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The Synthesis of Some Decahydronaphthoic Acid Lactones

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The Synthesis of Some Decahydronaphthoic Acid Lactones

by

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The author wishes to express his thanks to Dr. Desmond M. S. Wheeler for his assistance and guidance during the course of this work and to the Chemistry Department of the University of Nebraska for the use of its facilities.

He also wishes to thank a wonderful mother and father for their encouragement.

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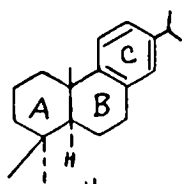
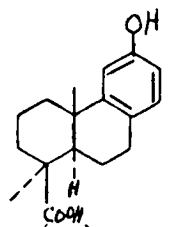
INTRODUCTION

The diterpenoid acids, dehydroabietic acid (I), podocarpic acid (II), abietic acid (III), and palustric acid (IV), have been synthesized.[1] Dehydroabietic acid (I)[2] was synthesized by building up a β tetralone (V);



(I)



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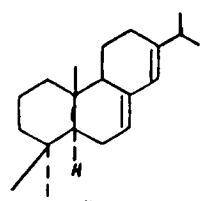

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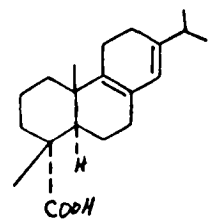
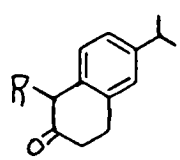


(IV)

the aromatic ring was the precursor of ring C; the reduced ring was to become ring B; ring A, with the methyl group (VI) of the gem methylcarboxyl was added by an alkylation reaction of the type developed by Robinson in the synthesis of steroids; a homocarboxyl group was put in using



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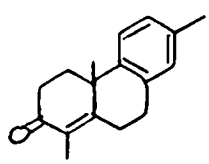
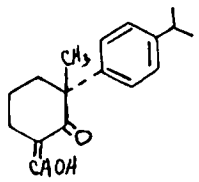


(VI)

an alkylation reaction with bromoacetic ester; the eventual product was homodehydroabietic acid which gave dehydroabietic acid (I) on Barbier-Wieland degradation.

Dehydroabietic acid (I) was also prepared by a highly stereoselective synthesis. 6-Hydroxymethylene-2-methyl-2-(p-isopropylphenyl) cyclohexanone (VII) was condensed with methyl vinyl ketone to give a diketone (VIII) which has rings A and C present and has the proper relative stereochemistry at the two asymetric centers. Selective methylation of the

monoketal of VIII followed by base-catalyzed cyclization of the diketone gave an octalone (IX). An asymmetric center was stereoselectively introduced into the octalone by reduction of the double bond with lithium in



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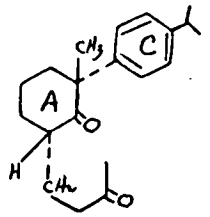
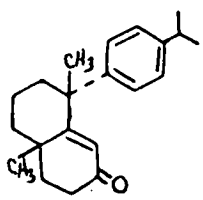


(VIII)

ammonia. The resulting β-decalone (X) was converted to a hydroxy methylene derivative which was then ozonized to a diacetic acid (XI). The diacid, on treatment with polyphosphoric acid, gave a tricyclic keto



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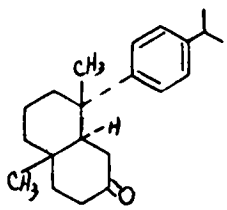

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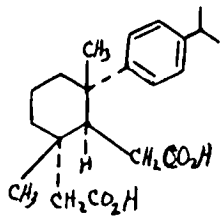
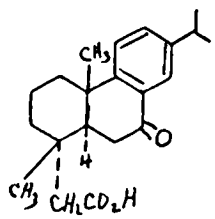


(XI)



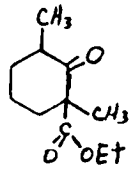
(XII)

acid (XII) which, on hydrogenolysis over palladium-on-carbon, gave homodehydroabietic acid. Degradation of the homoacid gave dehydroabietic acid (I).

The first synthesis of podocarpic acid[4] (II) was a non-stereospecific one in which an aromatic ring (ring C) was coupled through a chain of two carbon atoms to a cyclohexanone (XIII) (ring A); ring B was formed by an acid catalyzed cyclization, which was not stereospecific. Three racemates were found in the cyclization mixture, one of which (XIV) was converted into podocarpic acid (II).

Abietic acid (III) and palustric acid (IV) have been prepared[5] by applying the Benkeser[6] lithium-in-ethylamine reduction procedure under

carefully defined conditions to dehydroabietic acid (I) and then isomerising the double bonds into conjugation.



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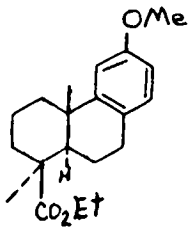
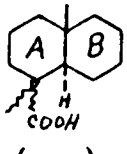


(XIV)

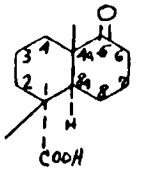
All of these syntheses and most of the others which have been reported, have the disadvantage in that they apply to one specific compound and are difficult to generalize. It is therefore desirable to develop a general synthetic scheme for diterpenoid acids. A new approach to diterpenoid synthesis would be to construct rings B and A (including the gem methylcarboxyl) first. Ring C would then be added. This means that the skeleton (XV), common to all diterpenoid acids, would first be made and so the scheme would be applicable not merely to compounds containing an aromatic ring C, but also to those which have ring C non-aromatic and to those which are based on a naphthalene rather than a phenanthrene skeleton.



