[CONTRIBUTION FROM THE CHANDLER LABORATORIES, COLUMBIA UNIVERSITY, NEW YORK, N. Y.]

A Stereospecific Route to the Dehydroabietic Acid Configuration[1]

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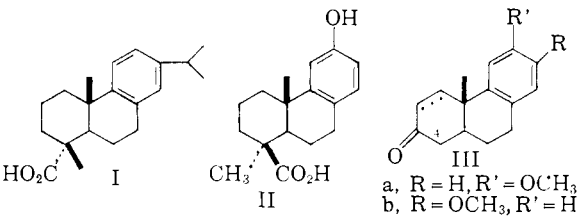
The intermediate 2-keto-6-methoxy-12-methyl-2,3,4,9,10,12-hexahydrophenanthrene (IX) was prepared for a study of the controlled formation of the asymmetric centers of the podocarpic or dehydroabietic acid series of resin acids. Lithium in ammonia and catalytic reductions led to the *trans*- and *cis*-octahydrophenanthrenones X and XI. Stereochemical assignments were established by configurationally controlled enamine bromination and dehydrohalogenation. Conversion of X to *trans*-2-keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XVII) and introduction of carbomethoxy or nitrile functions gave 1-carbomethoxy- and 1-cyno-2-keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XXIII and XXIV). Subsequent axial methylation with electronic rather than steric control resulted stereospecifically in compounds (XXVII) with the configuration of dehydroabietic acid (I). Methylation of the octahydrophenanthrene β-ketonitrile XXX led to a mixture of alkylation products. Analogously, the potential abietic acid intermediate 2-keto-7-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XXXIV) was synthesized. Podocarpic acid (II) was transformed into the nitrile methyl ether XXXVII for comparison with the C-4 epimeric synthetic material XXIX and the nitrile then reconverted to podocarpic acid.

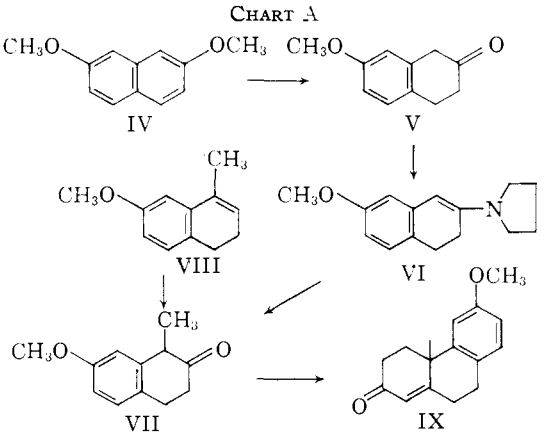
Concurrently with studies which led to the total synthesis of dehydroabietic acid[3] (I), we were interested in other stereoselective approaches which would result in either the abietic or the C-4 epimeric podocarpic acid (II) series of resin acids.[1,4] The presently considered scheme is based on our expectation that alternation in the stepwise introduction of methyl and potential carboxyl functions at C-4 in the tricyclic A–B *trans* fused ketones III (a,b) would selectively produce either of the epimeric series.



The tricyclic enone intermediate IX (m.p. 78–79°, 71% yield, D.N.P. m.p. 201–202°) was prepared by application of the Robinson ring-extension reaction to 7-methoxy-1-methyl-2-tetralone (VII). Similar preparations have since been reported.[5,6] While the tetralone VII was also obtained initially by oxidation of the dihydronaphthalene VIII, it was most conveniently prepared from 2,7-dimethoxynaphthalene (IV), by the sequence shown in Chart A. This route became practical by application of the enamine alkylation[7] to VI, whereby the otherwise difficult clean monomethylation of a β-tetralone is achieved.

Reduction of the tricyclic enone IX with lithium in liquid ammonia led to the A–B *trans* tricyclic ketone X, while catalytic reduction gave the *cis*-ketone XI. Configurational assignments could be made by analogy to the established course of catalytic reduction of the tricyclic enone XX to XXI[8] and

CHART A



by analogy to the reduction of Δ^4-3-ketosteroids by chemical[9–11] and catalytic[12] methods.[13] Confirmation of the stereochemical assignments to tricyclic ketones X and XI was obtained by an examination of their preferential directions of enolization. These are shown in Chart B and follow the expectations for *cis*- and *trans*-decalone systems,[15] in accord with the behavior of A–B *cis*- and *trans*-3-ketosteroids.

In order to prevent simultaneous bromination of the aromatic portion of the molecule, activation of the ketonic function of the *trans*- X and *cis*- XI tricyclic ketones was desired and achieved by formation of the respective enamine derivatives XII and XIII. Direct bromination of the tricyclic ketone X produced a crystalline dibromide (infrared ketone C=O 5.85 μ) on immediate isolation of the reaction product and increasing amounts of oily bromoke-

(1) Part of doctoral dissertation, Martin E. Kuehne, Columbia University, 1955.

(2) CIBA Pharmaceutical Products, Inc., Summit, N. J.

(3) G. Stork and J. W. Schulenberg, *J. Am. Chem. Soc.*, **78**, 250 (1956).

(4) A. W. Burgstahler, Ph.D. Thesis, Harvard University, 1952.

(5) K. Raman and P. N. Rao, *Experientia*, **12**, 472 (1956): oil, 62% yield, D.N.P. m.p. 241–242°.

(6) F. H. Howell and D. A. H. Taylor, *J. Chem. Soc.*, 1248 (1958), report m.p. 63°, 50% yield.

(7) (a) G. Stork, R. Terrell and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954); (b) G. Stork and H. K. Landesman, *ibid.*, **78**, 5128, 5129 (1956).

(8) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

(9) O. Diels and E. Abderhalden, *Ber.*, **39**, 884 (1906).

(10) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5360 (1953).

(11) D. H. R. Barton, D. A. J. Ives and R. R. Thomas, *J. Chem. Soc.*, 903 (1954).

(12) H. Grasshof, *Z. physiol. Chem.*, **223**, 249 (1934).

