good agreement with the reported chemical shifts of two other 6β-methoxy-4-en-3-ones.[15]

(15) S. Julia, B. Decouvelaere, and F. Engelmann [*Bull. Soc. Chim. France*, 2277 (1966)] reported the following for 6β-methoxy-4-cholesten-3-one and 6β-methoxy-4-androstene-3,17-dione, respectively: δ 1.28, 1.31 (19-H_3); 3.19, 3.23 (6β-OCH_3); 3.65, 3.73 (t, 6α-H); 5.77, 5.83 (4-H).

Registry No.—Ia, 2066-13-9; Ib, 2944-79-8; Id, 13871-44-8; Ie, 13871-45-9; IIIa, 13871-46-0; IIIb, 13970-31-5; IIId, 13871-47-1; IV, 13871-48-2; V, 13871-49-3; 17α-ethynyl-17β-acetoxyestra-3,5-dieno-[3,4-*b*]dithiane, 13970-30-4.

Terpenoids. LX.[1] Revised Structures of the Cactus Triterpene Lactones Stellatogenin and Thurberogenin[2]

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A combination of chemical and spectral evidence is presented demonstrating that the pentacyclic triterpene lactones, thurberogenin and stellatogenin, previously believed to have structures I and II, respectively, are in fact correctly represented as III (thurberogenin) and IV (stellatogenin). By optical rotatory dispersion measurements on appropriate derivatives, the C-19 stereochemistry of III and IV has been shown to be the same (19α side chain) as in betulinic acid (XIII) and other lupane derivatives. The results of certain previously described experiments which appeared to support the earlier structural assignments (I and II) for thurberogenin and stellatogenin, respectively, are discussed and shown to be in accord with the revised structures.

Earlier papers in this series described the isolation and characterization of the title compounds from the cactus species *Lemaireocereus stellatus*[3] and *Lemaireocereus thurberi*,[4] respectively. Thurberogenin and stellatogenin were shown to possess the structural feature, unprecedented at that time among naturally occurring triterpenes,[5] of a lactone ring,[3,4] and thurberogenin was correlated with stellatogenin by the demonstration that the latter could be converted in a facile manner to the former, without skeletal rearrangement, by dehydrative elimination of a side-chain tertiary hydroxyl group.[3]

On the basis of biogenetic considerations and of a series of chemical transformations, structures I and II were proposed for thurberogenin and stellatogenin, respectively.[6] Subsequent confirmation for the presence of the lupane skeleton came from interrelation of a thurberogenin degradation product (XXIII) with one of known structure derived from betulinic acid (XIII).[7] (See Chart I.)

At the time that these structure assignments were made, nuclear magnetic resonance and mass spectrometry had not yet been employed in triterpene chemistry. Recently, we had occasion to examine the nmr and mass spectra of certain thurberogenin and stellatogenin derivatives, which showed that the earlier assignments were untenable. We have now accumulated a combination of chemical and spectral data that permits the conclusive assignment of structures III and IV to thurberogenin and stellatogenin, respectively. It is our present purpose to set forth the evidence which dictates these findings, as well as to discuss some of the chemical transformations reported previously[6,7] in the light of the structures now known to be correct.

For the sake of convenience much of the experimental and spectral information was obtained from thurberogenin derivatives. Since the relationship of stellatogenin to thurberogenin has been rigorously demonstrated,[3] any structural conclusions concerning the latter compound apply as well to the former.

It can be seen that the difference between the originally proposed (I) and revised (III) structures for thurberogenin involves the position and nature (*i.e.*, tertiary *vs.* secondary) of the hydroxylic terminus of the lactone bridge. Important information on this point comes from the nmr spectrum of dihydrothurberogenone (now known to have structure V), obtained from thurberogenin by catalytic hydrogenation of the side chain and oxidation of the C-3 hydroxyl function.[6] A complex resonance integrating for one proton is observed at δ 4.60, indicative of the grouping $H\overset{|}{C}OR$. This function must involve the lactonic hydroxyl group, since the other two oxygens above in V are carbonyls, *and the hydroxyl group involved in lactone formation must therefore be secondary.*

Supporting spectral evidence for this conclusion was obtained in the following manner. Lithium aluminum hydride reduction of dihydrothurberogenin (III with saturated side chain) cleaves the lactone ring and furnishes a triol VI, readily esterifiable with acetic anhydride–pyridine.[6] The acetylation product VIa, originally thought to be a diacetate, shows a molecular ion peak in the mass spectrum at *m/e* 586 as well as a prominent fragment ion at 526 (M − CH_3COOH), indicating it to be in fact a *triacetate* ($C_{36}H_{58}O_6$). The

(1) Paper LIX: T. Nakano, M. Hasegawa, T. Fukumaru, S. Tobinaga, C. Djerassi, L. J. Durham, and H. Budzikiewicz, *Tetrahedron Letters*, 365 (1967). The preseut article represents also part XIV in the series "Triterpenes" by B. Tursch, *et al.* (for preceding paper, see *Tetrahedron Letters*, 2129 (1967)).

(2) Financial support from the National Institutes of Health (Grant No. GM-06840) is gratefully acknowledged.

(3) C. Djerassi, L. H. Liu, E. Farkas, A. E. Lippman, A. J. Lemin, L. E. Geller, R. N. McDonald, and B. J. Taylor, *J. Am. Chem. Soc.*, **77**, 1200 (1955). In the same paper the isolation of stellatogenin from still another cactus genus is described.