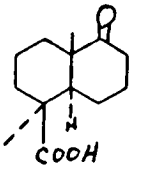
(XV)

The two major intermediates in this type of synthetic scheme would be the C.1 epimers (XVI) and (XVII) or compounds closely related to them. It should be possible to convert the intermediate (XVI) by suitable reactions into the various acids in the abietic acid stereochemical series, e.g. abietic acid (III) and dehydroabietic acid (I). The intermediate (XVII)

could similarly act as the precursor of the various compounds stereochemically related to podocarpic acid (II).

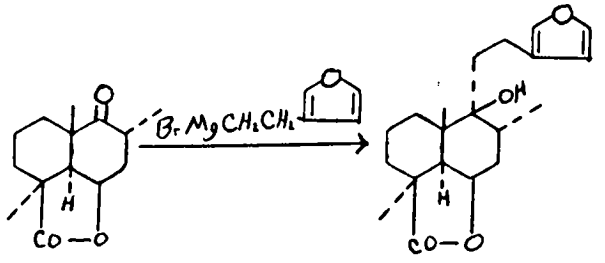


(XVI)



(XVII)

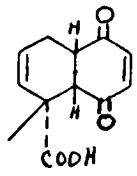
The intermediate (XVII) of the podocarpic acid series should also be a suitable starting material for the synthesis of marrubiin (XIX) by the way of intermediate (XVIII). The compound (XVIII) has already been obtained as a degradation product of marrubiin.[7]



(XVIII) (XIX)

The original plan for the synthesis of the intermediates (XVI) and (XVII) involved making the Diels-Alder adduct (XX). From compound (XX) it should be possible to devise a sequence of reactions which would involve a selective epimerization of C.4a and which would eventually lead to the compound (XXI). Compound (XXI) on alkylation would then give an intermediate of the type (XVII). Similarly, if (XX) is taken through a sequence of reactions in which C.8a is epimerized, compound (XXII) would be obtained. Compound (XXII) on alkylation would give a material corresponding to (XVI). This work was started by Dr. Roy,[10] who found it impossible to obtain the Diels-Alder adduct (XX). Dr. Roy, therefore, started with the adduct (XXIII)[13] and converted it to compound (XXIV)[9].

In later work, Roy, Mori, and Rieke have protected 0.6 in (XXIV) [(XXIV)→ (XXIVb)] and have alkylated (XXIVb).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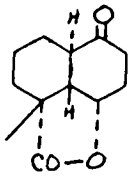
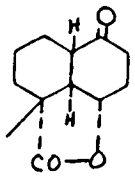
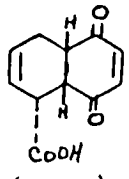
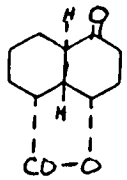

(XXI)

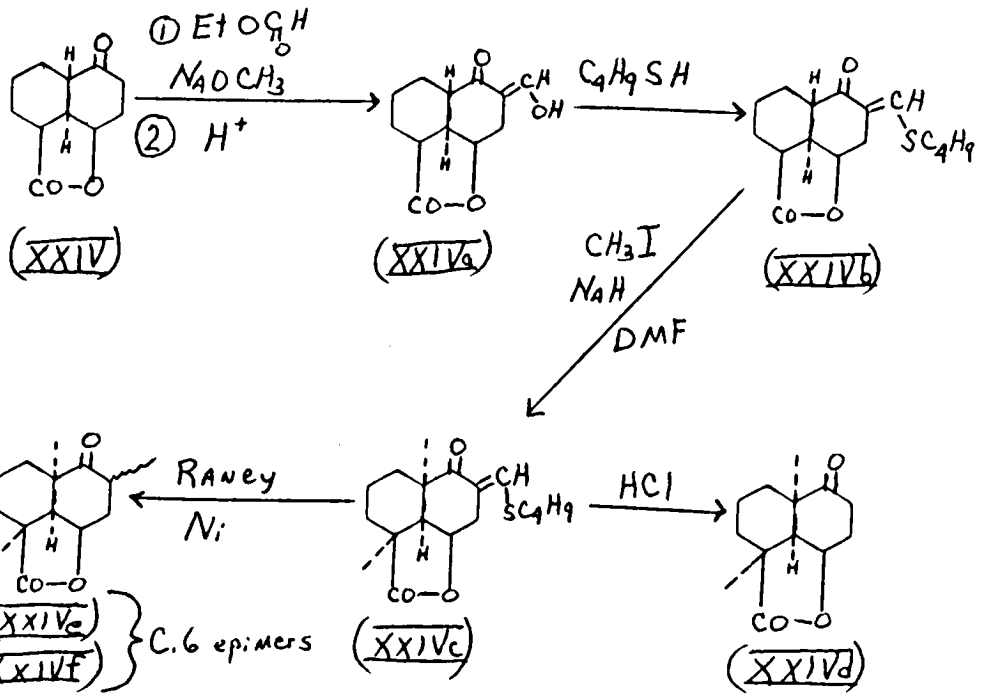

(XXII)

Removal of the protecting group has given one dimethyl (XXIVd) and two


(XXIII)


(XXIV)

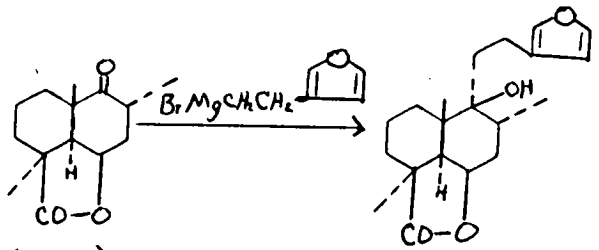
trimethyl compounds (XXIVe and XXIVf)[11].



