izing microscope. Talomucic acid could not be found.

Products from D-Galactal.—These products were similarly examined (Table I). Attempts to isolate a crystalline derivative of the non-volatile acid found were not successful. The presence of D-lyxonic acid is surmised.

Summary

1. Four unsaturated sugar derivatives, diacetyl-D-arabinal, D-arabinal, triacetyl-D-galactal and D-galactal were treated with hydrogen peroxide in *t*-butanol with osmium tetroxide as a catalyst.
2. D-Arabinose was identified as a reaction product from both arabinal and its diacetate and the yield was determined roughly. D-Ribose was not found.
3. D-Galactose was identified and roughly estimated as a product from galactal and its triacetate. D-Talose was not found.
4. D-Arabinal and D-galactal were partially oxidized by the reagent producing, respectively, D-erythronic acid and (probably) D-lyxonic acid.
5. The stereochemical aspects of the reaction are discussed.

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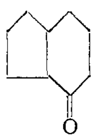
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

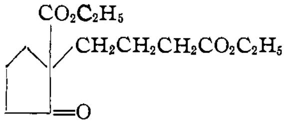
A New Synthesis of 4-Ketohexahydroindan

BY W. E. BACHMANN AND W. S. STRUVE[1]

4-Ketohexahydroindan (I), which has been prepared previously from indan[2] and from δ-ketosebacic acid,[3] has now been synthesized from 2-carboethoxycyclopentanone. The potassium derivative of the latter compound reacted with ethyl γ-bromobutyrate to give ethyl γ-(1-carboethoxy-2-ketocyclopentyl)-butyrate (II) in good yield. By hydrolysis of the ester followed by decarboxylation of the dicarboxylic acid, γ-(2-ketocyclopentyl)-butyric acid (III) was obtained. The methyl ester of this keto acid was converted to the cyanohydrin, methyl γ-(2-hydroxy-2-cyanocyclopentyl)-butyrate (IV). When the cyanohydrin was dehydrated with thionyl chloride and pyridine according to the procedure used by Cook and Linstead on an analogous compound,[4] and the unsaturated cyanide was hydrolyzed with concentrated hydrochloric acid, a crystalline unsaturated acid was obtained which is probably γ-(2-carboxycyclopenten-1-yl)-butyric acid (V), but the results were not reproducible. By dehydrating the cyanohydrin by means of thionyl chloride and pyridine entirely in the cold and hydrolyzing the resultant unsaturated cyanide with dilute alkali, a different unsaturated acid was obtained which is probably γ-(2-carboxycyclopenten-2-yl)-butyric acid (VI). Both unsaturated acids gave the same reduced acid γ-(2-carboxycyclopentyl)-butyric acid (VII) on hydrogenation with Adams platinum catalyst. It is not known whether this saturated acid is the *cis* or *trans* form.



I



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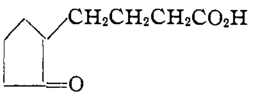

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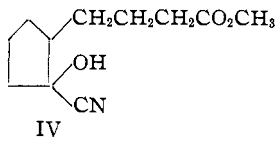

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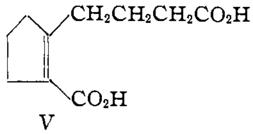

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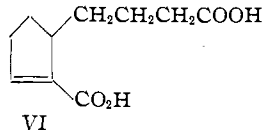

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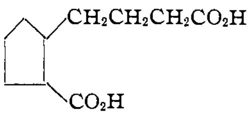
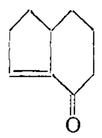


VII



VIII

γ-(2-Carboxycyclopenten-2-yl)-butyric acid (VI) was cyclized by means of acetic anhydride to what is probably 4-ketohexahydroindene-3 (VIII). This is an isomer of the compound obtained by Hückel and Schlüter[3] by treating δ-ketosebacic acid with acetic anhydride and believed by them to be 4-ketohexahydroindene-8, although the position of the double bond was not definitely

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[1] Du Pont Post-doctoral Fellow.

[2] Hückel and Goth, *Ber.*, **67**, 2104 (1934).

[3] Hückel and Schlüter, *ibid.*, **67**, 2107 (1934).