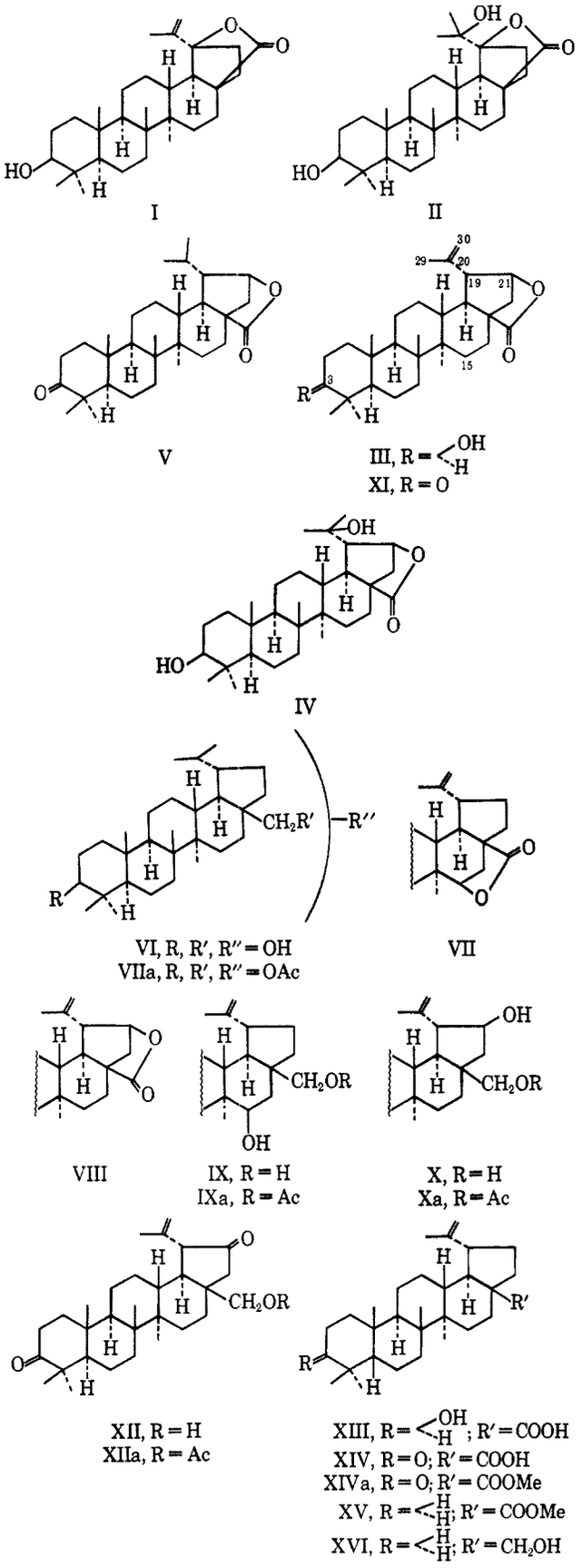
(4) C. Djerassi, L. E. Geller, and A. J. Lemin, *ibid.*, **75**, 2254 (1953).

(5) The list of pentacyclic triterpenes reported to contain lactone rings has grown somewhat in recent years. For a compilation, as well as for reviews of structural progress in this field, see T. G. Halsall and R. T. Aplin in "Progress in the Chemistry of Organic Natural Products," Vol. 22, L. Zechmeister, Ed., Springer-Verlag, Vienna, 1964, pp 153–202, as well as P. Boiteau, B. Pasich and A. R. Ratsimamanga, "Les Triterpénoides," Gauthier-Villars, Paris, 1964.

(6) C. Djerassi, E. Farkas, L. H. Liu, and G. H. Thomas, *J. Am. Chem. Soc.*, **77**, 5330 (1955).

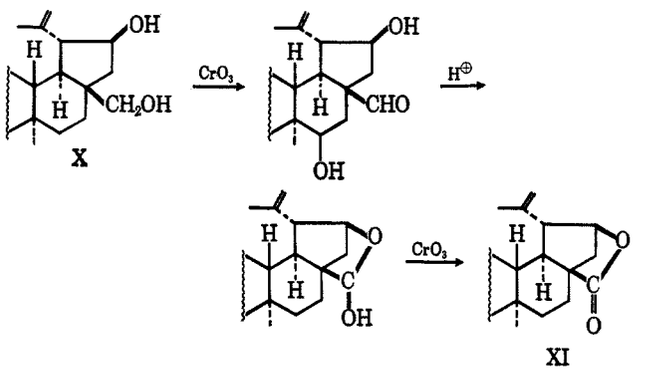
(7) C. Djerassi and R. Hodges, *ibid.*, **78**, 3534 (1956).

CHART I



presence of three acetyl groups is confirmed by the nmr spectrum, which displays signals at 1.96 δ (singlet, 3 H) and 2.04 (singlet, 6 H). A complex absorption pattern in the δ 4.2–5.2 region integrating for four protons is partially resolved in the 100-Mc spectrum to an AB quartet (2 H, $-CH_2OAc$) and two one-proton multiplets (2 HCOAc). The presence of a primary alcohol (from reduction of the lactonic carboxyl), a secondary alcohol (ring A), and yet another secondary alcohol (lactonic hydroxyl) in triol VI is thus confirmed.