(XXIV) (XXIVa) (XXIVb) (XXIVc) (XXIVd) (XXIVe) (XXIVf)

Unfortunately, the alkylation gave cis fused compounds. Work is still in

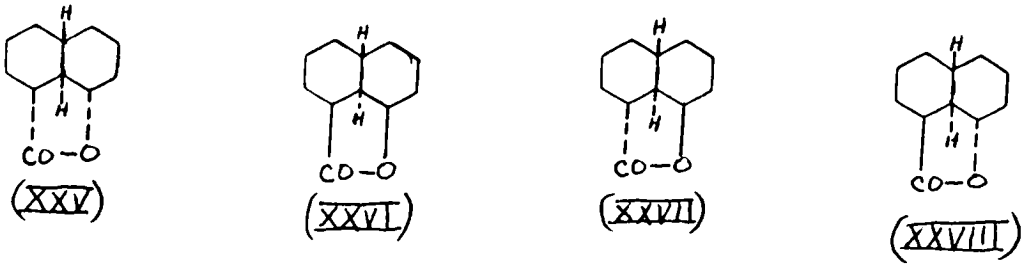
progress to get the compound (XVIII) which could be used as a starting material for the synthesis of marrubiin (XIX).



(XVIII) (XIX)

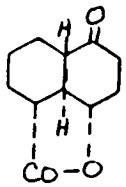
Recently, other workers[12] have tried to prepare the intermediate (XVIII) by cyclization of a highly substituted cyclohexene with polyphosphoric acid and have also failed.

Originally, the work for this thesis was aimed at obtaining the following four decahydronaphthoic acid lactones (XXV - XXVIII). These compounds would be useful model substances (e.g. for n.m.r. studies) in connection with some of the synthetic work.



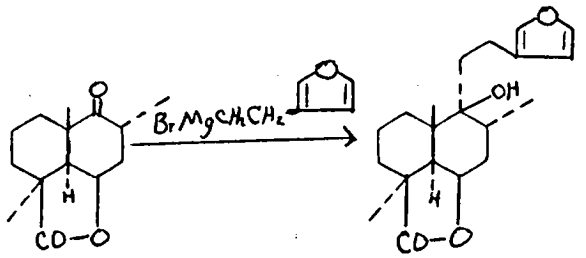
(XXV) (XXVI) (XXVII) (XXVIII)

The lactone (XXV) had been previously prepared by Mrs. Margaret Wheeler.[8] However, shortly after the thesis work started, it was decided to attempt to prepare the keto lactone (XXIX) from the adduct (XXIII). This lactone corresponds to the keto lactone (XXII) of the original synthetic scheme.



(XXIV)

progress to get the compound (XVIII) which could be used as a starting material for the synthesis of marrubiin (XIX).



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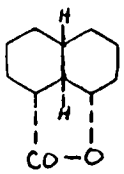
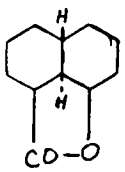


(XXV)



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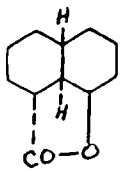
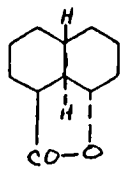


(XXVII)



(XXVIII)

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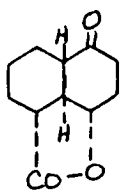


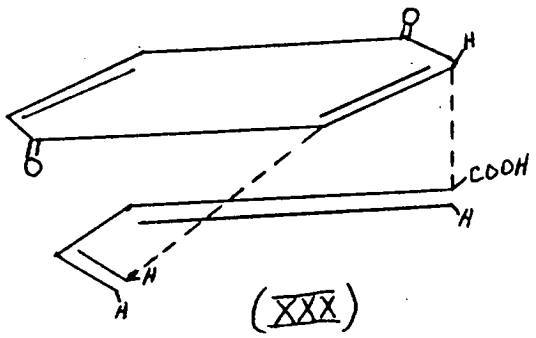
(XXIX)

This thesis records the successful completion of this task which involves a selective epimerization of C.8a. It is hoped that (XXIX) on alkylation will give an intermediate of the type (XVI) which is required for the synthesis of the abietic acid series.

DISCUSSION

Originally, it had been hoped to synthesize a gem methylcarboxyl compound such as (XVI) or (XVII) from the Diels-Alder adduct of 2-methyl-2, 4-pentadienoic acid with ρ-benzoquinone. After several attempts to prepare the adduct had failed,[10] it was decided to make the Diels-Alder adduct (XXIII) of vinyl acrylic acid and ρ-benzoquinone which would directly lead to compounds (XXVI)-(XXVIII).

The adduct (XXIII) (see Chart I and II, pages 12 and 13) was prepared by the method of Woodward et al with minor modifications. The only known form of vinyl acrylic acid possesses a trans double bond, and the combination of that isomer with ρ-benzoquinone, proceeding through an intermediate (XXX) of the geometrical type generally accepted for the Diels-Alder reaction, can only lead to an adduct with the stereochemistry defined by (XXIII).