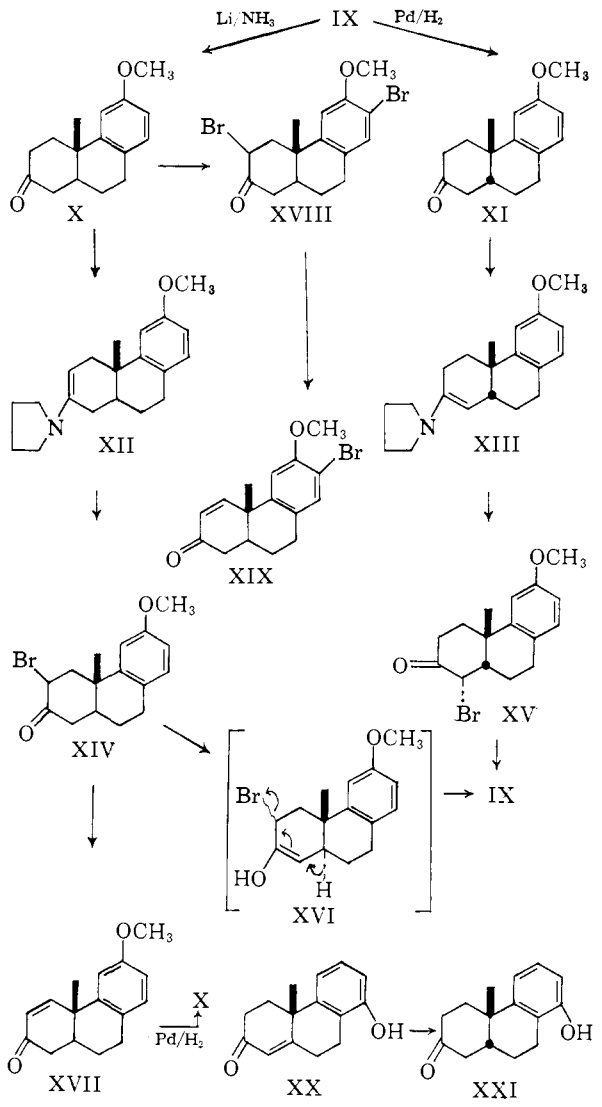
(13) Inherent in the latter analogy is the assumption that the present formation of substituted *cis*- and *trans*-octalones can be compared with that of the steroidal decalone moiety. A consideration of conformational factors in the course of lithium–ammonia reductions of cyclic enone systems has been presented previously[14] and can be extended to the present tricyclic case IX. See E. Wenkert and T. E. Stevens, *J. Am. Chem. Soc.*, **78**, 2318 (1956), for reduction of desmethoxy IX.

(14) G. Stork and S. D. Darling, *ibid.*, **82**, 1512 (1960).

(15) (a) A. Butenandt and L. Mamoli, *Ber.*, **68**, 1850, 1854 (1935); (b) A. Butenandt and A. Wolff, *ibid.*, **68**, 2091 (1935).

tone on prolongation of the reaction time. This observation is consistent with the formation of an initial axial α-bromoketone and epimerization in the acetic acid–hydrogen bromide reaction mixture.[16]

CHART B



While dehydrohalogenation of the dibromide XVIII in dimethylformamide readily produced the enone XIX (m.p. 144°, infrared enone C=O 6.05 μ), this product was obtained in poor yield from the corresponding oily equatorial α-bromoketone, accompanied by undehydrohalogenated material (5.80 μ).

In the A–B *trans* series, the Δ^1-enone XVII was accompanied by small amounts of the saturated ketone X and the Δ^4-enone IX. Formation of the latter compound was not quite unexpected in view of the analogous collidine dehydrohalogenation of *trans*-2α-bromo-9β-methyl-3-decalone,[17] and may be visualized as the product of vinylogous dehydrohalogenation in the enol XVI, or equivalent processes. Whereas the enone IX contaminant was readily removed by recrystallization, the saturated ketone X could not be completely removed even by chromatography. Two chemical methods of separation were thus developed. In the first, borohydride reduction of the mixture and subsequent treatment with manganese dioxide, a selective reagent for oxidation of allylic alcohols, gave the enone XVII, which could readily be separated by crystallization from the saturated hydroxylic material. Alternatively, it was found that the Girard T derivative of X was cleaved back to the ketone at *p*H 5–6, but that the corresponding derivative of the enone XVII required much more acidic conditions.[18]

For further elaboration of our synthetic scheme, it was necessary to block position 2 in X in order to effect condensation at C-4.[19] This was achieved in XVII by the presence of a double bond. As alternatives to the enamine bromination sequence, bromination of an enol acetate and acid hydrolysis or epoxidation of the enol acetate and Serini rearrangement were less successful. Bromination of the anion of 2-formyl or oxalyl derivatives and controlled basic hydrolysis, however, gave fair yields of bromoketone, which could be dehydrohalogenated.

Direct introduction of a carbomethoxy group by condensation of the enone XVII with dimethyl carbonate or methyl phenyl carbonate was not satisfactory, but condensation with methyl oxalate readily yielded the oxalyl derivative XXII. Decarbonylation to the β-ketoester XXIII proceeded poorly, in agreement with other studies on oxalylcyclohexenones.[21] Of interest is the lack of enolization of the β-ketoester XXIII, caused partly by steric strain which would be inherent in the enolic cyclohexadiene. Similar lack of enolization has even been observed in closely analogous saturated β-ketoesters in a *trans* fused octalin and yohimbinone and ascribed to the *peri* effect.[22] The compound is insoluble in 10% sodium hydroxide and does not give a color reaction with ferric chloride. To circumvent the difficult carbethoxylation, a nitrile group was introduced by formylation, isoxazole formation and base-catalyzed rearrangement of the heterocycle to the β-ketonitrile XXIV.[23,24]

Alkylation of the carbanion corresponding to the ketonitrile XXIV is controlled by two factors: Maximum charge overlap with the carbonyl and nitrile functions favors axial introduction[25] of an electrophilic group, whereas steric repulsion by the axial angular methyl group should shield XXIV from axial attack and favor the equatorially alkyl-

(16) (a) E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2301, 3297, 4832 (1953); (b) **76**, 175 (1954).

(17) M. Yanagita, *et al.*, *J. Org. Chem.*, **18**, 792 (1953); **21**, 500 (1956); **22**, 291 (1957).

(18) A. Zaffaroni, R. B. Burton and E. H. Keutmann, *J. Biol. Chem.*, **177**, 109 (1949).

(19) Condensation at 2 would be expected by the preferred direction of enolization as well as the high steric requirement of the Claisen condensation. The latter is seen in the formation of 3-acyl-2-tetralones from β-tetralones.[20]

(20) G. Stork and R. K. Hill, *J. Am. Chem. Soc.*, **79**, 495 (1957).

(21) R. Meyer, *Ber.*, **88**, 1859 (1955).

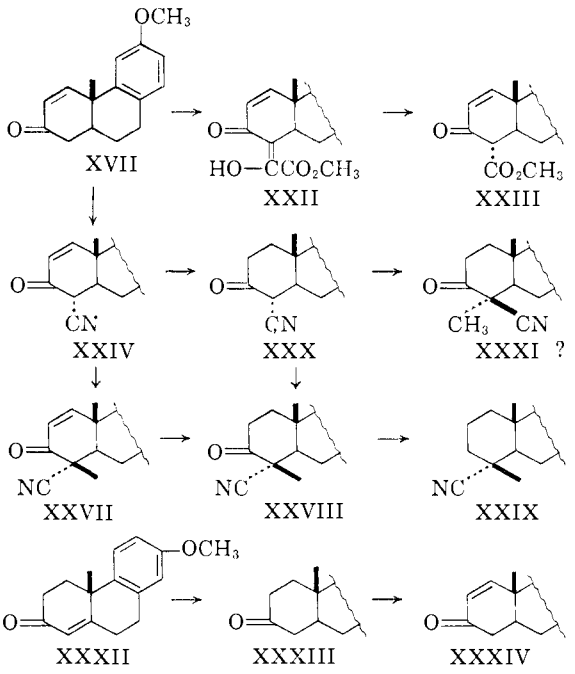
(22) E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **81**, 5601 (1959).