With the lactonic hydroxyl established as secondary, only two termini (C-15 and C-21, see partial structures VII and VIII) for the five-membered lactone ring of thurberogenin need now be considered. A choice between these alternatives is possible, in principle, by oxidation of the lithium aluminum hydride reduction product (partial structure IX or X) of thurberogenin or some suitably protected derivative thereof. A cyclohexanone system should arise from IX, while X would generate a cyclopentanone. Initial attempts to oxidize thurberogenintriol directly with the Jones reagent[8] produced a mixture, the major component of which was shown to be thurberogenone (XI) by its infrared spectral properties and thin layer chromatographic mobility. This result is not unexpected[9] if the primary hydroxyl is the first to undergo oxidation, *e.g.*, X → XI.



To circumvent this difficulty an attempt was made to protect the primary hydroxyl group of thurberogenintriol (IX or X) as a trityl ether. Surprisingly, however, selective tritylation could not be achieved;[10] in fact, only under forcing conditions was any significant reaction of the primary hydroxyl group observed. Eventually it was found that simple acetylation under carefully controlled conditions produced the desired primary monoacetate (IXa or Xa) in satisfactory yield. Oxidation of this material with the Jones reagent[8] followed by mild basic hydrolysis furnished a diketo alcohol, $C_{30}H_{46}O_3$, with the appropriate molecular ion peak at m/e 454 in the mass spectrum and displaying two cleanly separated carbonyl bands ($\lambda_{max}^{CHCl_3}$ 5.77 and 5.90 μ) in the infrared spectrum. The higher wavelength absorption is attributable to the C-3 carbonyl function, while that at lower wavelength falls precisely at the position anticipated for a cyclo-

(8) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

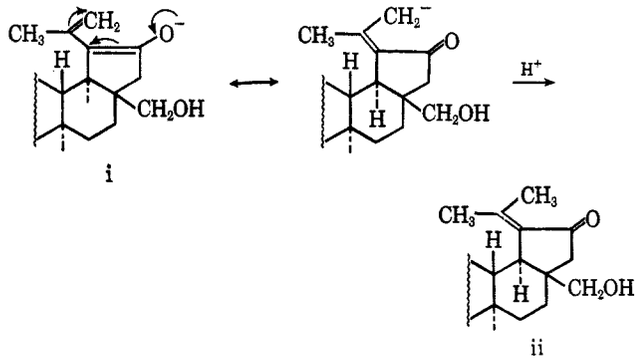
(9) See, for example, H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p. 87.

(10) This result was unexpected, because similarly situated (neopentyl) hydroxyl groups in the β-amyrin triterpenes chichipegenin and longispinogenin could be selectively tritylated without difficulty (A. Sandoval, A. Manjarrez, P. R. Leeming, G. H. Thomas, and C. Djerassi, *J. Am. Chem. Soc.*, **79**, 4468 (1957)). The greater rigidity of the *trans*-hydrindan *vs.* the *cis*-decalin skeleton, as well as the additional steric hindrance imposed by the presence of a hydroxyl group *cis*-1,3 to the bridgehead hydroxymethyl group of thurberogenin triol, are presumably the factors accounting for the lack of reactivity in the present case.

pentanone.[11] Structure XII is therefore established for the diketo alcohol, whereupon it follows that thurberogenin triol must be X and its progenitor, thurberogenin, III.

To assure that no gross skeletal rearrangement had occurred in its preparation, a correlation of the diketo alcohol XII with a compound of known structure was achieved in the following manner. Betulinic acid (XIII) was oxidized with the Jones reagent[8] to betulonic acid (XIV). Modified Wolff–Kishner reduction[12a] of the latter, followed by esterification with diazomethane, furnished methyl 3-deoxybetulinate (XV), which was reduced with lithium aluminum hydride to 3-deoxybetulin (XVI),[12b] mp 140–142°. When the diketo alcohol XII derived from thurberogenin was subjected in the form of its acetate XIIa to the same Wolff–Kishner reaction conditions,[12a] a nonketonic product was obtained in good yield. This material, although homogeneous by thin layer chromatography and exhibiting the same mobility as authentic XVI, proved difficult to crystallize and exhibited a wide melting range (mp 106–137°) even after repeated recrystallizations. However, both its mass and infrared spectra are identical in every respect with those of 3-deoxybetulin (XVI). Clearly a mixture of epimers at C-19 is involved, since the combination of an adjacent carbonyl group and the strongly basic conditions of the Wolff–Kishner reduction provides ample opportunity for isomerization at that center.

