filtered. The crude precipitate was treated directly with diazomethane in ether and subsequently acetylated with acetic anhydride in pyridine. Chromatography on 10 g. of Merck alumina, elution with benzene–ether (95:5 and 90:10) and recrystallization from methanol–chloroform led to colorless plates of the **diacetoxy lactone XVIII**,[25] m.p. 320–322°; $\lambda_{max}^{CHCl_3}$ 5.60, 5.75, 5.96, 6.10 and 8.0 μ (broad).

Anal. Calcd. for $C_{34}H_{48}O_7$: C, 71.80; H, 8.51; O, 19.69. Found: C, 71.74; H, 8.41; O, 19.45.

Treleasegenic Acid Bromolactone Triacetate (V).—Treleasegenic acid triacetate (Id) (50 mg.) in 5 cc. of chloroform was treated with a slight excess of bromine for 5 min. at room temperature. Crystallization of the product from methanol afforded prisms, m.p. 265° with sintering from 255°, $[\alpha]_D$ +90°; $\lambda_{max}^{CHCl_3}$ 5.60, 5.75 and 8.0 μ.

Anal. Calcd. for $C_{36}H_{57}BrO_8$: C, 62.34; H, 7.70; Br, 11.52; O, 18.45. Found: C, 61.98; H, 7.72; Br, 11.71; O, 18.60.

Methyl Treleasegenate 3,21-Diacetate 30-Trityl Ether (VIb).—Methyl treleasegenate (Ib) (200 mg.) and trityl chloride (600 mg.) in 16 cc. of 1:1 dioxane–pyridine were heated on the steam-bath for 6 hr. and then left at room temperature overnight. Dilution with water, extraction with ether, washing, drying and evaporation yielded an oil which was chromatographed on 15 g. of alumina. Elution with benzene removed triphenylcarbinol, while benzene–ether (9:1) afforded 230 mg. of the oily **trityl ether VIa** ($\lambda_{max}^{CHCl_3}$ 2.85, 5.76 and characteristic aromatic triplet bands at 6.7 μ) which resisted all attempts at crystallization.

Acetylation with acetic anhydride–pyridine produced the **diacetate VIb**, which separated from methanol as an amorphous solid, m.p. 155–165°, $[\alpha]_D$ +110°; $\lambda_{max}^{CHCl_3}$ 5.76, 6.7 (triplet) and 8.0 μ.

Anal. Calcd. for $C_{54}H_{68}O_7$: C, 78.22; H, 8.27; O, 13.51. Found: C, 78.43; H, 8.22; O, 13.21.

Cleavage of the diacetoxy trityl ether VIb by heating for 50 min. with 5% sulfuric acid in acetic acid yielded methyl treleasegenate triacetate (Ic).

Chromium Trioxide–Pyridine Oxidation of Methyl Treleasegenate 30-Trityl Ether (VIa).—The oily trityl ether VIa (207 mg.) was treated overnight with 300 mg. of chromium trioxide in 20 cc. of pyridine. Isolation with ether gave 150 mg. of the **3,21-dioxo-30-trityl ether VII** ($\lambda_{max}^{CHCl_3}$ 5.80 with shoulder at 5.76 μ) as a resin which could not be crystallized.

(26) All melting points were determined on the Kofler block. Unless noted otherwise, all rotations were measured in chloroform solution in 1-dcm. tubes. We are indebted to Mrs. Dolores Phillips for the ultraviolet and infrared spectra and to Dr. Alfred Bernhardt (Mülheim, Germany) for the microanalyses.

The product was heated under reflux for 3 hr. with 20 cc. of 5% sulfuric acid in 75% dioxane–water and isolated in the usual manner by ether extraction. Triphenylcarbinol was separated by benzene elution from an alumina column, while ether removed a yellowish oil which crystallized from hexane–acetone as needles (70 mg.), m.p. 220°. The analytical sample of **methyl 3,21-dioxo-30-hydroxy-Δ^{12}-oleanen-28-oate (XIa)** was recrystallized from aqueous methanol whereupon it exhibited m.p. 222–225°, $[\alpha]_D$ +50°; $\lambda_{max}^{CHCl_3}$ 2.90, 5.79 (infl.) and 5.85 μ.

Anal. Calcd. for $C_{31}H_{46}O_5$: C, 74.66; H, 9.30; O, 16.04. Found: C, 74.57; H, 9.45; O, 15.84.