(23) K. v. Auwers, Th. Bahr and E. Frese, *Ann.*, **441**, 68 (1925).

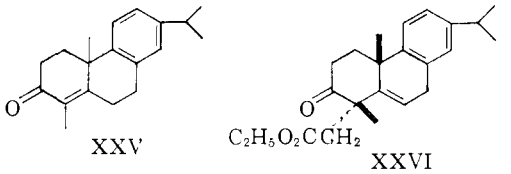
(24) W. S. Johnson and W. E. Shelberg, *J. Am. Chem. Soc.*, **67**, 1745 (1945); W. S. Johnson, J. W. Petersen and C. D. Gutsche, *ibid.*, **69**, 2942 (1947).

(25) W. S. Johnson, *Chemistry & Industry*, 167 (1956).

CHART C



ated product. That steric direction is given to similar alkylations of carbanions has been observed with hydroxyl, alkoxyl and acyloxy groups placed in an analogous 1,3-diaxial relationship.[26-28] It was also found that the Δ^4-4-methyl tricyclic enone intermediate XXV in the synthesis of dehydroabietic acid was alkylated at C-4 on the side opposite the angular methyl group.[3] Methylation of the keto-



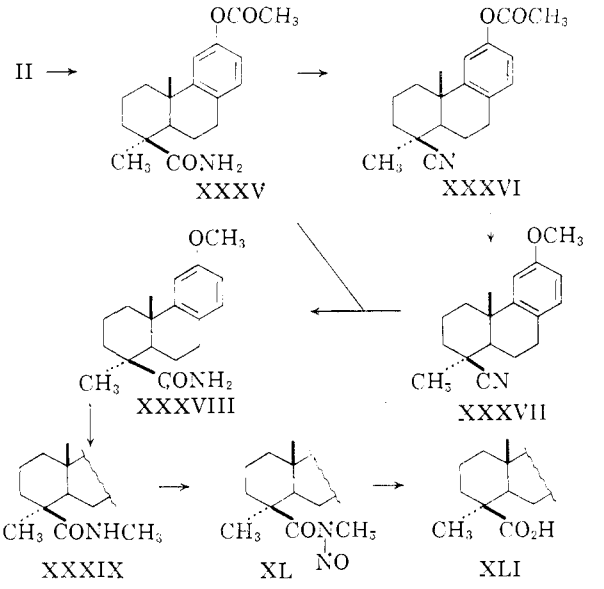
nitrile XXIV led to a single crystalline product XXVII in 80% yield, the balance of material appearing as tars. Catalytic reduction of the double bond (XXVIII) and desulfurization of the corresponding thioketal gave the crystalline nitrile methyl ether XXIX. Infrared (CS_2 and CCl_4) comparison with the nitrile methyl ether XXXVII, derived from podocarpic acid, showed a sufficiently large number of differences in the fingerprint region to ensure the epimeric nature of the compounds at C-4. *The present sequence thus represents a stereospecific route to compounds with the stereochemistry of dehydroabietic acid.*

The observed lack of steric hindrance by the axial angular methyl group to axial alkylation at C-4 is of special interest[29] in view of contrary experience in other cases.[26-28] Examination of models shows that the presence of the double bond in the ketonitrile XXIV causes a flattening of the ketonic ring, further augmented in the enolate undergoing alkylation. Shielding to C-4 alkylation by the angular methyl group thereby becomes sufficiently low to permit the electronically favored axial attack to take place. In the saturated β-ketonitrile XXX, hindrance by the angular methyl group is increased and thus its methylation led to a mixture of products which could not be readily separated.

By an analogous series of steps, the tricyclic enone XXXII[6,30] was reduced (XXXIII)[30] and converted to the enone XXXIV,[31] a suitable intermediate for the synthesis of abietic acid by the reaction sequence above.

Chart D shows the conversion of podocarpic acid (II) to the nitrile methyl ether XXXVII and a reconversion to podocarpic acid. The steps leading from the nitrile XXXVII to the acid XLI may be of general interest as a method for the hydrolysis of extremely hindered amides[32]: Monomethylation of the sodium salt of the amide XXXVIII in dimethylformamide, followed by nitrosation with nitrosyl chloride, yielded the N-nitrosoamide XL, which was smoothly cleaved by base to the acid XLI. In contrast, the common drastic hydrolysis methods did not affect the amide XXXVIII, and treatment with amyl nitrite and hydrogen chloride[33] gave only a 9% yield of acid and the balance of material as nitrile.

CHART D



Acknowledgment.—The author wishes to thank Professor Gilbert Stork for his inspiring guidance throughout this work and Columbia University for a Quincy Ward Boese fellowship (1954–1955).

Experimental

7-Methoxy-1-methyltetralone-2 (VII).—Methylation of 2,7-dihydroxynaphthalene with a large excess of dimethyl sulfate and sodium hydroxide gave a quantitative yield of

(26) L. H. Sarett, *et al.*, *J. Am. Chem. Soc.*, **75**, 2112 (1953).
(27) A. Wettstein, *et al.*, *Helv. Chim. Acta*, **40**, 1034, 1438 (1957).
(28) J. H. Fried, *et al.*, *J. Am. Chem. Soc.*, **82**, 1684 (1960).
(29) Methylation of analogous tricyclic enone- and ketoesters gave comparable results: E. Wenkert, private communication, and E. Wenkert and A. Tahara, *J. Am. Chem. Soc.*, **82**, 3229 (1960).
(30) J. T. Rundquist, Ph.D. thesis, Harvard University, 1951.
(31) For an elegant different synthesis of the desmethoxy compound see E. Wenkert and T. E. Stevens, *J. Am. Chem. Soc.*, **78**, 5627 (1956).
(32) An alternative method of hydrolysis of the nitrile XXXVII is given in ref. 29.
(33) N. Sperber, D. Papa and E. Schwenk, *J. Am. Chem. Soc.*, **70**, 3091 (1948).

2,7-dimethoxynaphthalene (IV), m.p. 139°, reported[34] 139°. Reduction with sodium in ethanol[35] gave the methoxy-β-tetralone V in 65% yield, b.p. 130–140° (0.3 mm.), reported[36,37] 123–125° (0.4 mm.). Nitrogen was passed through a solution of 85.0 g. (0.48 mole) of V in 200 ml. of dry benzene, 40.0 g. (0.57 mole) of pyrrolidine added and the reaction refluxed with a water separator for 3 hours under nitrogen. After concentration *in vacuo*, the residual oil was refluxed for 5 days in 350 g. of methyl iodide. The quaternary amine salt was decomposed by stirring in 500 ml. of water for 40 hours at 25° and 1 hour at 100°. Ether extraction, drying and evaporation gave 83 g. of crude tetralone, b.p. 123–124° (0.25 mm.), 91% yield. The D.N.P. derivative, m.p. 164.0–164.5°, showed no depression with the derivative formed from the product of perphthalic acid oxidation of 7-methoxy-1-methyl-3,4-dihydronaphthalene[5,6] in 75% yield. A very slow tetralone blue test could be observed with aqueous base. The two products had identical infrared spectra.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.38; H, 4.87. Found: C, 58.35; H, 4.94.