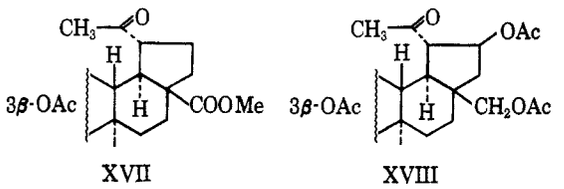
The stability of the β,γ-enone system of XII deserves some comment. One might normally anticipate rearrangement to the conjugated ketone (i → ii) in the presence of base. No such migration was observed, however, in the base-catalyzed hydrolysis of acetate XIIa, and deliberate attempts to generate the α,β-unsaturated enone system by subjecting XII to the action of refluxing methanolic sodium methoxide were likewise unavailing. Even under the strenuous conditions of the Wolff–Kishner reduction we detected no double-bond migration. This behavior reflects the severe steric interaction which models indicate would



i ii

be generated between the C-12 methylene group and an isopropylidene group at C-19 in a molecule possessing the lupane skeleton.[13] Other manifestations of this potential interaction include the findings that dehydration of the C-20 tertiary hydroxyl group of stellatogenin (IV) affords only thurberogenin (III) and not the isopropylidene isomer,[3] and that acid-catalyzed rearrangement of lupane derivatives containing the terminal isopropenyl group inevitably leads to skeletal rearrangement rather than simple double-bond migration. In fact we are unaware of any reported example, naturally occurring or otherwise, of the lupane system with a terminal isopropylidene group.[14]

While the results described so far define the gross structure of thurberogenin, they do not permit an unequivocal assignment of stereochemistry at C-19. Optical rotatory dispersion (ORD) measurements enabled this final ambiguity to be resolved. Preparation of the 30-norketo ester XVII by oxidative cleavage of the terminal methylene group of betulinic acid



XVII XVIII

(XIII) under conditions mild enough to preclude epimerization at C-19 has been previously described.[15] Application of a similar reaction sequence to the triacetate of thurberogenintriol (X) afforded the corresponding 30-nor ketone XVIII, and the ORD curves of XVII and XVIII proved to be very similar, both exhibiting moderately strong positive Cotton effects (see Experimental Section). Steroidal analogies demonstrate that a vicinal substituent *trans* to an acetyl side chain has very little effect on the ORD curve.[16] This fact, in conjunction with the gross differences shown to exist between the ORD curves of various steroidal epimeric pairs differing only in the configuration of an acetyl function, particularly in those instances where the rotation of that group is restricted,[17] as is almost certainly the case in the present instance (see preceding discussion concerning the nonexistent C-19 isopropylidene group), provides conclusive evidence that the C-19 configurations of XVII and XVIII are the same.

The structure of thurberogenin is therefore correctly represented by III and that of stellatogenin by IV, with the C-19 stereochemistry being the same as in betulinic acid (XIII).[18]

It is now appropriate to examine two reactions, the results of which were originally thought to provide

(11) Characteristic absorption wavelengths, in chloroform solution, are, for cyclopentanones, 5.76–5.80 μ; for cyclohexanones, 5.87–5.90 μ (K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1964, p 42).

(12) (a) W. Nagata and H. Hazaki, *Chem. Ind.* (London), 1194 (1964). (b) L. Ruzicka and S. D. Heineman (*Helv. Chim. Acta*, **23**, 1512 (1940)) reported mp 140–141° for a specimen prepared by a somewhat different route.

(13) T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 1905 (1954).

(14) Barbier–Wieland degradation of the lupene side chain *via* the C-19 diphenylmethylidene derivative has, however, been reported (L. Ruzicka, W. Huber, and O. Jeger, *Helv. Chim. Acta*, **28**, 195 (1945); G. S. Davy, E. R. H. Jones, and T. G. Halsall, *Rec. Trav. Chim.*, **69**, 368 (1950)).

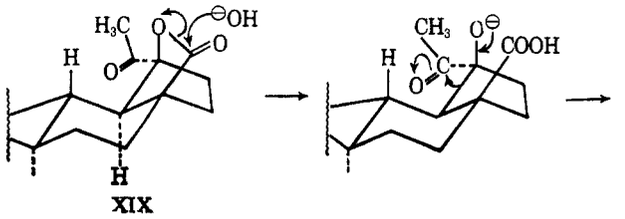
(15) The key step (see ref 7) involved periodic acid cleavage of the 20,30-glycol system. Interestingly, a hydroxy acid, platanic acid, has recently been isolated from natural sources (A. F. Thomas and J. M. Muller, *Chem Ind.*, (London), 1794 (1961)) and demonstrated to have the structure corresponding to XVII (R. T. Aplin, T. G. Halsall, and T. Norin, *J. Chem. Soc.*, 3269 (1963)).

(16) P. Crabbé, F. McCapra, F. Comer, and A. I. Scott, *Tetrahedron*, **20**, 2455 (1964); J. C. Danilewicz and W. Klyne, *J. Chem. Soc.*, 1306 (1965); K. M. Wellman and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 60 (1965).

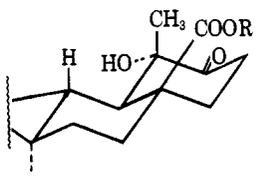
(17) For a discussion and references, see P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, pp 134–140; C. Djerassi, *Proc. Chem. Soc.* (London), 314 (1964).