(XXX)

The adduct (XXIII) may selectively be reduced with sodium borohydride by the method of Woodward et al using modifications suggested by Wheeler[8] to give the dihydrocompound (XXXI).

The structure and the stereochemistry of both (XXIII) and (XXXI) were readily established by Woodward through the formation of the δ-transannular lactones (XXXII)-(XXXIII). The infrared spectrum of the δ-transannular lactone (XXXIII) possessed a normal ketonic carbonyl band at 5.83μ and a second band at 5.77μ characteristic of the carbonyl group of a six-membered lactone.

As Woodward originally suggested,[13] the selective reduction at C.5 of the adduct (XXXIII) is due to the carboxylate ion exerting an electrostatic repulsion on the borohydride ion.[8] This shields one side of the carboxyl (C.8); the other side is shielded by the folded nature of the cis-decalin system.

Starting with (XXXIII), it should be possible to make the γ-lactones with varying stereochemistry as was intended in the original research problem. However, it was then felt that it was more important to proceed to intermediate (XXIX), which was directly involved in the general synthetic scheme.

The δ-lactone (XXXIII) was hydrolyzed; the cis product (XXXV) was not isolated because it was immediately epimerized under the basic conditions to the trans hydroxy keto acid (XXXIV). Compound (XXXIV) has also been obtained by a direct reduction of the dihydro compound (XXXI) to give the hexahydro compound (XXXV) followed by epimerization with 5% alcoholic potassium hydroxide. The latter route is the method of choice. The δ-lactone (XXXIII) had been previously converted into (XXXIV)[18]. Protiva et al[18] also obtained it by hydrolyzing esters of the cis hydroxy acid (XXXV) or by epimerizing the acid itself. The properties of their compounds agree with those reported in this thesis.

Originally, it was difficult to obtain a good yield of (XXXV), but a high yield was finally obtained by using 5% rhodium on charcoal as the catalyst and t-butanol as the solvent. Working up the reaction mixture gave an oil which was crystallized by dissolving in ethyl ether, introducing a boiling stick into the flask and evaporating to dryness on the steam bath. The present results suggest that the use of t-butanol as a solvent for catalytic hydrogenation ought to be investigated more closely. The yield of the hexahydro-compound (XXXV) was unsatisfactory when palladium

and acetic acid, rhodium and ethyl acetate, and palladium and ethyl acetate were used as the catalyst and solvent, respectively. An attempted reduction of (XXXI) was done using diimide, Cu^{++}, and air[19] without any known materials being isolated.

The trans-hydroxy keto acid (XXXIV) was easily transformed to a diol (XXXVI) by reduction in aqueous sodium bicarbonate with sodium borohydride in the cold. The structure of the diol is consistent with its analysis and infrared spectrum. By analogy with earlier work,[8] it was assumed that the hydroxyl group at C.8 was equatorial.

The diol (XXXVI) does not lactonize easily. The conditions tried included heating at 225° for up to 12 hours in a stream of nitrogen, treatment with strong mineral acid, and treatment with p-toluene sulfonic acid using ethyl acetate, benzene, and dioxane as solvents. Only starting material was recovered in each case. Finally, the diol was dissolved in methanol and was kept with N,N-dicyclohexylcarbodiimide[13] for 14 hours at room temperature. The γ-hydroxy lactone (XXXVII) was recovered in 71% yield; its structure was established from its analysis and infrared spectrum (band at 2.80μ for -CH and 5.63μ for γ-lactone).

Previously,[8] it had been shown that the γ-lactone (XXV) formed easily from the corresponding hydroxy acid either by heating or by treating it with acetic anhydride. The difficulty in obtaining (XXXVII) suggested the possibility that reduction of (XXXIV) had given a diol (XXXVII) in which the C.8 hydroxyl group is axial. A possible way in which this could happen would be reaction of the borohydride ion with the C.5 hydroxyl group of (XXXIV) to give an alkoxyborohydride (XXXIVa) and subsequent intramolecular hydride transfer from the top side of the molecule. The γ-hydroxy lactone formed from this type of diol would have the interesting skew structure of (XXXVIII). The assignment of

structure (XXXVII) to the lactone is discussed below.

The γ-hydroxy lactone (XXXVII) was oxidized by the Jones method[16] to the γ-keto lactone (XXIX) which had bands in the infrared spectrum at 5.62μ and 5.82μ corresponding to a γ-lactone and a saturated cyclohexanone.

Originally, the keto lactone (XXIX) was obtained with a melting point of 65.5-67°. When the work was repeated, the material isolated had a m.p. of 114-115°. In later work, A. Ghosh has prepared the keto lactone m.p. 114-115° several times and has never obtained the lower melting material. The n.m.r. spectrum of the higher melting material has a peak corresponding to C.8-H at δ =4.4 p.p.m. The width of this peak at half height is 22 c.p.s. These widths are in good accord with the structure (XXIX). If structure (XXXVIII) were correct, the peak would be less broad.[17] Very recently, A. Ghosh has confirmed this assignment of structure by converting (XXIX) into (XXV). The identity of the 65.5-67° material is still not clear. As indicated in the introduction, the keto lactone (XXIX) will be used as a starting material for the dimethyl keto lactone (XXXIX).