2-Keto-6-methoxy-12-methyl-2,3,4,9,10,12-hexahydrophenanthrene (IX).—To 195 ml. of methanol, through which nitrogen was bubbled, 7.8 g. of potassium hydroxide (0.14 mole) in 16 ml. of water was added. The solution was cooled to 0° and 19.5 g. of VII (0.103 mole) in 35 ml. of methanol added. After cooling to −20°, 7.2 g. of methyl vinyl ketone (0.103 mole) was added slowly, with rapid stirring, keeping the temperature at −10 to −20°. After 1 hour the reaction was permitted to warm to room temperature and stirred overnight, followed by refluxing for 3 hours. The cooled mixture was poured into ice-water, 11.5 ml. of concd. hydrochloric acid (0.14 mole) added, extracted with chloroform, the latter washed with water, dried and evaporated. A quantitative yield of oily product, b.p. 165–195° (0.01 mm.) (jacketed flask temp.), was obtained. Crystallization from ethanol gave 17.7 g. of tricyclic enone, 71% yield, m.p. 78.5–79.0°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.76. Found: C, 78.98; H, 7.56.

The D.N.P. derivative showed m.p. 201.0–201.5°, λ_{max} 387–388 mμ.

Anal. Calcd. for $C_{22}H_{22}N_4O_5$: C, 62.56; H, 5.21. Found: C, 62.47; H, 5.24.

***trans*-2-Keto-6-methoxy- and 7-methoxy-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (X and XXXIII). a.**—To a stirred solution of 1.3 g. of lithium (0.19 mole) in 2 l. of liquid ammonia, 11.0 g. of IX (0.045 mole) was added rapidly in 22 ml. of dry tetrahydrofuran. After 10 minutes dry *t*-butyl alcohol was added in a slow stream. The dark blue solution discolored after 450 ml. had been added; 16.0 g. of ammonium chloride (0.16 mole) was added and the ammonia evaporated overnight. The residue was poured into water, extracted with ether and washed with water. Drying, evaporation and distillation, b.p. 150–180° (0.01 mm.) (jacket temperature), and crystallization from ethanol gave 3.7 g. of X, 34% yield, m.p. 129.5–130°.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.68; H, 8.20. Found: C, 78.68; H, 8.49.

The D.N.P. derivative showed m.p. 169–171°.

Anal. Calcd. for $C_{22}H_{24}N_4O_5$: C, 62.26; H, 5.66. Found: C, 62.17; H, 5.67.

Similarly reduction of XXXII[6,30] gave a 40% yield of XXXIII,[6,30] m.p. 107–108°. Mother liquor oils with CrO_3–pyridine gave further 11% XXXIII.

b.—To 2.4 g. of IX (0.010 mole), dissolved in 20 ml. of dry tetrahydrofuran, 160 ml. of liquid ammonia was added, followed, with rapid stirring, by 2.0 g. of lithium (0.29 mole). After exactly 10 minutes, 22 g. of sodium bromate (0.15 mole) was added and stirring continued for 1 hour. The reaction was cooled in a Dry Ice–acetone-bath, stirred for 1.5 hours, 16 g. of ammonium chloride (0.32 mole) introduced, followed by an additional 22 g. (0.41 mole) after 1 hour. The reaction was worked up as under a, giving 1.1 g. of X, yield 46%. *Note*: Violent eruptions have been observed by other workers using this method in our laboratories.

***trans*-3-Bromo-2-keto-6-methoxy-12-methyl-1,2,3,4,9,10,-11,12-octahydrophenanthrene (XIV).**—Water was azeotropically removed over 5 hours from 2.4 g. of X (0.010 mole), under nitrogen, in 50 ml. of benzene and 5.0 g. of pyrrolidine (0.070 mole). After concentration in vacuum and drying for 2 hours under high vacuum, 3.0 g. of the enamine (0.010 mole) was collected, showing practically no carbonyl absorption in the infrared. The crude XII was dissolved in 100 ml. of dry ether and 1.6 g. of bromine (0.010 mole) in 75 ml. of dry ether added rapidly, with stirring and cooling in a Dry Ice–acetone-bath. The reaction was stirred at low temperature for 1 hour, then at room temperature for 2.5 hours, 100 ml. of water was added and then left overnight. The ether layer was separated, the aqueous portion extracted once with ether and the combined organic extracts dried and concentrated under vacuum to 3.2 g. of bromoketone, yield 100% of crude product (infrared 5.85 μ).

***trans*-2-Keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XVII). With Collidine.**—The crude bromoketone XIV (10.8 g., 0.034 mole) was added to 40 ml. of refluxing collidine, causing the amine hydrobromide to separate after about 5 minutes. Refluxing was contined for 20 minutes, the reaction cooled and poured into water. Extraction with chloroform, washing with 3% hydrochloric acid, drying and evaporation gave a gum, distilled at 160–180° (bath) (0.01 mm.). The distillate, 6.2 g., contained saturated and unsaturated ketonic material (infrared 5.9 and 6.0μ).

Separation of Saturated and Unsaturated Material by Girard T Reagent.—The mixture, 6.2 g., was refluxed in 110 ml. of absolute ethanol with 16 g. of glacial acetic acid and 16 g. of Girard T reagent, for 2.8 hours under nitrogen, poured into water and the acidity adjusted to *p*H 5–6 with sodium carbonate. After 7 hours, the saturated fraction was removed by several extractions with ether and the aqueous portion acidified to below *p*H 4. Repeated extractions with chloroform, the last one after 12 hours, washing of the extracts with 5% aqueous sodium hydroxide and water, subsequent evaporation and distillation at 160–190° (bath) (0.01 mm.), yielded 3.5 g. of unsaturated ketonic material (44% yield from saturated tricyclic ketone, neglecting recovered material). The product showed no saturated ketone (5.9 μ) in the infrared. Crystallization from ethanol and water gave 3.3 g. of material, m.p. 90–110°. Repeated crystallization from ethanol produced 2.0 g. of XVII, m.p. 119–120° (25% yield from saturated tricyclic ketone, neglecting recovered material.) White, crystalline material was obtained from the mother liquors of fractional crystallization from ethanol; m.p. 60–95°.

