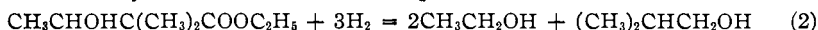


carbon atoms with the formation of two molecules of ethyl and one molecule of isobutyl alcohol as shown in Equation 2.



Unsuccessful attempts were made to hydrogenate malonic and phenylacetic esters. Both of these esters reduced the catalyst so that it was inactive for the hydrogenation of esters. It is hoped that work now in progress will make it feasible to reduce such esters.

Other catalysts for the hydrogenation of esters have been used in this Laboratory but none of them have proved as effective as copper chromite. For example, the nickel catalyst obtained by reducing nickel chromite catalyzed the hydrogenation of ethyl laurate to the extent of only 40% after seven hours at 250°.

Summary

Ethyl laurate, myristate, valerate, cinnamate, trimethylacetate and succinate have been hydrogenated over a copper chromite catalyst with the formation of the corresponding alcohols in yields of from 80 to 98%. The carboxy group in 2,2-dimethyl-3-hydroxybutyrate was hydrogenated to a carbinol group, and in addition the molecule underwent cleavage between the 2 and 3 carbon atoms.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, No. 651]

STUDIES ON π -CAMPHOR DERIVATIVES. II. THE IDENTITY OF DIHYDRO-TERESANTALIC ACID WITH 7- π -APOCAMPHAN-CARBOXYLIC ACID

By TORSTEN HASSELSTRÖM

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In a previous paper the complete synthesis of 7- π -apocamphancarboxylic acid has been reported.¹ The present investigation was undertaken in order to prove the identity of this acid with dihydro-teresantalic acid. The preparation of dihydro-teresantalic acid itself was accomplished by new methods which furnish further evidence of the structure of the π -camphor derivatives.

By adding hydrogen chloride to teresantalic acid the trimethylene ring is opened and chlorodihydro-teresantalic acid formed.² This action of hydrogen chloride, however, does not yield a homogeneous product.³ Rupe and Tomi⁴ have investigated the action of hydrogen chloride on the methyl ester of teresantalic acid and found that two different chlorodi-

¹ Hasselström, *Ann. Acad. Fenn.*, **30**, 12 (1929).

² Muller, *Arch. Pharm.*, **238**, 366 (1900).

³ Semmler and Bartelt, *Ber.*, **40**, 3140 (1907).

⁴ Rupe and Tomi, *ibid.*, **49**, 2563 (1916).

hydro-teresantalic methyl esters were formed; namely, a labile liquid form which easily split off hydrogen chloride, and a more stable solid form which could be distilled without decomposition. The removal of hydrogen chloride from both forms gives the methyl ester of iso-teresantalic acid. Thus iso-teresantalic acid and teresantalic acid are stereoisomeric compounds.

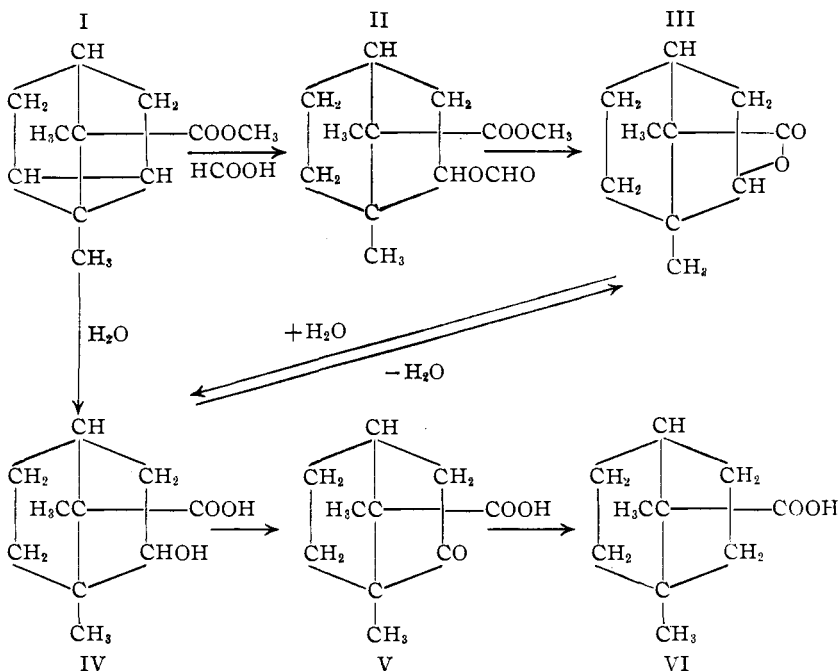
By the action of dilute alkali on chlorodihydro-teresantalic acid, Muller² obtained a lactone, which Semmler and Bartelt⁵ later converted into the corresponding hydroxy acid and glycol. The action of formic acid on teresantalic acid results in the partial formation of a lactone, which is not identical with Muller's previously prepared lactone. Semmler and Bartelt explained the formation of their lactone by the addition and splitting off of formic acid and suggested that the lactone formed does not have the carboxyl group located in the bridge but in the ring. In order to obtain further data on this lactone formation, the preparation of dihydro-teresantalic acid was first accomplished from Semmler and Bartelt's lactone.