CHART I

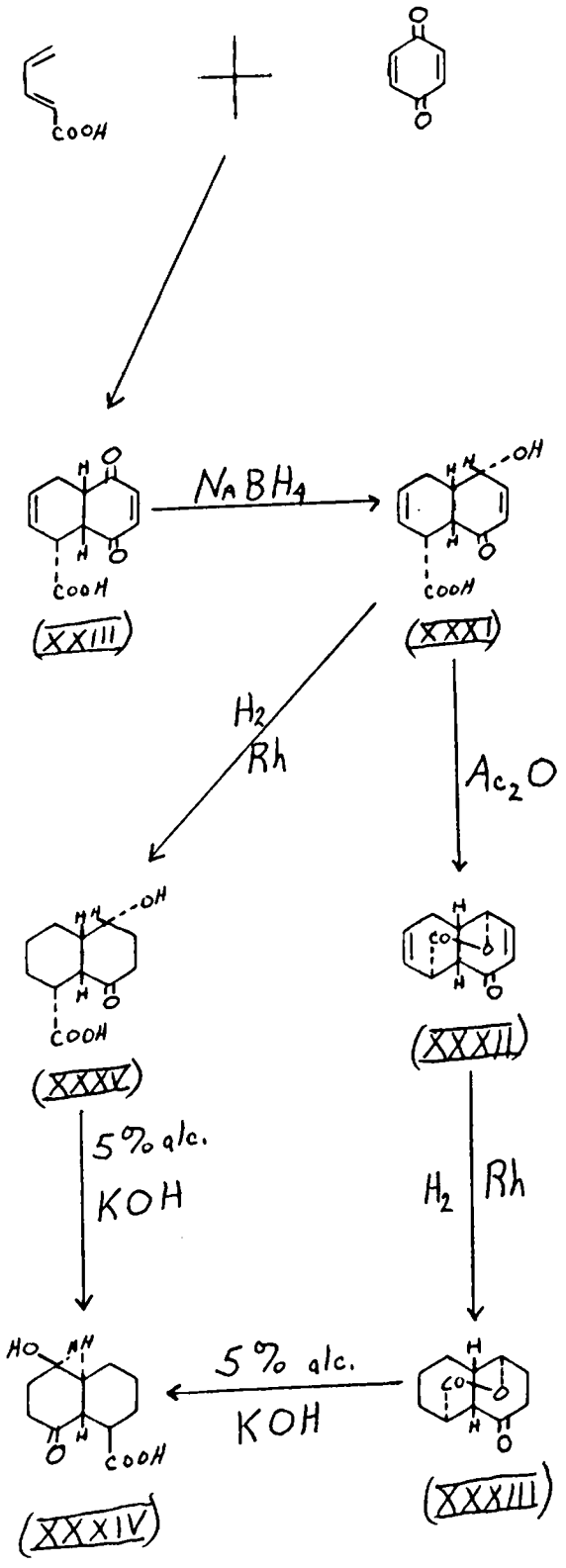
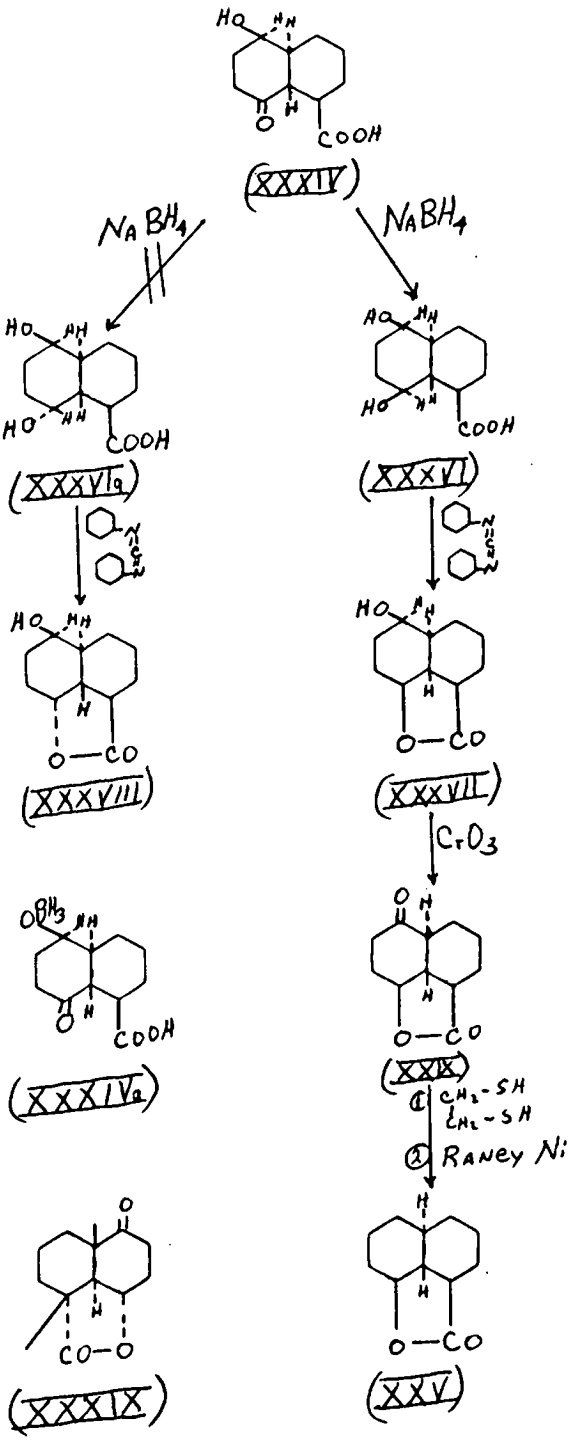