With Dimethylformamide.—Alternatively 10.8 g. (0.034 mole) of XIV was refluxed with 10 g. of lithium chloride in 75 ml. of dimethylformamide for 5 hours under nitrogen. On pouring into water, extracting with ether and distillation, 6.1 g. of enone-ketone mixture was obtained. Separation through the Girard derivatives gave 2.8 g., m.p 70–95°, recrystallized from ethanol to 1.6 g., m.p. 119–120° (20% yield). Chromatography of 2.8 g. of mother liquor material from several runs, m.p. 60–95°, on 150 g. of alumina, *p*H 7.5, activity II, and elution with cyclohexane gave very small amounts of XVII, m.p. 120°, and IX, m.p. 79°, and the bulk of material as a mixture of the two, progressively changing over many fractions.

Separation of Saturated and Unsaturated Ketonic Material by Reduction and Oxidation.—A solution of 700 mg. of crystalline enone and ketone mixture (0.003 mole) was dissolved in 50 ml. of 95% ethanol and cooled in ice. Then 200 mg. of sodium borohydride (0.0058 mole) was added with 25 ml. of 95% ethanol and the reaction left in the cold for 1 hour and at room temperature for 3 hours. Ethanol was removed at 50° under vacuum. The residue, showing no carbonyl absorption in the infrared, was stirred overnight in 50 ml. of chloroform with 7.0 g. of manganese dioxide (0.080 mole). The reaction was filtered, the residue washed with hot chloroform and the solvent evaporated (infrared 6.0 μ, no band 5.9 μ). One crystallization from ethanol gave 150 mg. of enone mixture (21% yield). Purification by fractional crystallization (ethanol) produced a sample, m.p. 121–122°, λ_{max} 226–227 mμ (log ε 4.35).

(34) H. Buenzly and H. Decker, *Ber.*, **38**, 3268 (1905).

(35) J. W. Cornforth, R. H. Cornforth and R. Robinson, *J. Chem. Soc.*, 689 (1942).

(36) B. W. Horrom and H. Zaugg, *J. Am. Chem. Soc.*, **72**, 721 (1950).

(37) F. B. Diamond and M. D. Soffer, *ibid.*, **74**, 4126 (1952).

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.76. Found: C, 79.25; H, 7.73.

Catalytic Reduction of 2-Keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene.—A solution of 120 mg. of tricyclic enone XVII (0.00050 mole) in 20 ml. of absolute ethanol and a few milligrams of 10% Pd–C catalyst absorbed the theoretical amount of hydrogen at 33°, in 10 minutes. No further uptake could be observed. After filtration, 110 mg. of the saturated ketone crystallized by addition of water (92% yield); m.p. 129°, with no depression on mixed m.p. with authentic tricyclic ketone X.

2-Keto-7-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XXXIV). Through the Enamine.—Following the procedure for X to XVII, enamine formation with 2.4 g. of XXXIII and bromination gave 3.2 g. of crude bromoketone, dehydrohalogenated with dimethylformamide–lithium chloride to 1.7 g. of enone–ketone mixture. Separation through the Girard derivatives and recrystallization from ethanol gave 0.81 g. of XXXIV, m.p. 123–124°, λ_{max} 229–230 mμ; D.N.P. derivative m.p. 110–111°; λ_{max} 382–385 mμ.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.76. Found: C, 79.23; H, 7.38.

Through the Formyl Ketone.—Sodium methoxide, prepared from 1.41 g. of sodium (0.0613 mole) and dried at 150° (0.01 mm.) for 3 hours, was suspended in 50 ml. of dry benzene and 5.00 g. of XXXIII (0.020 mole) in 20 ml. of dry benzene added under nitrogen. After stirring for 10 minutes, 7.55 g. of ethyl formate was added in 10 ml. of dry benzene. The reaction was stirred overnight, poured into ice-water, ether added and the organic layer extracted 2 times with ice-cold 5% aqueous sodium hydroxide. The combined aqueous fractions were acidified, extracted 3 times with ether and the extracts dried and evaporated to give 4.53 g. of crude formyl ketone (81% yield). The crude hydroxymethylene compound (3.3 g., 0.012 mole) was dissolved in 15 ml. of methylene chloride and added to 367 ml. of cold 0.05 *N* sodium hydroxide solution (0.018 mole). The resulting sodium salt solution was extracted once with ether to remove 0.13 g. of neutral material, and 1.9 g. of bromine (0.012 mole) in aqueous potassium bromide solution added dropwise with rapid stirring, followed by 105 ml. of 0.05 *N* cold sodium hydroxide solution (0.006 mole) and sufficient tetrahydrofuran to clear the solution of all bromoformyl ketone which precipitated. The reaction was left at 5° for 6 hours and at room temperature for 15 hours. Tetrahydrofuran was removed from the neutral solution under vacuum and the water suspension extracted with ether. After drying over magnesium sulfate and evaporation, a quantitative yield of crude bromoketone was collected. Leaving the crude α-bromo-α-formyl ketone for 1 hour at room temperature with a tenfold excess of 1.25 *N* sodium hydroxide converted it completely to the carboxylic acid Favorsky rearrangement product, obtained by acidification, extraction with ether and crystallization from methanol–water; m.p. 158–159°.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.85; H, 7.69. Found: C, 73.74; H, 7.36.

Catalytic Reduction of 2-Keto-7-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene.—An equivalent of hydrogen was absorbed by 120 mg. of XXXIV (0.00050 mole) in 10 ml. of ethanol, with 5 mg. of 10% Pd–C at room temperature. Filtration, evaporation and crystallization gave a quantitative yield of XXXIII, m.p. 107–108°, undepressed on mixed m.p. with the product of lithium–ammonia reduction of XXXII.

***cis*-2-Keto-6-methoxy-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (XI).**—A solution of 1.0 g. (0.0041 mole) of IX in 50 ml. of ethanol with 10 mg. of 10% Pd–C absorbed the theoretical amount of hydrogen at 32° in 90 minutes. No further uptake could be observed. After filtration and concentration to 10 ml. the saturated ketone (1.0 g.) crystallized with addition of a few drops of water (100% yield); m.p. 75–76°, steady over 4 crystallizations.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.68; H, 8.20. Found: C, 78.69; H, 8.35.

Bromination of *cis*-2-Keto-6-methoxy-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (XI to IX).—Conversion of 900 mg. (0.0037 mole) of ketone XI to the enamine XIII and bromination with 590 mg. of bromine (0.0037 mole) was carried out as described for the *trans* tricyclic ketone X. Dehydrohalogenation with lithium chloride in dimethylformamide at reflux for 4 hours gave 450 mg. of gum showing a strong enone band in the infrared (6.0 μ) with slight broadening toward the saturated ketone region (5.9 μ). Separation of saturated and unsaturated material was again achieved through selective cleavage of the Girard T derivatives (above). A D.N.P. derivative of the enone fraction, m.p. 197–198°, had undepressed mixed m.p. with the derivative of IX; λ_{max} 387–389 mμ.