The 30-acetate XIb crystallized from hexane as needles, m.p. 184–188°, $[\alpha]_D$ +37°.

Anal. Calcd. for $C_{33}H_{48}O_6$: C, 73.30; H, 8.95; O, 17.75. Found: C, 73.09; H, 8.79; O, 17.70.

A 100-mg. sample of the 3,21-dioxo-30-hydroxy methyl ester XIa was heated under reflux for 2.5 hr. with 10% methanolic potassium hydroxide. Attempts to isolate formaldehyde as the dimedone derivative by distilling part of the solution failed, but dilution with water, acidification, filtration of the resulting acid (XIIa?) and remethylation with diazomethane afforded an oil, which resisted crystallization even after chromatography. In contrast to the starting material XIa, the substance showed no hydroxyl band in the infrared and may represent the retroaldolization product XIIb.

Methyl 3-Deoxyqueretaroate (VIIIa). (a) From Treleasegenic Acid.—The crude product VII (1.8 g.) from the chromium trioxide–pyridine oxidation of methyl treleasegenate trityl ether (VIa) was heated under reflux for 1 hr. in 60 cc. of diethylene glycol with 6 cc. of 85% hydrazine hydrate. Potassium hydroxide (6.0 g.) was added and heating was continued for an additional 30 min. Excess water and hydrazine were then boiled off until the temperature rose to 205° and heating under reflux was continued for 4 hr. Dilution with water, acidification and isolation with ether gave a product which was remethylated with diazomethane to yield 1.62 g. of a light colored resin ($\lambda_{max}^{CHCl_3}$ 2.85, 5.75 and aromatic triplet at 6.7 μ). Detritylation was accomplished by heating under reflux for 3 hr. with 100 cc. of 5% sulfuric acid in 75% dioxane–water and the crude product was chromatographed on 45 g. of Merck alumina. Triphenylcarbinol was removed with benzene while benzene–ether (9:1) eluted an oil, which crystallized from hexane as needles (405 mg.), m.p. 118–135°, raised to 137–140° after three recrystallizations from nitromethane. The melting point of methyl 3-deoxoqueretaroate (VIIIa) could not be improved on further recrystallization and was not changed by drying in a high vacuum; $[\alpha]_D$ +75°, $\lambda_{max}^{CHCl_3}$ 2.8 and 5.75 μ.

Anal. Calcd. for $C_{31}H_{50}O_3$: C, 79.10; H, 10.71; O, 10.20. Found: C, 78.72; H, 10.39; O, 10.83.

For adequate characterization, the alcohol was acetylated with acetic anhydride–pyridine overnight at room temperature. Crystallization of the product from methanol led to the **acetate VIIIb** as thick needles, m.p. 164–166°, $[\alpha]_D$ +90°, $\lambda_{max}^{CHCl_3}$ 5.75 and 8.0 μ.

Anal. Calcd. for $C_{33}H_{52}O_4$: C, 77.29; H, 10.22; O, 12.48. Found: C, 76.90; H, 10.61; O, 12.56.

(b) **From Queretaroic Acid.**—Methyl queretaroate (IXa)[15] (1.48 g.), trityl chloride (3.0 g.) and pyridine (60 cc.) were heated on the steam-bath overnight. The products were isolated with ether and chromatographed on 70 g. of Merck alumina in 1:1 hexane–benzene. Development of the chromatogram with the same solvent mixture afforded triphenylcarbinol while elution with benzene and benzene–ether (9:1) gave **methyl queretaroate 30-trityl ether (IXb)** as a non-crystallizable resin ($\lambda_{max}^{CHCl_3}$ 2.85, 5.78 and 6.7 μ (triplet)).

A portion (840 mg.) of the trityl ether IXb was oxidized in pyridine solution (30 cc.) with 700 mg. of chromium trioxide overnight at room temperature and the resulting crude oxidation product Xa (620 mg., $\lambda_{max}^{CHCl_3}$ 5.8 (broad) and triplet near 6.7 μ) was detritylated in the customary fashion by boiling for 3 hr. with 5% sulfuric acid in 75% dioxane–water. **Methyl 3-dehydroqueretaroate (Xb)** was separated from triphenylcarbinol by chromatography and crystallized from methanol as needles showing m.p. 254–256°, $[\alpha]_D$ +42°, $\lambda_{max}^{CHCl_3}$ 2.8 and 5.8 μ (broad).