(18) Every lupane triterpene reported to date (*cf.* ref 5) possesses this same configuration at C-19.

strong evidence for I as the correct structure of thurberogenin.[6,7] The first of these involved treatment with methanolic alkali of the 30-nor ketone obtained by ozonolysis of thurberogenin acetate to give a dihydroxy keto acid with one esterifiable hydroxyl group (C-3), characterized as the methyl ester and methyl ester acetate. On the assumption that the nor ketone had the partial structure XIX, this acid was formulated as an E-homo derivative XX, produced as indicated below in accord with the analogous behavior of 17-hydroxy-20-keto steroids to give D-homo derivatives.[19] Such a reaction path is of course incompatible

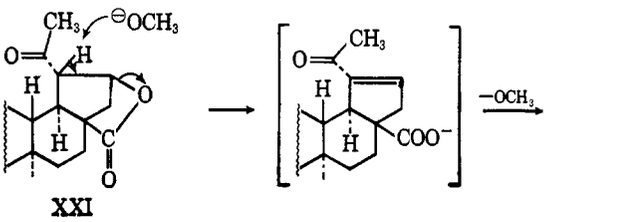


XIX

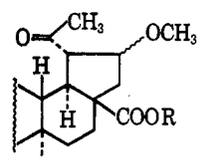


XX, R = H; 3β-OH
XXa, R = CH_3; 3β-OH
XXb, R = CH_3; 3β-OAc

with structure XXI for the 30-nor ketone, based on the revised expression III for thurberogenin. The mass spectrum of the keto acid methyl ester indicates a molecular composition $C_{31}H_{50}O_5$ (*m/e* 502, M^+), which formula differs from that of XXa by the presence of an extra CH_2 unit.[20] In addition there is a prominent fragment ion at *m/e* 470 ($M - CH_3OH$). The presence of an ethereal $-OCH_3$ group was confirmed by a proton singlet at δ 3.21 in the nmr spectrum, which displays as well signals at δ 3.70 (singlet, 3 H) and 2.17 (singlet, 3 H) corresponding to $-COOCH_3$ and $-C(=O)CH_3$ groups, respectively. Consideration of these data suggested structure XXII for the keto acid, which can be derived mechanistically from the nor



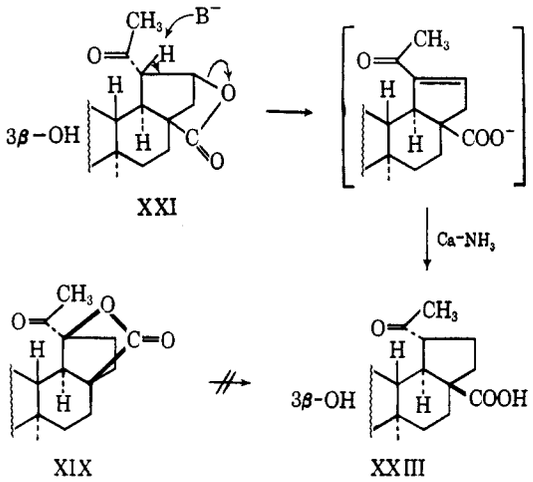
XXI



XXII, R = H; 3β-OH
XXIIa, R = CH_3; 3β-OH
XXIIb, R = CH_3; 3β-OAc

ketone XXI as indicated. The 19α configuration of the keto acid XXII follows from the positive ORD Cotton effect of XXIIa which was virtually identical with that of XVII and XVIII.

The second reaction of interest is the conversion[7] of the nor ketone XXI to the 30-nor-20-ketobetulinic acid derivative XXIII by calcium–ammonia reduction. Originally thought to proceed *via* reduction of an α-acyloxy ketone system (XIX → XXIII), the reaction may now be formulated as indicated in the accompanying diagram (XXI → XXIII). The proton-abstracting agent involved in the initial step may be either amide ion ($^-NH_2$) or alkoxide ion generated by reaction of a hydroxyl group, *i.e.*, that at C-3, with calcium, while ample precedent exists for the double-bond reduction of α,β-unsaturated ketones in metal–ammonia systems.[21]



XXI

XIX XXIII

The presence of an oxygen function at C-21 places thurberogenin and stellatogenin in a unique position among triterpenes possessing the lupane skeleton. However, C-21 oxygenation is by no means unknown among cactus triterpenes since in the β-amyrin series, machaeric acid,[22] machaerinic acid,[22] and treleasegenic acid[23] are all distinguished by oxygenation at that position.

Experimental Section[24]

Proton magnetic resonance spectra were obtained using Varian A-60 and HR-100 nmr spectrometers, and chemical shifts are reported in parts per million (δ) relative to an internal tetramethylsilane standard. Infrared spectra were recorded on Perkin-Elmer Model 137 and 421 spectrometers. Ultraviolet spectra were recorded on a Cary 14 instrument. ORD measurements were carried out using a JASCO Model 5 ORD/CD/UV recording spectropolarimeter. Mass spectra were determined at 70 ev using A. E. I. MS-9 and Atlas CH-4 instruments equipped with direct inlet systems. Melting points were determined on a Kofler micro hot stage and are uncorrected. Analytical thin layer chromatography (tlc) was carried out

(19) It should be kept in mind that the lactone ring of thurberogenin itself is stable to base.[6]

(20) Such differences in molecular composition are not amenable to detection by conventional C,H analysis. For example, the calculated values for XXa are C, 73.73; H, 9.90, while those for XXIIa are C, 74.06; H, 10.03.

(21) Lithium appears to be the reagent of choice for such reductions; *cf.* J. E. Starr in "Steroid Reactions," C. Djerassi, Ed., Holden-Day, San Francisco, Calif., 1963, Chapter 7; H. Smith, "Organic Reactions in Liquid Ammonia," Interscience Publishers, Inc., New York, N. Y., 1963, p 231. The use of calcium may therefore be at least partly responsible for the low yield of XXIII actually obtained.[7]

(22) C. Djerassi and A. E. Lippman, *J. Am. Chem. Soc.*, **77**, 1825 (1955).