The teresantalic methyl ester (I) was used as starting material, instead of the free acid. This was done in order to prevent, if possible, the formation of the formate of π -norborneol. This reaction resulted in a good yield of the lactone of 2-hydroxy-7- π -apocamphan-carboxylic acid (III), from which the hydroxy acid (IV) was prepared by saponification with alkali. The melting points of the lactone and the hydroxy acid corresponded with those given by Semmler and Bartelt.⁵ By oxidation with potassium permanganate in alkaline solution an optically active keto acid (V) was obtained, the semicarbazone of which, when treated according to the method of Wolff,⁶ gave a good yield of nearly optically inactive dihydro-teresantalic acid (VI). Furthermore, the dihydro-teresantalic acid had the same melting point as the synthetically prepared 7- π -apocamphan-carboxylic acid¹ and did not give a depression by the mixed melting point test. Thus this reaction completes the synthesis of a dihydro-teresantalic acid which is identical with 7- π -apocamphan-carboxylic acid.

The action of formic acid on the methyl ester of teresantalic acid shows that the trimethylene ring is split without a rearrangement of the symmetric system and also that the carboxyl group remains in the bridge. Whether or not an intermediate formate of dihydro-teresantalic methyl ester (II) is formed during this reaction was not evident. The splitting of the trimethylene ring might perhaps take place by the addition of water according to the well-known reaction of Bertram and Walbaum. The saponification of the ester group might be a secondary reaction of saponification and therefore the formation of the lactone would be due to the primary hydroxy acid (IV).

² Semmler and Bartelt, *Ber.*, **40**, 4465 (1907).

⁶ Wolff, *Ann.*, **394**, 86 (1912).