Anal. Calcd. for $C_{31}H_{48}O_4$: C, 76.81; H, 9.98; O, 13.20. Found: C, 76.45; H, 10.27; O, 13.42.

Wolff–Kishner reduction of 100 mg. of the ketone Xb was carried out in the above-described manner and furnished 52 mg. of methyl **3-deoxoqueretaroate (VIIIa)**, m.p. 133–138°, $[\alpha]_D$ +76°, the infrared spectrum of which was identical with that of the specimen prepared according to procedure a.

Anal. Calcd. for $C_{31}H_{50}O_3$: C, 79.10; H, 10.71; O, 10.20. Found: C, 78.71; H, 10.66; O, 10.46.

Identity was confirmed by the preparation of the **acetate VIIIb**, m.p. 163–165°, undepressed upon admixture with the sample derived from treleasegenic acid, $[\alpha]_D$ +89°; the infrared spectra of the two acetate specimens proved to be superimposable.

Anal. Calcd. for $C_{33}H_{52}O_4$: C, 77.29; H, 10.22; O, 12.48. Found: C, 76.84; H, 10.47; O, 12.61.

Treleasegenic Acid 28 → 21-Lactone (XIIIa). (a) **From Methyl Treleasegenate (Ib).**—Methyl treleasegenate (2.0 g.) was heated under reflux for 3 hr. with 150 cc. of 5% sulfuric acid in 75% dioxane–water[27] and the solution was concentrated somewhat until a precipitate appeared. On cooling, the lactone XIIIa separated as needles (1.35 g.),[28] m.p. 288–292°. Recrystallization from nitromethane gave the analytical sample which exhibited m.p. 300–303°, $[\alpha]_D$ +48° (pyridine); λ_{max}^{Nujol} 2.90, 2.95, 5.72 μ but no band at 8.0 μ.

Anal. Calcd. for $C_{30}H_{46}O_4$: C, 76.55; H, 9.85; O, 13.60. Found: C, 76.02; H, 9.71; O, 14.01.

Acetylation with acetic anhydride–pyridine at room temperature overnight and crystallization from methanol–chloroform yielded the **lactone diacetate XIIIb** as plates, m.p. 308–310°, $[\alpha]_D$ +25°; $\lambda_{max}^{CHCl_3}$ 5.62, 5.76 and 7.96 μ.

Anal. Calcd. for $C_{34}H_{50}O_6$: C, 73.61; H, 9.09; O, 17.31. Found: C, 73.73; H, 8.98; O, 17.75.

That no rearrangement (skeletal or stereochemical) had occurred during lactone formation was demonstrated by the following reactions:

(i) When 60 mg. of the lactone diacetate XIIIb was heated under reflux for 2 hr. with 5% ethanolic potassium hydroxide, diluted with water, acidified with hydrochloric acid, again made basic and extracted with ethyl acetate virtually no neutral material was isolated.[29] Reacidification and filtration gave an acid fraction which was methylated with diazomethane and acetylated to furnish 50 mg. of methyl treleasegenate triacetate (Ic).

(ii) The lactone diacetate XIIIb (100 mg.) was treated with methanolic hydrochloric acid under the conditions used for the acid cleavage of the crude cactus triterpenoid glycosides and after acetylation provided 70 mg. of methyl treleasegenate triacetate (Ic).

(iii) Lithium aluminum hydride reduction of 100 mg. of the lactone diacetate in the manner described earlier (Ic → II) followed by acetylation gave 90 mg. of the tetrol tetraacetate IIb, m.p. 150–156°, $[\alpha]_D$ +76°.

(b) **From Methyl Treleasegenate Diacetate Trityl Ether (VIb).**—A solution of 160 mg. of the trityl ether VIb in 20 cc. of 5% sulfuric acid in 75% dioxane–water was heated under reflux for 2 hr. and the product was isolated by ether extraction. Leaching with hexane–benzene (1:1) removed triphenylcarbinol and the insoluble residue was recrystallized from methanol and from nitromethane to give the lactone XIIIa, m.p. 297–301°. Identity with the specimen prepared according to (a) was established by mixture melting point determination and infrared comparison.