[4] Cook and Linstead, *J. Chem. Soc.*, 946 (1934).

established. The derivatives of the new unsaturated ketone are different from those of Hückel and Schlüter's compound; hence, we consider our ketone to have the structure VIII and the corresponding acid to have the structure VI. Unfortunately, enough of the isomeric unsaturated acid (V) was not obtained to allow a cyclization to be carried out on it.

In order to prepare 4-ketohexahydroindan (I), a mixture of the methyl esters of the unsaturated acids V and VI was hydrogenated and the mixture of reduced esters was cyclized by sodium methoxide in benzene. The resulting carbomethoxy derivative of the cyclic ketone was converted to 4-ketohexahydroindan by the action of a hot mixture of acetic and hydrochloric acids. The product is presumably the equilibrium mixture of the *cis* and *trans* forms described by Hückel and Doll,[5] which consists mainly of the *cis* form. The 4-ketohexahydroindan also was formed by hydrogenation of the unsaturated ketone 4-ketohexahydroindene-3 (VIII).

Experimental

Ethyl γ-(1-Carboethoxy-2-ketocyclopentyl)-butyrate (II).—To a cold suspension of 12.5 g. of powdered potassium in 250 cc. of toluene was added 50 g. of 2-carboethoxycyclopentanone. After the mixture had been warmed on a steam-bath for half an hour to form the potassium salt, 50 g. of ethyl γ-bromobutyrate[6] was added to the cooled mixture, which was then refluxed on a sand-bath overnight. Dilute hydrochloric acid was added to the cooled reaction mixture, the organic layer was washed with water and the residue obtained by evaporation of the toluene was distilled; b. p. 140–145° at 0.4 mm.; yield, 55 g. (79%) of a colorless liquid.

Anal. Calcd. for $C_{14}H_{22}O_5$: C, 62.2; H, 8.1. Found: C, 61.8; H, 8.1.

γ-(2-Ketocyclopentyl)-butyric Acid (III).—A mixture of 180 g. of the aforementioned compound and 300 cc. of concentrated hydrochloric acid was refluxed for three hours. The hydrochloric acid was removed under reduced pressure, the residue was taken up in benzene, and the benzene solution was shaken with sodium carbonate solution. The acid liberated by acidification of the alkaline extract was taken up in ether and the residue obtained by evaporation of the dried ether extract was distilled; b. p. 153–156° at 0.2 mm.; yield, 60 g. (53%) of a colorless, viscous liquid.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.2; H, 8.2. Found: C, 63.5; H, 8.3.

The **methyl ester** was prepared by refluxing 70 g. of the acid with 400 cc. of 3% methanolic hydrochloric acid for three hours. It was obtained as a colorless liquid; b. p. 143–146° at 14 mm.; yield, 67.5 g. (87%).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.2; H, 8.7. Found: C, 64.9; H, 8.4.

Methyl γ-(2-Hydroxy-2-cyanocyclopentyl)-butyrate (IV).—To a mixture of 15 cc. of liquid hydrogen cyanide and 2 drops of 45% aqueous potassium hydroxide solution cooled in an ice–salt-bath was added dropwise 15 g. of the aforementioned methyl ester. After twelve hours in a refrigerator the mixture was neutralized with sulfuric acid, the excess of hydrogen cyanide was removed under reduced pressure and the residue was distilled; b. p. 163–165° at 3 mm.; yield, 15.45 g. of a colorless liquid, which was not analytically pure.

Anal. Calcd. for $C_{11}H_{17}NO_3$: C, 62.5; H, 8.0. Found: C, 63.4; H, 8.5.

γ-(2-Carboxycyclopenten-1-yl)-butyric Acid (V).—The following procedure worked satisfactorily only occasionally; frequently only an intractable tar was produced. To a mixture of 15.45 g. of the cyanohydrin (IV) and 12.2 cc. of pyridine cooled in an ice–salt-bath was added dropwise 11 cc. of thionyl chloride, and the resulting mixture was heated on a steam-bath for one hour. Ice and hydrochloric acid were then added to the cooled mixture, the organic layer was taken up in ether, and the ether solution was washed with 10% sodium hydroxide solution and then dried with sodium sulfate. The residue obtained by removal of the ether was distilled; b. p. 130–133° at 3 mm.; yield, 9.9 g. (70%) of an almost colorless liquid.