(23) C. Djerassi and J. S. Mills, *ibid.*, **80**, 1236 (1958).

(24) We are pleased to thank Dr. Lois J. Durham for obtaining the nmr spectra, Dr. A. M. Duffield for the mass spectral determinations, and Mrs. R. Records for the ORD measurements.

using microscope slides coated with silica gel G or GF (Merck A.-G., Darmstadt) and development systems containing varying proportions of methanol in benzene as indicated, while preparative tlc was effected on 20 × 20 cm plates employing the same adsorbents and solvent systems.

Nmr Data on Dihydrothurberogenone (V).—The preparation of V has been previously described.[6] The integrated nmr spectrum (deuteriochloroform solution) showed a multiplet at 4.60 (1 H, C-18 hydrogen). There were no other resonances below 2.7.

Spectral Data on Dihydrothurberogenintriol Triacetate (VIa).—The preparation of VIa (mistakenly identified as a diacetate) has been previously described.[6] The nmr spectrum (100 Mc, deuteriochloroform solution) indicates the presence of three acetyl groups: singlet, 1.96 (3 H); singlet, 2.04 (6 H); and a total of four hydrogens on carbon bonded as well to oxygen. The two hydrogens of the primary $-CH_2OAc$ group attached at C-18 appear as an AB quartet ($J \simeq 7$ cps) due to the adjacent asymmetric center, centered at 4.27 (2 H). Multiplets at 4.48 (1 H) and 5.00 (1 H) can be assigned to the C-3 and C-18 hydrogens, although not necessarily in the order indicated.

The mass spectrum of VIa shows peaks at *m/e* 586 (M^+), 526 ($M - CH_3COOH$), 466 ($M - 2CH_3COOH$), etc.

Direct Oxidation of Thurberogenintriol (X).—To a stirred solution of 230 mg (0.5 moles) of thurberogenintriol (X)[6] in 90 ml of acetone was added dropwise the Jones reagent (1.5 equiv) under ice cooling during 30 min, at which time very little starting material could be detected by tlc (4:1 benzene–methanol). Solid sodium bicarbonate and isopropyl alcohol were added to neutralize the reaction mixture and destroy any excess reagent, respectively. The reaction mixture was dried over magnesium sulfate and filtered, followed by evaporation of the filtrates under reduced pressure. Preparative tlc (4:1 benzene–methanol) on the resulting residue furnished a semicrystalline product, 150 mg, which was recrystallized from methanol to give 68 mg of cream-colored crystals. This material, although homogeneous by tlc, was apparently a mixture. The infrared spectrum showed all the absorptions anticipated for thurberogenone (XI) as well as peaks (λ_{max}^{KBr} 3.68, 5.73, 5.81(sh) μ, etc.) suggesting the presence of the originally anticipated product, 3,21-dioxolup-20(30)-en-28-al.

Several other experiments in which the dilution, reaction temperature, and relative proportions of reactants were varied produced no material effect on the over-all reaction course.

Attempted Tritylation of Thurberogenintriol (X).—A solution of X (200 mg) and freshly prepared trityl chloride (600 mg) in 8 ml of pyridine and 8 ml of dioxane was heated for 8 hr on the steam bath. Work-up followed by chromatography on neutral alumina (activity II) furnished 112 mg of X, 16 mg of a glass corresponding in tlc mobility to a monotrityl derivative, and 34 mg of a glass having the mobility of a ditrityl derivative. In view of the low yield and apparent nonselectivity of the tritylation reaction as evidenced by this and other experiments, this approach was not pursued further. In a control experiment using the same reagents and conditions described above, chichipegenin was smoothly converted to its 28-monotrityl derivative.[10]

Thurberogenintriol 28-Monoacetate (Xa).—To a stirred ice cooled solution of 500 mg (1.09 mmoles) of thurberogenintriol (X) in 8 ml of dry pyridine was added 0.3 ml of acetic anhydride, and stirring at ice bath temperature was continued for 100 min. The reaction mixture was treated with excess methanol, concentrated under reduced pressure, and diluted with ether. The ether solution was washed successively with dilute hydrochloric acid, water, and saturated brine, followed by drying over magnesium sulfate and evaporation of the solvent. Chromatography of the residue on neutral alumina (activity III) and elution with benzene–ether (1:9–1:4) furnished 143 mg of the crystalline monoacetate Xa, homogeneous by tlc (4:1 benzene–methanol). Several recrystallizations from acetone–hexane afforded the analytical sample, which apparently contained 0.5 mole of acetone of crystallization and exhibited a double melting point: mp 124–127°; resolidified, mp 206–207°.

Anal. Calcd for $C_{32}H_{52}O_4 \cdot 0.5C_3H_6O$: C, 76.12; H, 10.35; mol wt (without solvent of crystallization) 500. Found: C, 76.17; H, 10.57; *m/e* 500.

From earlier and later column eluates, which were combined and hydrolyzed with methanolic sodium methoxide, there was recovered 343 mg of thurberogenintriol (X). The yield of Xa based on unrecovered starting material was therefore 83.3%.