Cleavage of Methyl Treleasegenate Diacetate 30-Trityl Ether (VIb) with Hydrogen Chloride–Chloroform.—In

(27) Similar treatment of methyl cochalate, cochalic acid, dumortierigenin, methyl Δ^{16}-oleanolate, echinocystic acid and methyl epimachaerinate (XVIIc) resulted only in unchanged starting material, no lactone being formed as demonstrated by infrared examination of the total crude product. On the other hand, the infrared spectrum of the methyl machaerinate (XVIIa) reaction product exhibited a lactone band ($CHCl_3$ solution) at 5.62 μ in addition to one at 5.74 μ due to unreacted methyl ester.

(28) A similar yield of lactone could be realized when treleasegenic acid was subjected to the same acid treatment.

(29) Thus demonstrating that lactonization does not occur under those conditions in marked contrast to the behavior of the 11-keto lactone IV (→ XVIII) – see footnote 25.

order to examine the feasibility of retaining the acetate protecting groups under detritylation conditions, hydrogen chloride gas was passed for 2 hr. at room temperature through a solution of 1.4 g. of the trityl ether diacetate VIb in 50 cc. of dry chloroform. The solvent was removed *in vacuo* and the residue was adsorbed from 1:1 hexane–benzene on 70 g. of Merck alumina. Elution with this solvent mixture gave 365 mg. of triphenylcarbinol, while benzene led to an oil and then to a crystalline solid (265 mg.). Crystallization from methanol–chloroform and from benzene produced needles, m.p. 290–294°, which were shown by mixture melting point determination, infrared comparison and analysis to be somewhat impure lactone diacetate XIIIb.

Anal. Calcd. for $C_{34}H_{50}O_6$: C, 73.61; H, 9.09; O, 17.31. Found: C, 73.52; H, 9.21; O, 16.88.

Further development of the chromatogram with benzene–ether (1:1) and crystallization of the resulting solid from methanol afforded 240 mg. of **methyl treleasegenate 3,21-diacetate (XIV)** as needles showing m.p. 224–228°, $[\alpha]_D$ +80°; $\lambda_{max}^{CHCl_3}$ 2.85, 5.77 and 8.0 μ.

Anal. Calcd. for $C_{35}H_{54}O_7$: C, 71.64; H, 9.28; O, 19.09. Found: C, 71.74; H, 9.26; O, 19.19.

Treleasegenic Acid 28 → 21-Lactone 3-Acetate 30-Trityl Ether (XVb).—The lactone XIIIa (1.3 g.) was heated on the steam-bath overnight with 3.0 g. of trityl chloride in 60 cc. of pyridine. The products were isolated with ether in the usual manner and chromatographed on 70 g. of Merck acid-washed alumina. Elution with hexane–benzene (1:1) gave 2.69 g. of triphenylcarbinol, while benzene and benzene–ether (9:1) removed 1.61 g. of oil, which appeared to be the desired lactone trityl ether XVa by infrared examination. For adequate characterization, this material was transformed into the acetate XVb, which crystallized from methanol–chloroform as needles, m.p. 213–216°, $[\alpha]_D$ +41°, $\lambda_{max}^{CHCl_3}$ 5.65, 5.76, 6.7 (triplet) and 7.95 μ.

Anal. Calcd. for $C_{61}H_{62}O_5$: C, 81.13; H, 8.27; O, 10.60. Found: C, 80.73; H, 8.35; O, 10.70.

Cleavage of this acetate trityl ether (1.3 g.) was performed with hydrogen chloride–chloroform exactly as described above for the trityl ether diacetate VIb and there was obtained in addition to 150 mg. of unchanged starting material XVb (m.p. 211–215°), 360 mg. of the **lactone 3-monoacetate XVIa**, m.p. 300–304° (from methanol–chloroform), $[\alpha]_D$ +16°; $\lambda_{max}^{CHCl_3}$ 2.90, 5.65, 5.80 and 8.0 μ.

Anal. Calcd. for $C_{32}H_{48}O_5$: C, 74.96; H, 9.44; O, 15.60. Found: C, 74.60; H, 9.44; O, 16.21.

Δ^{12}-Oleanene-3β,21β-diol-30-al-28-oic Acid 28 → 21-Lactone-3-Acetate (XVIb) and Conversion to Methyl Machaerinate (XVIIa).—A solution of 250 mg. of the lactone 3-acetate XVIa in 40 cc. of acetone (distilled from potassium permanganate) was treated dropwise with 0.14 cc. of standard chromium trioxide–sulfuric acid reagent.[30] After 5 minutes, much water was added, the product was extracted with ether and chromatographed on 7.5 g. of alumina. Elution with benzene–ether (9:1) gave the aldehyde XVIb as needles (104 mg.) from hexane–benzene, m.p. 290–295°, $[\alpha]_D$ +42°; $\lambda_{max}^{CHCl_3}$ 5.60, 5.78 and 7.97 μ.