COOH
NaBH4
(XXIII)
(XXXI)
H2
Rh
Ac2O
(XXXV)
(XXXII)
5% alc.
KOH
H2
Rh
5% alc.
KOH
(XXXIV)
(XXXIII)

CHART II


NaBH4
NaBH4
(XXXIV)
(XXXVIa)
(XXXVI)
(XXXVIII)
(XXXVII)
CrO3
(XXXIVa)
(XXIX)
① CH2-SH
CH2-SH
② Raney Ni
(XXXIX)
(XXV)

EXPERIMENTAL

Infrared spectra were determined on Perkin Elmer models 21, 237 grating and 137 infrared spectrometers for chloroform solutions unless otherwise indicated. Ultraviolet spectra were determined on a Cary model 12 recording spectrophotometer for solutions in methanol. The melting points reported were determined in an oil-bath and are uncorrected. Analyses were by Alfred Bernhardt.

cis-1,4-Carboxy-5,8-dioxo-1,4,5,8,4a,8a-hexahydronaphthalene (XXIII).*

A solution of malonic acid (200 g.) in pyridine (450 ml.) was cooled to 10° and acrolein (146 ml.) was added at such a rate that the temperature did not exceed 12°. After the addition was complete (1.5 hr.), hydroquinone (1 g.) was introduced into the mixture. Stirring was continued for 3 hours at 0° and subsequently for 5 hours at 35-45°.

At the end of the stirring period, conc. sulfuric acid (420 ml.) was added with stirring to 4 l. of crushed ice. The reaction mixture was poured over the resulting icy slush with stirring and more ice was added as necessary to keep the temperature low.

The mixture was divided into three portions, and each portion was extracted three times with ether (200 ml.). The combined ether extracts were washed with water and dried (Na_2SO_4).

The etheral solution of vinyl acrylic acid was concentrated to 200 ml. and benzene (250 ml.) was added; the solution was again concentrated to 200 ml.

The vinyl acrylic acid solution was added to a solution of p-benzoquinone (118 g.) and hydroquinone (1 g.) in boiling benzene (500 ml.). After refluxing for 4 hours, the mixture was filtered at about 50°. The filtrate was cooled to room temperature and filtered again to give 85 g. (38%) of crude adduct.

*For nomenclature see ref. 8.

The filtrate was concentrated to 200 ml. and crystals formed upon standing. About 10 g. of crude adduct, rich in p-benzoquinone, was recovered.

After removing the p-benzoquinone by sublimation at 75°, the crude adduct was dissolved under reflux in a methanol-acetone (1:1) solution. Charcoal was added and the solution was filtered hot through Celite. n-Pentane was added to the cooled filtrate and crystals formed upon stirring. The crystals were collected and washed with acetone-n-pentane (1:2) until the filter cake did not darken on exposure to air. The adduct was washed with n-pentane and air dried. The m.p. of 215-225° agreed with that of Woodward et al[13].

ν_{max}^{KBr} 1700-1675(b), 1602, 1420, 1385(m), 1361, 1315, 1267, 1230, 1183, 1125, 1095, 1084, 1020(b), 993, 958, 940, 885, 833, 825 Cm^{-1}

cis-1α-Carboxy-5β-hydroxy-8-oxo-1,4,5,8,4a,8a-hexahydronaphthalene (XXXI).

A solution of sodium bicarbonate (6.2 g.) in water (100 ml.) was added slowly to a slurry of the adduct (XXIII) (15 g.) in water cooled to 0°, while maintaining a thin layer of ethyl acetate on top of the reaction mixture to prevent foaming. When nearly all of the adduct was dissolved, a solution of sodium borohydride (1.8 g.) in water was added in portions and the mixture was stirred for 15 minutes. Ethyl acetate (50 ml.) was added and the solution was treated with 20% sulfuric acid until acid to Congo Red. The acidic solution was seeded with a sample of the dihydro derivative and stirred at 0° for another 30 minutes. It is essential that the reaction mixture be cooled throughout the reduction.

The dihydro product (XXXI) (9.2 g.) (61%) was removed by filtration and was washed with water (100 ml.) After recrystallization from ethyl acetate, the dihydro product had a m.p. of 182-184° (lit.[13] 179-180°).

ν_{max}^{KBr} 3460, 3360, 2900, 2840, 1700-1660(b), 1418(m), 1385, 1358, 1313, 1252, 1210, 1120, 993, 1058(m), 1011, 975, 930(s), 895, 838, 810 cm^{-1}.

δ-Lactone of cis-1α-Carboxy-5β-hydroxy-8-oxo-1,4,5,8,4a,8a-hexahydronapthalene (XXXII).

A mixture of the dihydroderivative (XXXI) (10 g.), acetic anhydride (10 ml.), anhydrous sodium acetate (2 g.), and benzene (200 ml.) was heated to reflux with vigorous stirring. The dihydro derivative dissolved slowly and in about 15 minutes the reaction mixture was a clear yellow solution containing some undissolved sodium acetate. After the mixture was refluxed for 1 hour, it was cooled in an ice bath, and ethyl acetate (100 ml.) and cold saturated sodium chloride (25 ml.) were added.