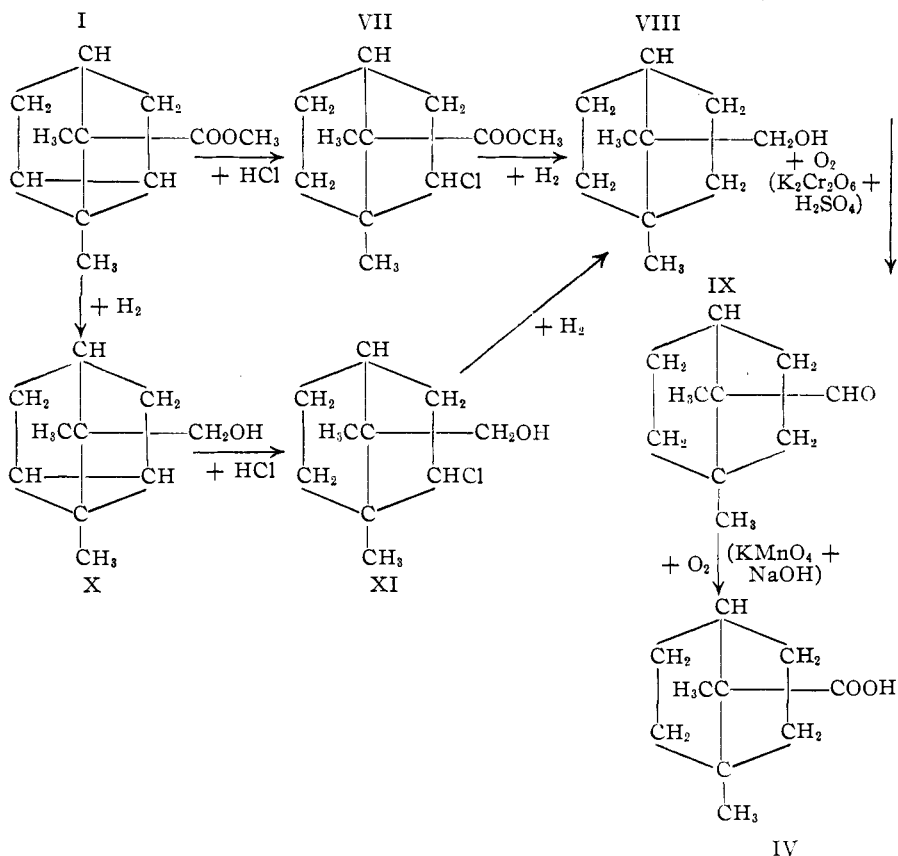


There still remains the question of the difference between the Semmler-Bartelt and the Muller lactones. The reaction of dilute alkali on chlorodihydro-teresantalic acid might, during the splitting of hydrogen chloride, cause a rearrangement. The lactone of Muller might here react as an intermediate product in the conversion of the teresantalic series into the santene series, since the formation of lactone, thus obtained, is accompanied by more or less santene.² This explanation would agree with the hypothesis that the rearrangements in the true camphor series are due to an intramolecular tertiary mobile halogen or hydroxyl atom.⁷ Further investigations of Muller's lactone will be necessary to provide more evidence.

Additional work was carried out on the preparation of dihydro-teresantalic acid. The crude mixture of chlorodihydro-teresantalic methyl ester (VII) was reduced to dihydro-teresantalol (VIII). This reaction was carried out with aluminum amalgam in moist ether solution at room temperature, in order to prevent the splitting off of hydrogen chloride, which readily occurs according to Rupe and Tomi.⁴ As the isolated product contained chlorine, the reduction was continued by the method of Bouveault and Blanc, by means of metallic sodium and alcohol. The

⁷ (a) Meerwein and van Emster, *Ber.*, **53**, 1815 (1920); *ibid.*, **55**, 2500 (1922); (b) Hasselström, *Ann. Acad. Fenn.*, **20**, 2 (1923); (c) Komppa and Hasselström, *ibid.* **24**, 14, (d) 15 (1925); (e) **26**, 2, (f) 13 (1926); (g) **30**, 13 (1929).

dihydro-teresantalol obtained was oxidized to dihydro-teresantalal (IX) with a mixture of potassium dichromate and sulfuric acid. By oxidation with potassium permanganate this aldehyde was converted into dihydro-teresantalic acid (IV), which did not depress the melting point of the previously prepared dihydro-teresantalic acid.



In order to obtain a more convenient method for the preparation of dihydro-teresantalic acid, the methyl ester of teresantalic acid was reduced to teresantalol (X) and the chlorodihydro-teresantalol (XI) obtained by the addition of hydrogen chloride was reduced to dihydro-teresantalol (VIII). However, the addition of hydrogen chloride to teresantalol seems to be accompanied by side reactions, since a solid and a liquid form of chlorodihydro-teresantalol were obtained. Further investigations of the liquid chloride, to determine whether or not a rearrangement to the santene type had taken place, were not made. The solid form of chlorodihydro-teresantalol was reduced by sodium and alcohol to dihydro-teresantalol.

The complete synthesis of dihydro-teresantalic acid, combined with the work of Ruzicka and Liebl,⁸ completes the evidence for the structure of teresantalic acid.

These investigations on the π -camphor series will be continued.

Experimental

Raw Material.—The teresantalic acid was obtained from Schimmel and Co. by the courtesy of Fritzsche Bros., New York City. The purification was carried out by crystallizing the crude acid once from dilute acetic acid. The melting point was 156–157°, which corresponds with the data obtained by previous investigators.