A mixture of the unsaturated cyanide and 40 cc. of concentrated hydrochloric acid was refluxed for seventy-two hours. After removal of the hydrochloric acid under reduced pressure, the residue was extracted with benzene and ether, and the organic solution was washed with water and then evaporated. The acid which was obtained was refluxed with 25 cc. of 3% methanolic hydrochloric acid for twelve hours and the resulting ester was purified by distillation; b. p. 146–153° at 12 mm. The ester was hydrolyzed by refluxing with 20 cc. of concentrated hydrochloric acid for twelve hours, the liquids were removed under reduced pressure and the residue was crystallized from benzene–petroleum ether; yield, 1.7 g. (17%); m. p. 114–119°. After several recrystallizations from benzene–petroleum ether the acid was obtained as colorless prisms; m. p. 121–122°.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.6; H, 7.1. Found: C, 60.7; H, 7.3.

The **dimethyl ester** prepared by refluxing 0.77 g. of the acid with 5 cc. of 3% methanolic hydrochloric acid was obtained as a colorless liquid; yield, 0.71 g. (81%); b. p. 173–177° at 26 mm.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.7; H, 8.0. Found: C, 63.1; H, 8.1.

γ-(2-Carboxycyclopenten-2-yl)-butyric Acid (VI).—To a solution of 33 g. of methyl γ-(2-hydroxy-2-cyanocyclopentyl)-butyrate and 26 cc. of pyridine in 100 cc. of anhydrous ether cooled in an ice–salt-bath was added dropwise 23.5 cc. of thionyl chloride. The mixture was kept in the cooling bath for two hours and then at room temperature for an additional ten hours, after which it was hydrolyzed and worked up as described above; b. p. 130–135° at 3 mm.; yield, 16 g. (53%) of a colorless liquid. A mixture of it and 130 cc. of 10% sodium hydroxide solution

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(5) Hückel and Doll, *Ann.*, **526**, 103 (1936).

(6) Prill and McElvain, THIS JOURNAL, **55**, 1233 (1933).

was refluxed for twelve hours and then acidified. After a short time the oil which precipitated partially solidified. The oil was removed from the crystals as much as possible by suction and the solid was recrystallized from benzene–petroleum ether; yield, 2.8 g. (17%); m. p. 133–135°. After several recrystallizations the acid formed fine colorless needles; m. p. 137.5–138.5°. This acid depressed the melting point of the preceding acid.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.6; H, 7.1. Found: C, 60.4; H, 7.1.

The **dimethyl ester**, prepared like its isomer, was obtained as a colorless liquid in 88% yield; b. p. 137–139° at 3 mm.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.7; H, 8.0. Found: C, 63.2; H, 8.0.

4-Ketohexahydroindene-3 (VIII).—Following the procedure of Hückel and Schlüter[3] a mixture of 3 g. of γ-(2-carboxycyclopenten-2-yl)-butyric acid and 15 cc. of acetic anhydride was heated slowly in an oil-bath and then distilled, the fraction boiling at 200–300° (bath temperature) being collected. The distillate was made alkaline with sodium carbonate solution and the product, after being washed and dried in ethereal solution, was distilled; b. p. 120–126° at 20 mm.; yield, 0.74 g. of an almost colorless liquid.

The **semicarbazone** formed cream colored leaflets from alcohol; m. p. 236–237°. Hückel and Schlüter[3] give 255° as the melting point of the semicarbazone of their isomeric 4-ketohexahydroindene-8.

Anal. Calcd. for $C_{10}H_{15}N_3O$: N, 21.8. Found: N, 22.3.

The **oxime**, prepared from ketone regenerated from the semicarbazone, crystallized from petroleum ether in two interconvertible modifications: leaflets, m. p. 128–129°, and needles, m. p. 136.5–138°.

Anal. Calcd. for $C_9H_{13}NO$: N, 9.3. Found: N, 9.6.