3,7-Dibromo-2-keto-6-methoxy-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (XVIII).—To 244 mg. of X (0.00100 mole) in 10 ml. of purified glacial acetic acid, 320 mg. of bromine (0.00200 mole) in 10 ml. of glacial acetic acid was added dropwise over 15 minutes. After standing at room temperature for 10 minutes, the reaction was poured into ice-water, extracted with ether, washed with 2.5% sodium hydroxide, with water and dried over magnesium sulfate. Evaporation left a foamy residue which crystallized from ether–petroleum ether, giving 402 mg., 100% yield, m.p. after 4 crystallizations 163.3–163.7°.

Anal. Calcd. for $C_{16}H_{18}Br_2O_2$: C, 47.76; H, 4.48. Found: C, 47.66; H, 4.39.

An infrared spectrum showed considerable modification of the anisole absorption characteristic of all other tricyclic compounds in the series. When the sequence was repeated, leaving the reaction for 1 hour after addition of bromine, 120 mg. of crystalline dibromide was obtained (30% yield), accompanied by the balance of material as the non-crystalline dibromide. After 3 hours, only 40 mg. of crystalline dibromide was obtained (10% yield).

7-Bromo-2-keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XIX).—A solution of 100 mg. of XVIII (0.000250 mole) in 10 ml. of dimethylformamide and 100 mg. of lithium chloride (0.00240 mole) was refluxed under nitrogen for 4 hours, poured into ice-water, extracted with chloroform, dried and evaporated. Crystallization from ethanol gave 56 mg. of bromoenone, m.p. 137–138°; recrystallized from ethanol, m.p. 144.0–144.5°, λ_{max} 227 mμ. A D.N.P. derivative decomposed above 240° over a broad range.

Anal. Calcd. for $C_{22}H_{21}BrN_4O_3$: C, 52.70; H, 4.23. Found: C, 52.68; H, 4.38.

1-Carbomethoxy-2-keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XXIII).—Sodium methoxide, prepared from 150 mg. of sodium (0.0066 mole) and dried for 4 hours at 150° (0.1 mm.) was suspended in 10 ml. of dry benzene, under nitrogen, and 800 mg. of XVII (0.0033 mole) added in 10 ml. of dry benzene, with rapid stirring and cooling in ice. After 10 minutes, a solution of 1.65 g. of dimethyl oxalate (0.014 mole) in 10 ml. of dry benzene was added and stirring continued for 1 hour with cooling, and at room temperature overnight. Then 30 ml. of ice-cold 2% NaOH was added, the benzene layer separated and extracted twice with further portions of cold base. Acidification with ice-cold, dilute hydrochloric acid and extraction with ether led to a nearly quantitative yield of glyoxalate XXII, giving a strong, almost black, color reaction with ferric chloride. The crude glyoxalate (1.08 g., 0.0033 mole) was heated with 0.5 g. of powdered soft glass, under nitrogen, at 180–190° for 30 minutes. Evolution of carbon monoxide had practically ceased at the end of this period. Distillation at 185–205° (bath temperature) (0.001 mm.) gave 370 mg., recrystallized from ether–heptane to 150 mg., m.p. 140–141°, 15% yield; ultraviolet λ_{max} 227 mμ; infrared 5.80 and 6.00 μ.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 72.00; H, 6.67. Found: C, 71.96; H, 6.69.

1-Cyano-2-keto-6-methoxy-12-methyl-1,2,9,10,11,12-hexahydrophenanthrene (XXIV).—Dry sodium methoxide, prepared from 0.57 g. of sodium (0.025 mole), was suspended in 10 ml. of dry benzene under nitrogen and 2.0 g. of XVII (0.0083 mole) in 20 ml. of dry benzene added with rapid stirring, at room temperature. After 10 minutes, 2.9 g. of freshly distilled ethyl formate (0.041 mole) in 10 ml. of dry benzene was introduced and the reaction stirred overnight. Extraction of the benzene with ice-cold 2% sodium hydroxide, acidification, extraction with ether and evaporation produced 2.2 g. of hydroxymethylene compound (0.0082 mole), m.p. 178–179° dec., 98% yield (deep red ferric chloride test). A solution of 2.2 g. of hydroxymethylene compound (0.0082 mole), in 90 ml. of glacial acetic acid,

and 0.96 g. of hydroxylamine hydrochloride (0.014 mole) was heated under nitrogen for 2 hours at 100°. After removal of acetic acid under vacuum, the residue was taken up in chloroform, washed with 2% aqueous sodium hydroxide and water, dried and concentrated to give 2.2 g. of crude isoxazole. A solution in 98 ml. of dry benzene was added to 0.33 g. of sodium (0.014 mole) dissolved in 8 ml. of dry methanol. The reaction was stirred for 30 minutes at room temperature and extracted several times with ice-cold 0.5% potassium hydroxide. Acidification, extraction with chloroform, drying, evaporation and crystallization from chloroform–ether gave 1.4 g. of crude nitrile, 63% yield. Purification by chromatography over Florisil in benzene, followed by crystallization from benzene–heptane, gave 0.90 g. of nitrile, m.p. 185–187°, 50% yield; analytical sample, m.p. 188.5–189.2°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41. Found: C, 76.10; H, 6.32.

1-Cyano-1,12-dimethyl-2-keto-6-methoxy-1,2,9,10,11,12-hexahydrophenanthrene (XXVII).—To a solution of 0.175 g. of XXIV (0.00066 mole) in 15 ml. of dry *t*-butyl alcohol was added a solution of 103 mg. of potassium (0.0026 mole) in 17 ml. of dry *t*-butyl alcohol, under nitrogen. The reaction was stirred for 15 minutes, a few drops of dry methyl iodide added, followed by 2 further portions after half-hour intervals. Stirring was continued for 12 hours, 5 ml. of methyl iodide added and the reaction heated at 40° for 2.5 hours. Then 0.10 g. of ammonium chloride (0.0020 mole) was added and the reaction mixture evaporated to dryness under vacuum. The residue was taken up in chloroform, extracted six times with 0.5% potassium hydroxide, dried, concentrated and chromatographed over Florisil (3 g.) in benzene. Crystallization from benzene–heptane yielded 148 mg. (yield 79%), twice recrystallized to 111 mg. of XXVII, m.p. 150–152°. Acidification of the basic washings gave a very small amount of recovered XXIV. Concentration of the mother liquors from crystallizations yielded only further quantities of XXVII. No oils, gums or other crystalline isomer could be found; analytical sample, m.p. 152–153°.

Anal. Calcd. for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81. Found: C, 77.18; H, 6.79.

1-Cyano-1,12-dimethyl-2-keto-6-methoxy-1,2,3,4,9,10,-11,12-octahydrophenanthrene (XXVIII).—Hydrogenation of 0.590 g. of XXVII (0.00210 mole) in 30 ml. of absolute ethanol with 10 mg. of 10% Pd–C at 31° stopped after 60 minutes, when the theoretical amount had been absorbed. Filtration, removal of ethanol under vacuum and crystallization from benzene–heptane gave 0.557 g. (yield 95%), m.p. 117–120°, recrystallized to 0.540 g., m.p. 118–120°.