Semmler and Bartelt's Lactone: Lactone of 2-Hydroxy-7- π -apocamphan-carboxylic Acid.—The methyl ester of teresantalic acid was prepared by the action of methyl sulfate on the sodium salts of teresantalic acid in water solution, according to the data given by Rupe and Tomi.⁴

To a solution of 30 g. of teresantalic methyl ester in 90% formic acid was added 5 cc. of water. The reaction mixture was allowed to boil under a reflux for one hour. After cooling to room temperature, the solution was poured into 500 cc. of a mixture of water and ice. During the treatment a solid mass separated. The product was filtered and dried on a porous plate: yield, 20 g. It was recrystallized from ethyl acetate and melted between 190–191°. Thus the melting point of the lactone corresponded to that given by Semmler and Bartelt.

Oil was obtained as a by-product. This is probably identical with the formate of π -norborneol. However, the amount was too small for an investigation.

Hydroxy Acid from Semmler and Bartelt's Lactone (2-Hydroxy-7- π -apocamphan-carboxylic Acid).—Two grams of Semmler and Bartelt's lactone was boiled under a reflux until dissolved with 150 cc. of 2% sodium hydroxide solution. After cooling, the hydroxy acid was precipitated with dilute sulfuric acid. It was filtered and dried upon a porous plate. The crude acid was crystallized from ethyl acetate and melted at 195–196°. This melting point of the hydroxy acid corresponds to that given by Semmler and Bartelt.

Ketodihydro-teresantalic Acid (2-Keto-7- π -apocamphan-carboxylic Acid).—Five grams of the lactone was saponified by 100 g. of an alkaline solution containing 2% of sodium hydroxide. After dissolving, little by little, 120 cc. of permanganate solution, containing 8 g. of potassium permanganate, was added to the boiling solution. The mixture was stirred vigorously. The manganese dioxide was filtered off after the color of the permanganate had disappeared. The filtrate was evaporated on a boiling water-bath until 30 cc. of solution remained. After cooling, the mixture was made acid. The precipitate had all the properties of the original material. The filtrate was extracted repeatedly with ether and the ether solution dried with anhydrous sodium sulfate. After evaporating the ether, a pale yellow oil remained. This gradually solidified: yield, 4.3 g. The oil was dissolved in water, filtered, and gave a more insoluble hydroxy acid. By standing overnight, the keto acid crystallized in colorless plates. Repeatedly recrystallized from water, the acid melted at 269–270°.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.89; H, 7.75. Found: C, 66.10; H, 7.77. *Rotation.* $[\alpha]_D^{25} -55^\circ$ (0.5l, $\alpha = 2.7^\circ$, in 10% alcohol solution).

In comparison, the 2-keto-7- π -apocamphan-carboxylic acid previously prepared by complete synthesis melted at 249–250°.¹

The semicarbazone of 2-keto-7- π -apocamphan-carboxylic acid was prepared in the

⁸ Ruzicka and Liebl, *Helv. Chim. Acta*, 9, 140 (1926).

usual way. It melted at 204–205°, with decomposition, after one recrystallization from dilute alcohol.

7- π -Apocamphan-carboxylic Acid (Dihydro-teresantalic Acid).—Sodium ethylate was prepared in a bomb tube from 0.6 g. of sodium and 3 cc. of absolute alcohol. To the hot solution was added 0.5 g. of the crude semicarbazone of 2-keto-7- π -apocamphan-carboxylic acid. After closing the tube, the mixture was heated at 170–180° during fifteen hours. After cooling, the mixture was diluted with water and the dihydro-teresantalic acid precipitated by dilute sulfuric acid. The crude acid was recrystallized from dilute alcohol and melted at 228–229° (corr.). The acid was nearly optically inactive.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 71.42; H, 9.52. Found: C, 71.35; H, 9.37.

In comparison, the dihydro-teresantalic acid obtained by complete synthesis melted at 229–230°.¹ No depression of the mixed melting point was obtained.

Dihydro-teresantalol (π -Borneol).—By the method of Rupe and Tomi,⁴ teresantalic methyl ester was converted into chlorodihydro-teresantalic methyl ester. The oil obtained partly solidified on cooling, but the solid α -form was not separated from the labile liquid α -form, on the assumption that the α - and the β -forms are stereoisomeric compounds. Rupe and Tomi found that the hydrochlorides, by splitting off hydrogen chloride, gave the same iso-teresantalic acid, which easily was converted into teresantalic acid. Therefore the crude mixture of the chloro esters was used and the reduction carried out in such a way that the splitting off of hydrogen chloride from the labile α -form would be prevented as much as possible.