γ-(2-Carboxycyclopentyl)-butyric Acid (VII). (a) **From γ-(2-Carboxycyclopenten-1-yl)-butyric Acid.**—A solution of 0.5 g. of the acid in 5 cc. of alcohol and 0.05 g. of Adams platinum catalyst was shaken under a slight pressure of hydrogen for thirty minutes when the theoretical amount of hydrogen had been absorbed. The product obtained from the alcohol solution crystallized when triturated with petroleum ether; yield, 0.3 g.; m. p. 72–78°. After several recrystallizations from benzene–petroleum ether the acid was obtained in clusters of small colorless needles; m. p. 80–82°. No other crystalline acid was obtained.

(b) **From γ-(2-Carboxycyclopenten-2-yl)-butyric Acid.**—Hydrogenation of 0.5 g. of this acid in the same manner as its isomer yielded 0.32 g. of crystalline product; m. p. 70–72°. After several recrystallizations from benzene–petroleum ether, the acid melted at 81–83° alone and when mixed with the acid obtained in (a).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.0. Found: C, 59.5; H, 8.0.

4-Ketohexahydroindan (I).—A mixture of the dimethyl esters (1.17 g.) of the two unsaturated acids in 5 cc. of alcohol was hydrogenated (0.05 g. of Adams catalyst; one-half hour of shaking) and the resulting **dimethyl ester** of **γ-(2-carboxycyclopentyl)-butyric acid** (presumably a mixture of the *cis* and *trans* forms) was purified by distillation; b. p. 133–137° at 3 mm.; yield, 1.11 g. (94%) of a colorless liquid.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.1; H, 8.8. Found: C, 62.8; H, 8.7.

A mixture of dry sodium methoxide prepared from 0.1 g. of sodium, 0.92 g. of the dimethyl ester and 10 cc. of dry benzene was refluxed in an atmosphere of nitrogen for six hours. Dilute acetic acid was added, the benzene layer was washed with water and the residue obtained by removal of the benzene was distilled; b. p. 115–119° at 3 mm.; yield, 0.65 g. (80%) of a colorless liquid, which gave a deep purple color with an alcoholic solution of ferric chloride. A mixture of 0.3 g. of the cyclic keto ester, 1 cc. of acetic acid and 1.5 cc. of concentrated hydrochloric acid was refluxed in a nitrogen atmosphere for five hours, the acids were neutralized and the ketone was extracted with ether. The ketone obtained from the washed and dried ether solution was distilled and identified by means of its characteristic benzoyl oxime; m. p. 111–114° (reported,[2] 114°).

A further quantity of the ketone was obtained from the oil which was separated from the crystalline γ-(2-carboxycyclopenten-2-yl)-butyric acid. By esterification with 3% methanolic hydrochloric acid it yielded 8.5 g. of dimethyl ester (b. p. 157–160° at 12 mm.) which on hydrogenation gave 7 g. of a mixture of the reduced esters. Cyclization of 4 g. of the esters by sodium methoxide in the manner described gave 2.1 g. of the cyclic keto ester (b. p. 135–145° at 15 mm.) which was hydrolyzed and decarboxylated to yield 0.55 g. of 4-ketohexahydroindan as a colorless liquid with a peppermint-like odor; b. p. 101–103° at 15 mm. (reported,[2] 100° at 17 mm.). The benzoyl oxime melted at 111–113°, alone and when mixed with the benzoyl oxime prepared above. The semicarbazone melted at 193° (reported,[2] 193°).

A mixture of 0.42 g. of 4-ketohexahydroindene-3, 0.05 g. of palladium–charcoal catalyst,[7] and 15 cc. of absolute alcohol was shaken under a slight pressure of hydrogen for twenty minutes at which time the theoretical amount of hydrogen had been absorbed. The product obtained from the solution was converted into its benzoyl oxime, which separated from petroleum ether in clusters of leaflets and needles. The clusters of leaflets, separated by hand from the mixture, after several recrystallizations from petroleum ether melted at 112–114°, alone and when mixed with the benzoyl oxime prepared above.

Summary

4-Ketohexahydroindan has been built up from cyclopentanone. A butyric acid side chain was introduced into the 2-position and a carboxyl group was put into the 1-position, the latter through the cyanohydrin reaction. The six-membered ring was constructed by cyclization of the reduced dicarboxylic acid. In addition, a 4-ketohexahydroindene with the double bond probably in the 2-position was prepared.

ANN ARBOR, MICHIGAN

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[7] Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).