Acetoxydione XIIa.—A solution of thurberogenintriol monoacetate Xa (100 mg) in 20 ml of acetone maintained at ice bath temperature was oxidized with 0.16 ml of the Jones reagent[8] during 15 min. The reaction mixture was treated with 2-propanol and solid sodium bicarbonate, dried over magnesium sulfate, and filtered through Florisil. Evaporation of the filtrates under reduced pressure furnished XIIa as a residue, homogeneous by tlc (4:1 benzene–methanol), which crystallized partially on trituration with methanol: $\lambda_{max}^{CHCl_3}$ 5.76 (acetate and cyclopentanone C=O), 5.90 (cyclohexanone C=O), 6.08, 8.1–8.3 μ (broad), etc. This material was used for the next step without further purification.

Hydroxydione XII.—The acetoxydione XIIa prepared from 100 mg of monoacetate Xa was hydrolyzed for 1 hr at room temperature by treatment with a solution of 200 mg of sodium methoxide in 20 ml of methanol. The reaction mixture was then neutralized with saturated ammonium chloride solution, concentrated under reduced pressure, and extracted with chloroform. Evaporation of the extracts after washing with saturated brine and drying over magnesium sulfate furnished a partially crystalline residue, homogeneous by tlc (4:1 benzene–methanol), which was recrystallized from acetone–ether to give 58 mg of the hydroxydione XII as white needles, mp 214–216°. Recrystallization from the same solvent pair furnished the analytical sample: mp 215–217°; $\lambda_{max}^{CHCl_3}$ 2.77, 5.76 (cyclopentanone C=O), 5.90 (cyclohexanone C=O), 6.08 μ, etc.; ORD data (*c* 0.06, dioxane), $[\Phi]_{589}$ +216°, $[\Phi]_{328}$ +9648° (peak), $[\Phi]_{322}$ +7488° (trough), $[\Phi]_{317}$ +8064° (peak), $[\Phi]_{280}$ −7992° (trough).

Anal. Calcd for $C_{30}H_{46}O_3$: C, 79.24; H, 10.20; mol wt, 454. Found: C, 79.18; H, 10.23; M^+, *m/e* 454.

Betulonic Acid (XIV) and Methyl Betulonate (XIVa).—A solution of 0.92 g (2 mmole) of betulinic acid (XIII) in 200 ml of acetone was treated for 10 min at room temperature with 0.80 ml of the Jones reagent,[8] at which time tlc indicates essentially complete absence of starting material. After quenching with 2-propanol, the reaction solution was filtered through cellulose. Dilution of the filtrates with water followed by concentration under reduced pressure produced a white precipitate which was collected, washed with aqueous acetone, and dried, giving 0.87 g of XIV, homogeneous by tlc (4:1 benzene–methanol). This material was used directly for subsequent reactions.

A portion of the above material was esterified with an ethereal solution of diazomethane. Chromatography of the reaction production neutral alumina (activity III) and elution with 2:1 hexane–benzene furnished methyl betulonate (XIVa) as white needles, mp 167–169° (lit.[25] mp 165°).

Methyl 3-Deoxybetulinate (XV).—Betulonic acid (XIV) was subjected to the modified Wolff–Kischner reduction conditions of Nagata.[12a] A solution of 0.440 g (0.97 mmole) of XIV in 10 ml of *n*-butanol and 50 ml of triethylene glycol was purged with nitrogen, followed by the addition of 10 ml of 95% hydrazine dihydrochloride. The mixture was stirred for 2.5 hr at 130°, then 4.5 g of solid potassium hydroxide was added. Slow distillation of the mixture was then allowed to proceed until the pot temperature reached 210° (~1.5 hr), and refluxing at this temperature was continued for 3 hr. The mixture was cooled, diluted with water and ether, made slightly acidic with aqueous hydrochloric acid, and extracted several times with ether. The combined extracts were washed with saturated brine, dried over magnesium sulfate and evaporated under reduced pressure to give a residue which was esterified with ethereal diazomethane followed by chromatography on basic alumina (activity I). Elution with 1:4–3:2 benzene–hexane furnished 0.230 g of XV as white rods, homogeneous by tlc. Recrystallization from ether–methanol furnished white rods: mp 156–157.5° with previous sublimation (lit.[25] mp 153°); λ_{max}^{KBr} 5.75, 6.06 μ, etc.

3-Deoxybetulin (XVI).—A 0.120-g (0.26 mmole) portion of ester XV was reduced by refluxing for 3 hr with 0.70 g of lithium aluminum hydride in 20 ml of ether and 4 ml of tetrahydrofuran. There was obtained after work-up a colorless oil, 0.092 g, homogeneous by tlc (benzene). Crystallization from methanol afforded XVI as white needles: mp 140–142° with previous sublimation (lit.[26] mp 140–141°); λ_{max}^{KBr} 2.92, 3.26, 6.10, 9.77, 11.37 μ, etc.

Anal. Calcd for $C_{30}H_{50}O$: mol wt, 426. Found: M^+, *m/e* 426.

(25) L. Ruzicka and E. Rey, *Helv. Chim. Acta*, **24**, 529 (1941).
(26) L. Ruzicka and S. D. Heineman, *ibid.*, **23**, 1512 (1940).