Anal. Calcd. for $C_{32}H_{46}O_5$: C, 75.26; H, 9.08. Found: C, 75.04; H, 9.01.

The aldehyde (90 mg.) was heated under reflux for 1 hr. with 8 cc. of diethylene glycol and 0.4 cc. of 85% hydrazine hydrate. Potassium hydroxide (0.4 g.) was added, the mixture was heated under reflux for 30 min., the condenser was removed and the temperature was allowed to rise to 205°. After heating under reflux for an additional 3 hr., water and hydrochloric acid were added, the precipitated acid was collected and methylated with diazomethane. Crystallization from aqueous methanol gave 50 mg. of methyl machaerinate (XVIIa)[31] of m.p. 229–232°, $[\alpha]_D$ +72°; identity with an authentic sample[10] was established by mixture melting point determination and infrared comparison.

Acetylation with acetic anhydride–pyridine gave methyl machaerinate diacetate (XVIIb), m.p. and mixture m.p. 275–278°, $[\alpha]_D$ +89°. The infrared spectrum was identical with that of an authentic specimen.[10]

(30) See K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lemin, THIS JOURNAL, **75**, 2548 (1953).

(31) For comparison with methyl treleasegenate (Ib), 50 mg. of methyl machaerinate was boiled for 4 hr. with 10 cc. of 10% methanolic potassium hydroxide, diluted with water and extracted with ether. No neutral material was isolated, but acidification, extraction with ethyl acetate and crystallization afforded 38 mg. of machaerinic acid.

DETROIT, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY]

Azulenes. VIII.[1] 1- and 2-*t*-Butylazulene. Migration of the *t*-Butyl Group

BY WERNER HERZ

RECEIVED OCTOBER 3, 1957

2-*t*-Butylazulene has been synthesized from 2-*t*-butylindan by the diazoacetic ester method. Application of this procedure to 1-*t*-butylindan gave a mixture of 1- and 2-*t*-butylazulene, due to partial migration of the *t*-butyl radical, azulene and a small amount of a 1,3-disubstituted azulene, possibly 1,3-di-*t*-butylazulene.

Because the position of groups on the azulene nucleus determines the visible absorption spectrum,[2] investigations in the azulene series afford a unique and facile method for studying the migration of substituents on an aromatic ring. It was this circumstance which led to the discovery that in the dehydrogenation of guaiol with selenium, methyl group migration takes place from the 1- to the 2-position of the azulene nucleus.

Under the somewhat less rigorous conditions required by dehydrogenation with palladium–charcoal, migration of alkyl groups seems to be susceptible to steric factors. Thus, 1-methyl, 1-ethyl- and 1-isopropylazulene all have been prepared in pure form.[2] On the other hand, while no migration occurs in the preparation of 1,4,8-trimethylazulene,[3] replacement of the 1-methyl group by the bulkier isopropyl radical results in isopropyl group migration and formation of vetivazulene.[4,5] Similar results, apparently due to interference between isopropyl and methyl groups in position 1 and 8 of the azulene nucleus, were reported subsequently[6] in another series of compounds. Ukita and co-workers[7] also observed isopropyl group migration when the tertiary alcohol obtained from the reac-

(1) Paper VII, W. Herz, THIS JOURNAL, **78**, 1485 (1956).

(2) For a review, see M. Gordon, *Chem. Revs.*, **50**, 127 (1952).

(3) W. Herz, THIS JOURNAL, **74**, 1350 (1952).

(4) W. Herz, *ibid.*, **75**, 73 (1953).

(5) The same migration, but under very much milder conditions (dehydrogenation with chloranil of the product which results when 1-isopropylazulene is treated with excess methyllithium), has been observed recently by K. Hafner and H. Weldes, *Ann.*, **606**, 90 (1957).

(6) W. Herz and B. E. Cleare, THIS JOURNAL, **77**, 2318 (1955).

(7) T. Ukita, H. Watanabe and M. Miyazaki, *ibid.*, **76**, 4584 (1954).