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 80.25; H, 8.61. Found: C, 80.19; H, 8.61.

1-Cyano-2-keto-6-methoxy-12-methyl-1,2,3,4,9,10,11,-12-octahydrophenanthrene (XXX).—Hydrogenation of 75 mg. of XXIV (0.00028 mole) in 20 ml. of absolute ethanol and 10 mg. of 10% Pd–C, at 28°, stopped after 10 minutes when one equivalent of hydrogen had been absorbed. Filtration, with chloroform, evaporation and crystallization from benzene–heptane gave 75 mg. (0.00028 mole) of XXX (100% yield), m.p. 165–166°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11. Found: C, 75.84; H, 7.25.

Methylation of 1-Cyano-2-keto-6-methoxy-12-methyl-1,2,-3,4,9,10,11,12-octahydrophenanthrene.—A combination of 81 mg. of XXX (0.00030 mole) in 10 ml. of dry *t*-butyl alcohol and 2.44 ml. of 0.127 *N* potassium in *t*-butyl alcohol (0.00031 mole) was stirred for 2 hours, under nitrogen, at room temperature; 0.40 g. of methyl iodide (0.0026 mole) was then added in small portions over 1 hour. The reaction was stirred overnight, diluted with chloroform and extracted several times with 2% potassium hydroxide. Acidification of the basic extracts and extraction gave 14 mg. of recovered XXX, m.p. and mixed m.p. 165°. The neutral fraction contained 20 mg. of colorless crystalline material with a very large range in melting point which could not be reduced by numerous recrystallizations. The balance of material consisted of a dark, neutral gum which could not be crystallized.

1-Cyano-1,12-dimethyl-6-methoxy-1,2,3,4,9,10,11,12-octahydrophenanthrene (XXIX).—For 17 hours dry hydrogen chloride was passed into a solution of 250 mg. of XXVIII (0.00090 mole) in 10 ml. of ethanedithiol, cooled in ice. Excess ethanedithiol was then evaporated off under nitrogen and the amorphous residue dried under vacuum (2–3 mm.). An infrared spectrum showed no carbonyl band and retention of the nitrile absorption. The crude thioketal was refluxed overnight with 10 g. of deactivated Raney nickel (deactivated by refluxing for 4 hours in acetone with 2 drops of acetic acid) in ethanol, the reaction cooled and filtered, with thorough washing of the Raney nickel with benzene. The solution was evaporated and the residue distilled at temperatures to 180° (0.01 mm.). Chromatography over alumina, activity II, *p*H 7.5, using heptane with a very small amount of benzene for elution, gave 30 mg. of crystalline product (13% yield). After numerous crystallizations from heptane, 15 mg. of pure material, m.p. 134.5–135.5°, was obtained. An infrared spectrum, (Perkin-Elmer instrument) showed marked differences between this material and podocarponitrile methyl ether, obtained from natural podocarpic acid.

Anal. Calcd. for $C_{18}H_{23}NO$: C, 80.25; H, 8.61. Found: C, 79.88; H, 7.99.

Podocarpamide Acetate (XXXV).—A solution of podocarpic acid acetate[38] (1.0 g., 0.0032 mole), in 10 ml. of dry benzene, was mixed with 0.50 g. of oxalyl chloride (0.0039 mole), with cooling in an ice-bath. After 10 minutes, the reaction was allowed to come to room temperature and left standing for 2 hours. After warming at 100° for 10 minutes, the benzene was distilled off (infrared absorption at 5.75 μ and no absorption around 5.9 μ or in the hydroxyl region), the crude acid chloride dissolved in 10 ml. of anhydrous ether, and anhydrous ammonia passed through the cooled solution. The reaction was poured into water, extracted with chloroform, dried and concentrated. Crystallization of the amide from chloroform–ligroin gave 0.92 g., m.p. 153.5–154.5°.

Anal. Calcd. for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99. Found: C, 72.11; H, 7.98.

Podocarponitrile Acetate (XXXVI).—To 1.12 g. of XXXV (0.00356 mole), in 25 ml. of dry pyridine, 10 ml. of phosphorus oxychloride was added. After 3 hours, the mixture was poured into water, extracted with chloroform, the extracts washed with dilute hydrochloric acid, dried and evaporated; 850 mg. (80% yield) of nitrile recrystallized from chloroform–petroleum ether; m.p. 108–109°.

Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H 7.80. Found: C, 76.73; H, 7.95.

Podocarponitrile Methyl Ether (XXXVII).—The acetate XXXVI (0.85 g., 0.0029 mole) was suspended in 10 ml. of water and 1.0 g. of sodium hydroxide (0.025 mole), heated at 100° for 90 minutes, cooled and a large excess of dimethyl sulfate added. After standing at room temperature for 2 hours the reaction was heated again for 10 minutes, cooled and the methyl ether collected by filtration; crystallized from heptane, 0.72 g., 94% yield, m.p. 104.5–105.5°.

Anal. Calcd. for $C_{18}H_{23}NO$: C, 80.25; H, 8.61. Found: C, 80.19; H, 8.61.

Podocarpamide Methyl Ether (XXXVIII). a. **Hydrolysis of Nitrile.**—A suspension of 0.13 g. of XXXVII in 5 ml. of ethanol and 5 ml. of water, with 3.5 g. of potassium hydroxide, was heated in a steel bomb at 150° for 15 hours. The mixture was cooled, poured into water and extracted with chloroform. Evaporation gave a crystalline residue showing strong amide bands at 2.80, 2.90 and 6.05 μ in the infrared, as well as some residual nitrile. Chromatography over 15 g. of alumina, activity II, *p*H 4.5, gave the nitrile by elution with petroleum ether–benzene 10:2 and the amide, 0.050 g. (35% yield), with benzene–chloroform 1:1; crystallized from chloroform–heptane, m.p. 152.5–153.5°.

Anal. Calcd. for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77. Found: C, 75.17; H, 8.71.

b. From Amide Acetate.—A suspension of 2.7 g. (0.0086 mole) of XXXV in 30 ml. of water and 2.0 g. of sodium hydroxide (0.050 mole) was heated, under nitrogen, at 100° for 1.5 hours. To the cooled solution a large excess of dimethyl sulfate was added and the mixture left at room temperature overnight, followed by heating for 30 minutes. After cooling, filtration gave 2.4 g. of XXXVIII; crystallized from chloroform–heptane, m.p. 152.5–153.5°.

(38) I. R. Sherwood and W. F. Short, *J. Chem. Soc.*, 1006 (1938).