Wolff-Kischner Reduction of Acetoxydione XIIa.—The acetoxydione XIIa obtained by Jones oxidation[8] of 0.100 g of thurberogenin monoacetate (Xa) was subjected to modified Wolff-Kischner reduction[12a] as described in the preceding experiment. The reaction product, after work-up, was chromatographed on basic alumina (activity I). A fraction containing a major, more mobile and a small, minor, less mobile compound (tlc, 4:1 benzene–methanol) was obtained from the 3:2 ether–chloroform eluates. Preparative tlc (4:1 benzene–methanol) on this fraction furnished the major component as a pale yellow oil, 0.069 g, which crystallized on trituration with methanol. The product, although homogeneous by tlc, melted over a wide range, which behavior was not significantly altered by recrystallization. After three recrystallizations from methanol, it had mp 106–137°. The infrared spectrum (KBr pellet) of this material, however, was superimposable on that of authentic 3-deoxybetulin (XVI), and its mass spectrum (*m/e* 426) was identical in every detail with that of authentic XVI. The 3-deoxybetulin obtained from XIIa is apparently a mixture of C-19 epimers.

ORD Spectral Data Pertaining to the Stereochemistry at C-19. A. Methyl-3-acetoxy-30-nor-20-ketobetulinate (XVII).—The preparation of this compound has been described previously.[7] It exhibited the following ORD spectrum (*c* 0.087, dioxane): $[\Phi]_{305}$ +1368 (peak), $[\Phi]_{260}$ −1938° (trough).

B. Thurberogenintriol Triacetate 30-Nor 20-Ketone (XX).—This compound was prepared by a method similar to that described[7] for the preparation of XVII. It exhibited the following ORD spectrum (*c* 0.033, dioxane): $[\Phi]_{589}$ 0°, $[\Phi]_{305}$ +1848° (peak), $[\Phi]_{257}$ −2184° (trough).

C. Methyl 20-Keto-19-methoxy-30-norbetulinate (XXIIa).—The preparation of this compound (the "E-homo" derivative) has been described previously.[6] It exhibited the following ORD spectrum (*c* 0.045, dioxane): $[\Phi]_{589}$ 0°, $[\Phi]_{306}$ +1601° (peak), $[\Phi]_{255}$ −3937° (trough).

Attempted Double-Bond Isomerization of Hydroxydione XII.—A sample (*ca.* 20 mg) of XII was heated at reflux in a solution of 1.50 g of sodium methoxide in 20 ml of methanol. Aliquots for ultraviolet examination were withdrawn periodically during a 24-hr period, but the generation of any significant chromophore in the 240 mμ region was not observed. The major component of the reaction mixture after 24 hr was indicated to be unchanged starting material by tlc (4:1 benzene–methanol) examination.

Registry No.—III, 13950-48-6; IV, 13950-49-7; V, 13950-50-0; X, 13950-51-1; Xa, 13950-52-2; XII, 13952-73-3; XIIa, 13952-74-4; XIVa, 4356-31-4; XV, 13952-75-5; XVI, 13952-76-6; XX, 13952-77-7.

Electron-Transfer Polymers. XXXI. Preparation of Difunctional Benzoquinones and Related Derivatives and Polymers

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Synthesis of three 1,4-benzoquinonediols and their derivatives is described. It is shown that these diols form redox polymers through polycondensation reactions in which the quinone group need not be protected. As examples, syntheses of two polyesters and a polyurethane are described. A redox polyester could also be prepared from hydroquinonediacetic acid and 1,4-butanediol. Model compounds for these polyesters show that the ester bond is quite stable under suitable oxidative conditions.

The redox system hyrdoquinone–quinone is completely reversible. When one attempts to install this system in a polymeric structure, and then to describe its reactions, one is faced with certain problems.

(1) One or two functional groups must be introduced into the hydroquinone molecule to make it reactive in a polymerization reaction. This reaction must be such that it takes place at the functional group only and does not involve the hydroquinone or quinone functions in a side reaction. For example, vinylhydroquinone cannot be successfully polymerized[1] because the free hydroquinone group is a strong inhibitor for radical and ionic polymerizations. This difficulty is overcome either by protecting both phenolic hydroxyls with acetyl, benzoyl, ethoxy ethyl, or ether groups,[1] or to some extent by protecting *one* of the hydroxyls with an ether group.[2] The protected monomers can then yield high molecular weight polymers.

(2) The redox units in the resulting polymer are now protected, but the protecting groups must be removed without cross-linking the polymer and without damaging the very reactive redox groups. Depending on the nature of the protecting group it is more or less possible to prepare polymeric redox systems in this way.[1] However, it would be a major improvement to find polymerization reactions that avoid the problem of the protecting groups. (3) The redox properties of the polymers differ in some respects from those of hydroquinone.[3] This behavior, explainable as a kind of neighboring group effect in which internal electron transfer occurs between redox groups under the drive of internal quinhydrone formation[4] complicates the interpretation of the behavior of the polymers as electron exchangers and redox catalysts.

These considerations led us away from polyaddition toward polycondensation reactions. It is known that high molecular weight polymers can be obtained by treating diacyl chlorides with diols at very low temperatures in the presence of a suitable base.[5] The reaction of diols with diisocyanates at low temperature leads to polyurethanes.[6] Both reactions, as well as esterification of diacids with diols, should be suitable for our purposes if applied to quinone derivatives because the quinone group is quite stable under the conditions at which these polymerizations take place. Some redox polymers have been made by polycondensation.[7] We report a systematic study of some quin-

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(7) The literature is reviewed in ref 1.