The resulting phases were separated and the organic phase was dried (Na_2SO_4). The aqueous phase was back-washed with ethyl acetate, which was then washed with saturated sodium chloride, and dried (Na_2SO_4). The two solutions were combined and air was blown through the resulting solution to remove excess acetic anhydride. Evaporation of the solvent gave an oil which crystallized when kept with ethyl ether in the cold for a few hours. The crystalline product (XXXII) (6.8 g.) (75%) was collected, washed with ethylacetate-ether (10:90), and subsequently with ethyl ether and had a m.p. of 147-149° (lit.[8] 149-151).

ν_{max} 2940, 1740, 1677, 1380, 1358, 1323, 1150, 1130, 1080(b), 1031(m), 963, 910, 887 cm^{-1}.

δ-Lactone of cis-1α-Carboxy-5β-hydroxy-8-oxodecahydronapthalene (XXXIII).

A solution of the transannular six-membered lactone (XXXII) (0.95 g.) in ethyl acetate (150 ml.) was hydrogenated in the presence of 5% rhodium on charcoal (100 mg.). The uptake corresponded to two molar equivalents of hydrogen.

The mixture was filtered twice through Celite and then through a

gravity filter. Evaporation of the solvent gave an oil which crystallized from ether. The crude material (XXXIII) (0.50 g.) (52%) (m.p. of 123-125°) on further recrystallization from ethyl acetate had a m.p. of 125-126° (lit.[13] 126-127°).

ν_{max} 3500(b), 2940, 1732(b), 1714(m), 1468(s), 1448, 1384, 1345, 1290, 1135, 1087, 982, 973, 943(m), 910, 888(s) cm^{-1}.

cis-1α-Carboxy-5α-hydroxy-8-oxodecahydronapthalene (XXXV).

A solution of the dihydro compound (XXXI) (1.800 g.) in warm t-butanol (75 ml.) was filtered with suction and hydrogenated at room temperature in the presence of 5% rhodium on charcoal (200 mg.). The uptake corresponded to two molar equivalents of hydrogen.

Methanol (75 ml.) was added to the reaction mixture and the solution was filtered twice through Celite and then through a gravity filter. After evaporation of the solvent an oil resulted, which was dissolved in ether; the solution was filtered and evaporated to dryness on a steam bath with a wooden applicator in the flask. The crude cis-saturated hydroxy keto acid (XXXV) (1.758 g.) (96%) (m.p. of 151-153°) on further recrystallization from ethyl acetate had a m.p. of 152-154° (lit.[13] 153-155).

λ_{max} 288 mμ (ε 22), ν_{max} 3460(m), 2970, 1703(b), 1460, 1420, 1385, 1355, 1308, 1267, 1242, 1220, 1178, 1132(m), 1123, 1100, 1092, 1065(m), 1034, 1000(s), 975, 950, 925, 900(s), 845, 830 cm^{-1}.

trans-1β-Carboxy-5β-hydroxy-8-oxodecahydronapthalene (XXXIV).

(a) A solution of the transannular six-membered lactone (XXXIII) (428 mg.) in 5% alcoholic potassium hydroxide (15 ml.) was refluxed for 3 hours. Water (125 ml.) was added and the solution was extracted with ethyl acetate. The aqueous layer was acidified with hydrochloric acid to Congo Red and then extracted seven times with ethyl acetate. The combined extracts were washed with water and dried (Na_2SO_4). Evaporation gave the crude trans hydroxy keto acid (XXXIV) (351 mg.) (75%) (m.p. of

198-201°).

(b) A solution of the cis saturated hydroxy keto acid (XXXV) (3.315 g.) in 5% alcoholic potassium hydroxide (80 ml.) was refluxed for 6 hours. The mixture was filtered, water (150 ml.) was added and the solution was acidified with hydrochloric acid to Congo Red. The acidic solution was continuously extracted with ethyl acetate for 24 hours. The ethyl acetate was dried (Na_2SO_4). Evaporation of the solvent gave the crude trans hydroxy keto acid (XXXIV) (2.130 g.) (61%) (m.p. of 200-202°). Sublimation in vacuum gave an analytical sample of m.p. 200.5-202° (lit.[18] 206-208).

The infrared spectra of the materials from (a) and (b) were the same. The mixed melting point of the two materials showed no depression. λ_{max} 282mμ (ε 31), $\bar{\nu}_{max}$ 3410, 3960, 3880, 1700(b), 1447(m), 1434(m), 1418(m), 1310(b), 1327, 1314, 1287, 1265, 1247, 1233, 1197, 1145, 1132, 1111, 1073, 1053, 1012(b), 975, 949, 915, 875, 860(b), 845(m), 810(m)cm^{-1}.

Anal. Calcd. for $C_{11}H_{16}O_4$: C,62.25; H,7.60; O,30.15. Found: C,62.43; H,7.40; O,30.25%.

trans-1β-Carboxy-5β 8β-dihydroxydecahydronapthalene (XXXVI).

A mixture of trans hydroxy keto acid (XXXIV) (392 mg.) and sodium bicarbonate (180 mg.) was dissolved in water (15 ml.) A solution of sodium borohydride (250 mg.) in water (10 ml.) was added. The mixture was kept in the cold for 36 hours and then acidified with hydrochloric acid to Congo Red. The acidic solution was continuously extracted with ethyl acetate for 12 hours and dried (Na_2SO_4). Evaporation gave an oil which crystallized in a few minutes when kept with ethyl ether. The crude diol (XXXVI) (275 mg.) (70%) (m.p. of 206-208°) on further recrystallizations from ethyl acetate gave an analytical sample of m.p. of 206.5-208°. $\bar{\nu}_{max}$ 3495, 2955, 2882, 1703(m), 1457, 1439, 1418(s), 1359, 1348(s), 1326(s), 1308(m), 1287(s), 1258, 1215(doublet), 1190, 1150, 1133, 1094,

1078, 1060, 1035, 975, 955(b) cm^{-1}.