Aluminum amalgam was prepared from 25 g. of aluminum. To this moist aluminum amalgam was added 25 g. of chlorodihydro-teresantalic methyl ester, dissolved in 200 cc. of ether. After standing overnight, the mixture was filtered and the ether evaporated. The residue was a colorless oil, which gave a strong chlorine reaction. The product was therefore dissolved in 250 cc. of absolute alcohol and the reduction continued with 25 g. of sodium according to the well-known method of Bouveault and Blanc. When the reaction was complete, water was added and the solution extracted with ether repeatedly. The ether solution was dried and, after evaporation, the residue was distilled, b. p. 214–216°; yield, 18 g. The crystalline alcohol, after removal of some oil, melted at 171°, which corresponded with Semmler and Bartelt's previously found figure.⁵ The oily part was not further investigated.

Dihydro-teresantalal.—One gram of π -borneol dissolved in 10 g. of benzene was added to a solution of 1 g. of potassium dichromate, 1.1 g. of sulfuric acid and 10 cc. of water. The mixture was shaken and heated on a boiling water bath until the liquid became green. After cooling, the benzene layer was separated, dried, and the benzene evaporated. The residue gave a positive test for aldehyde with ammoniacal silver solution. The aldehyde was treated with semicarbazide mixture. The semicarbazone obtained was recrystallized from dilute alcohol and melted at 212–213° with decomposition.

Anal. Calcd. for $C_{11}H_{18}N_2O$: C, 63.16; H, 9.14. Found: C, 63.23, H, 8.9.

The aldehyde, recovered by adding dilute hydrogen chloride to the semicarbazone and distilling the mixture with steam, melted at 166.5–167.5°.

Dihydro-teresantalic Acid from Dihydro-teresantalal.—Six grams of dihydro-teresantalal was oxidized at room temperature with 9 g. of potassium permanganate and 6 g. of sodium hydroxide dissolved in 200 cc. of water. The mixture was shaken for twelve hours and the reaction mixture then decolorized with alcohol. The manganese dioxide was filtered off and the filtrate evaporated to about 50 cc. The dihydro-teresantalic acid was precipitated with dilute sulfuric acid and recrystallized from dilute alcohol;

m. p. 229–230°, and no melting point depression when mixed with the previously prepared acid; yield, 4.2 g. The acid was nearly optically inactive.

Chlorodihydro-teresantalol.—Two grams of teresantalol (m. p. 114°), prepared according to Semmler and Bartelt,^{8,9} was dissolved in methyl alcohol and the solution saturated with dry hydrogen chloride. The reaction mixture was cooled with a mixture of ice and salt. After standing for forty-eight hours, the mixture was poured on ice and extracted with ether. The ether solution was washed with water and a dilute sodium bicarbonate solution. After evaporation of the ether, a crystalline compound and an oil were obtained. However, the liquid part was formed in such small quantity that its further investigation was impossible. The solid part, 2-chloro-7- π -borneol melted as crude at 125–126° with decomposition.

Dihydro-teresantalol.—Two grams of 2-chloro-7- π -borneol was dissolved in 30 cc. of absolute ethyl alcohol and reduced with 5 g. of metallic sodium. The reaction mixture was diluted with water and extracted with ether. After evaporating the ether, dihydro-teresantalol was obtained, m. p. 171°, and did not give any melting point depression when mixed with the previously prepared dihydro-teresantalol.

The semicarbazone of dihydro-teresantalol prepared from dihydro-teresantalol obtained by oxidation of 7- π -borneol melted at 213–214° with decomposition, thus corresponding with the previously found melting point.

Summary

1. It is proved that dihydro-teresantalic acid is identical with 7- π -apocamphan-carboxylic acid.

2. The action of formic acid on teresantalic methyl ester results in a lactone which has the carboxyl group in the ring and not in the bridge.

3. The reactions of teresantal derivatives seem to be accompanied by side reactions, which may be due either to the formation of stereoisomeric compounds or to a rearrangement of the teresantal nucleus to the santene series.

4. The complete synthesis of dihydro-teresantalic acid completes the evidence for the structure of teresantalic acid.

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