Podocarpic Acid Methyl Ether (XLI).—To 574 mg. of XXXVIII (0.00200 mole) in 10 ml. of dry benzene, 63 mg. of sodium hydride (0.0026 mole) was added and the mixture refluxed for 4.5 hours, under nitrogen, with stirring. The reaction was cooled and 5 ml. of dimethylformamide added, causing the white, gelatinous precipitate to dissolve. Dry methyl iodide (3 ml.) was introduced and the reaction stirred overnight at room temperature. After pouring into ice-water, extraction with chloroform and evaporation left a product showing only one N–H band in the infrared at 2.82 μ. A solution of 1.9 g. of NOCl in 20 ml. of acetic anhydride was added dropwise to the N-methylamide XXXIX, dissolved in 7 ml. of glacial acetic acid, 3 ml. of acetic anhydride and 5.2 ml. of dry pyridine. Addition was stopped when an orange color and a positive potassium iodide–starch test persisted. The reaction was left in an ice-bath for 3 hours, poured into water, extracted with chloroform and evaporated under vacuum. The residue was refluxed for 10 hours with 30 ml. of a 10% solution of potassium hydroxide in ethanol, poured into chloroform and extracted with 10% aqueous potassium hydroxide. Acidification and extraction with chloroform, followed by drying over magnesium sulfate and evaporation, gave 380 mg. of crystalline podocarpic acid methyl ether; crystallized from ethanol, m.p. 157–158°, undepressed on mixed melting point with material obtained by saponification of the methyl ester methyl ether. Ether cleavage according to a reported procedure[39] gave podocarpic acid.

(39) R. D. Haworth and B. P. Moore, *J. Chem. Soc.*, 633 (1946).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE JOHNS HOPKINS UNIVERSITY, BALTIMORE 18, MD.]

Reactivity and Geometry in Allylic Systems. I. Stereochemistry of Photosensitized Oxygenation of Monoölefins[1,2]

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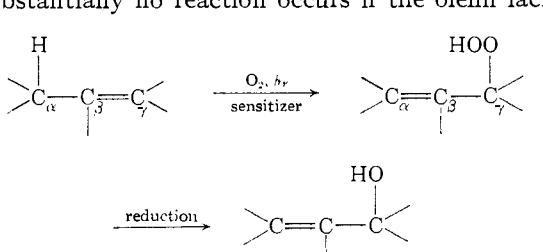
Steroid monoölefins have been used as substrates to study geometric aspects of photosensitized oxygenations. In pyridine solution with hematoporphyrin as a sensitizer, photoöxygenation of three Δ^6-cholestenes (Ia, b, c) gave the corresponding Δ^5-cholesten-7α-hydroperoxides (IIa, b, c) but no isolable amounts of the 7β-epimers. For characterization the hydroperoxides were reduced without purification to alcohols (and derived benzoates). Enone and dienone by-products resulted from breakdown of the hydroperoxides. Similar oxygenation of cholesterol-7α-*d* gave 3β-hydroxy-5α-hydroperoxy-Δ^6-cholestene (XII) that retained only 8.5% of the original deuterium, whereas cholesterol-7β-*d* gave XII with 95% of the original deuterium. These results show that such hydroperoxidations are stereospecific, and the new C–O bond bears a *cis* relationship to the C–H bond that is broken. Even on prolonged treatment Δ^6-cholesten-3β,5α-diol (XIII) is inert to photosensitized oxygenation; this is ascribed to steric shielding (of the β-side of the ring system and especially of the hydrogen at C-8) and demonstrates that the reaction can be sterically blocked. Δ^6-Coprostene has been synthesized from $\Delta^{4,6}$-cholestadien-3-one *via* 6α, 7α-oxido-Δ^4-cholesten-3-one (XIV), 6α, 7α-oxidocoprostan-3-one (XV) and Δ^5-coprosten-3-one (XVI). An unexpected occurrence in the transformation of XV → XVI was concomitant formation of XVII, presumably through a "Clemmensen-type" reduction of the ketone group. Δ^6-Coprostene (XVII) is inert to photosensitized oxygenation. The *quasi*-equatorial nature of the β-hydrogen at C-5 may contribute to this inertness and this suggests (but does not prove) the operation of a stereoelectronic factor in these oxygenations. Improved routes to cholestan-7-one and to Δ^6-cholestene have been developed. Decomposition of the secondary hydroperoxide IIa to the enone IVa occurs on treatment with Raney nickel in pyridine. A conformational factor in manganese dioxide oxidation of allylic alcohols is suggested by the faster oxidation of Δ^5-cholesten-7β-ol (*quasi*-equatorial OH) over the corresponding 7α-ol (*quasi*-axial OH).

The combination of molecular oxygen with olefins is a well-known phenomenon, but its use in syntheses has been limited. Oxygen (in the ground state) is a diradical and many of its laboratory reactions are of free-radical type, are initiated by peroxides, irradiation, etc., and involve chain mechanisms.[4] In contrast, when olefin oxygenation is conducted photochemically in *dilute solution* and in the presence of a small amount of sensitizing agent (usually a fluorescent dye) radical chains do not appear to be involved, the mode of oxygen attack is more specific, and the peroxidic products largely survive further breakdown.

One such type[5] of photosensitized oxygenation is of recent development and involves isolated olefinic links. Extensive studies by Schenck and his co-workers have shown that the initial products are allylic hydroperoxides and that the double bond always undergoes an allylic shift during the reaction, as shown in the adjoining scheme.[6] The oxygenation can be conducted in solvents such as pyridine, benzene or alcohols; and Schenck has established its generality by applying it to a variety of olefins, including terpenes and steroids. Substantially no reaction occurs if the olefin lacks



allylic hydrogens, or if the sensitizer, the irradiation or the oxygen is excluded. The initially formed hydroperoxide usually survives the reaction conditions and can be isolated and reduced to the allylic alcohol by any of a number of ways. That this method for introduction of an alcohol

(1) A preliminary communication of this work has been published [A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **81**, 6330 (1959)].

(2) This work was supported by the National Science Foundation and by the Alfred P. Sloan Foundation.

(3) Alfred P. Sloan Foundation Fellow.

(4) For a discussion see "Free Radicals in Solution" by C. Walling, John Wiley and Sons, Inc., New York, N. Y., 1957, Chapter 9.

(5) Another type is the formation of transannular peroxides from homoannular dienes on photosensitized oxygenation. This type is well documented [W. Bergmann and M. J. McLean, *Chem. Revs.*, **28**, 367 (1941)] and has been used as a key step in syntheses, and in structure elucidations [P. Bladon, *et al.*, *J. Chem. Soc.*, 4883, 4890 (1952); H. B. Henbest, *et al.*, *ibid.*, 4894 (1952); G. D. Laubach, *et al.*, *J. Am. Chem. Soc.*, **75**, 1514 (1953); G. O. Schenck and R. Wirtz, *Naturwiss.*, **40**, 581 (1953); W. H. Schuller, R. N. Moore and R. V. Lawrence, *J. Am. Chem. Soc.*, **82**, 1734 (1960)].

(6) For references and a review see G. O Schenck *Angew Chem.* **69**, 579 (1957).