Anal. Calcd. for $C_{11}H_{18}O_4$: C,61.66; H,8.47; O,29.87. Found: C,61.52; H,8.64; O,30.00%.

γ-Lactone of trans-1β-Carboxy-5β,8β-dihydroxydecahydronapthalene (XXXVII).

A solution of N,N-dicyclohexylcarbodiimide (453 mg.) in methanol (5 ml.) was added to a solution of the diol (XXXVI) (510 mg.) in methanol (15 ml.) and the mixture was kept at room temperature for 14 hours.

Evaporation of the solvent gave a semi-solid residue which was extracted 7 times with 10 ml. portions of water. The aqueous extracts were combined and continuously extracted with methylene chloride for 12 hours. Evaporation of the methylene chloride gave an oil which crystallized when kept with petroleum ether in the cold. The crude hydroxy lactone (XXXVII) (333 mg.) (71%) had a m.p. of 93-95°. Recrystallization from methylene chloride gave an analytical sample of m.p. 93-95°.

ν_{max} 3635, 3500(b), 2940, 1780(b), 1650, 1440(b), 1395, 1365, 1350, 1310 1155, 1090, 1020(m), 987, 953(m), 938(s), 925(s), 890, 873 cm^{-1}.

Anal. Calcd. for $C_{11}H_{16}O_3$: C,67.32; H,8.22; O,24.46. Found: C,67.35; H,8.19; O,24.46%.

γ-Lactone of trans-1β-Carboxy-8β-hydroxy-5-oxodecahydronapthalene (XXIX ~~XXXIV~~).

A solution of hydroxy lactone (XXXVII) (162 mg.) in acetone was cooled to 0° and a standard solution of Jones Reagent[16], cooled to 0°, was added to it until a slight red color developed. Cold isopropyl alcohol was added until a green color developed.

The reaction mixture was mixed with Celite, filtered, and the cake was thoroughly washed with acetone. Florisil was added to the filtrate and it was stirred for 5 minutes. The solution was filtered, the cake was washed thoroughly with acetone, and evaporated to an oil. The crude keto lactone (XXIV) (67 mg.) (42%) (m.p. of 68-70°) crystallized after

two days in the cold when kept with petroleum ether.

Sublimation gave an analytical sample of m.p. 65.5-67°.

λ_{max} 289 mμ (ε 24), ν_{max} 2940, 1780, 1713, 1635(m), 1450(b), 1350, 1340(s), 1270(m), 1190, 1160, 1080, 1035, 1000, 970, 920 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}O_3$: C,68.02; H,7.27; O,24.71. Found: C,68.21; H,7.64; O,24.13%.

γ-Lactone of trans-1β-Carboxy-8β-hydroxy-5-oxodecahydronaphthalene (XXXIX).

A solution of hydroxy lactone (XXXVII) (200 mg.) in acetone was cooled to 0° and a standard solution of Jones Reagent[16], cooled to 0°, was added to it until a slight red color developed. Cold isopropyl alcohol was added until a green color developed.

The reaction mixture was mixed with Celite, filtered, and the cake was thoroughly washed with acetone. Florisil was added to the filtrate and it was stirred for 5 minutes. The solution was filtered, the cake was washed thoroughly with acetone, and evaporated to an oil. The crude keto lactone (XXVIV) (120 mg.) (61%) (m.p. of 110-112°) crystallized when kept with petroleum ether in the cold.

Recrystallization from methylene chloride gave an analytical sample of m.p. 114-115°

λ_{max} 291mμ(ε 22), ν_{max} 3019, 2938, 1780, 1716, 1442, 1418, 1362,1343, 1269, 1185, 1158, 1080, 1036, 1000, 968, 918 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}O_3$: C,68.02; H,7.27; O,24.71. Found: C,68,31; H,7.47; O,24.14%.

SUMMARY

The synthesis of the cis-hydroxy keto acid (XXXV) from Woodwards adduct (XXIII) via (XXXI) was improved. The limited solubility of the dihydrocompound (XXXI) in the solvents commonly used in hydrogenation reactions was overcome by using t-butanol as the reaction solvent. It is suggested that the use of t-butanol as solvent in other catalytic hydrogenations should be investigated.

The trans-hydroxy keto acid (XXXIV) was obtained by either hydrolysis of the δ-transannular lactone (XXXIII) or (better) by epimerization with base of the cis-hydroxy keto acid (XXXV). The melting point of this compound compared favorably to that reported by M. Protiva et al.[18]

The trans-hydroxy keto acid (XXXIV) was reduced by aqueous sodium borohydride to the new diol (XXXVI). Some difficulty was experienced in lactonizing the diol (XXXV) but use of N,N-dicyclohexylcarbodiimide gave the new γ-hydroxy lactone (XXXVII).

The γ-hydroxy lactone (XXXVII) was oxidized with chromic oxide to give compounds on different occasions with different melting points. The analysis and infrared spectrum of each compound agrees with a structural assignment of a γ-keto lactone. However, the n.m.r. spectrum of the higher melting material was shown to be in good agreement with the structure (XXIX). This new compound will be used as a starting material for the synthesis of diterpenoid acids of the abietic acid type.

The identity of the lower melting material has not been established.

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