Anal. Subs., 0.4156: 22.90 cc. of 0.0842 *N* KOH. Calcd. for $C_{13}H_{26}O_2$: neutr. equiv., 214.2. Found: 215.5.

Summary

1. A satisfactory method is given for preparing various aldehyde esters by the ozonation of the methyl esters of unsaturated acids.
2. The use of the aldehyde esters in synthesizing hydroxy acids and unsubstituted acids is illustrated by the conversion of methyl η-aldehydo-octanoate by means of butylmagnesium bromide into methyl θ-hydroxytridecanoate and, finally, conversion of this latter compound through the bromide and olefinic acid to tridecanoic acid.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

SYNTHESIS OF DIHYDROCHAULMOOGRIC AND DIHYDROHYDNOCARPIC ACIDS. II

BY C. R. NOLLER[1] WITH ROGER ADAMS

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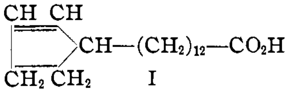
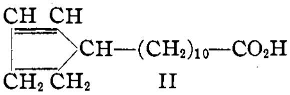
In a recent paper by Shriner and Adams[2] a careful consideration of the experimental work of Power[3] and collaborators together with the consideration of new experimental evidence led to the conclusion that chaulmoogric and hydnocarpic acids were not tautomeric substances but that all the reactions of these two compounds could be explained by one structural formula for each; chaulmoogric acid I; hydnocarpic acid II.

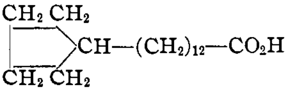


I



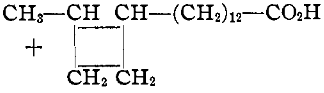
II

By reduction of the hydrogen bromide addition compound of chaulmoogric acid, Power[3c] obtained a dihydrochaulmoogric acid which he regarded as a mixture of μ-cyclopentyl-tridecanoic acid III and 2-methyl-μ-cyclobutyl-tridecanoic acid IV.

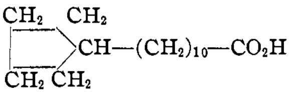


III

+



IV



V

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[1] This communication is an abstract of a portion of a thesis submitted by C. R. Noller in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

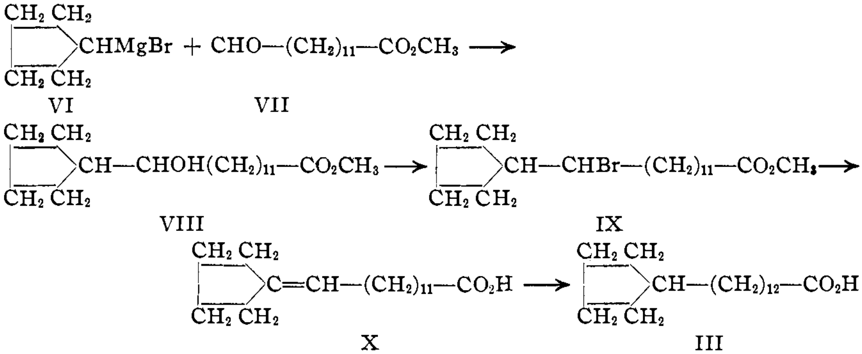
[2] Shriner and Adams, THIS JOURNAL, **47**, 2727 (1925).

[3] Power and Gornall, (a) *J. Chem. Soc.*, **85**, 838 (1904); (b) **85**, 851 (1904). (c) Barrowcliff and Power, *ibid.*, **91**, 557 (1907).

Dean and Wrenshall reduced both chaulmoogric[4] and hydnocarpic acids to dihydro compounds using hydrogen and a mixture of platinum and palladium black as catalyst. Shriner and Adams[2] found that these acids could be far more satisfactorily reduced using hydrogen and platinum-oxide platinum black as a catalyst. If Formulas I and II are correct for chaulmoogric and hydnocarpic acids, the dihydro derivatives are not mixtures and dihydrochaulmoogric acid must be represented by Structure III and dihydrohydnocarpic acid by Structure V.

The object of this research was the synthesis of compounds of Structures III and V. This has been accomplished and the products have been shown to be identical with reduced chaulmoogric and hydnocarpic acids. This demonstrates conclusively the cyclopentene structure of these natural acids as pointed out by Power[3] and Shriner and Adams.[2] It shows also that the views of Schmidt[5] are incorrect.

The synthesis of dihydrochaulmoogric acid was completed through the following series of reactions: (a) cyclopentylmagnesium bromide VI and methyl λ-aldehydo-dodecanoate[6] VII were condensed to give methyl μ-cyclopentyl-μ-hydroxy-tridecanoate VIII; (b) the hydroxy ester was converted into the corresponding bromide, methyl μ-cyclopentyl-μ-bromo-tridecanoate IX, with phosphorus tribromide; (c) the bromo compound yielded the unsaturated acid, μ-cyclopentyl-λ-tridecanoic acid, X, with alcoholic potassium hydroxide; (d) the unsaturated acid was reduced by means of hydrogen and platinum-oxide platinum black to μ-cyclopentyl-tridecanoic acid III (dihydrochaulmoogric acid).



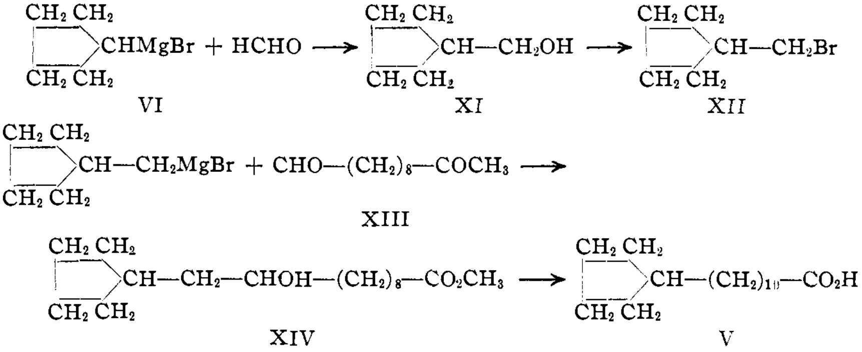
The identity of this product with that of reduced chaulmoogric acid was shown by similar melting point, a mixed melting point which gave no depression, and finally the melting points and mixed melting points of the corresponding amides.

[4] Dean and Wrenshall, *U. S. Pub. Health Bull.*, **141**, 25 (1924).

[5] Fritz Schmidt, Doctor's *Dissertation*, Hessischen-Ludwigs Universität, Giessen, 1923.

[6] Noller with Adams, This Journal, **48**, 1074 (1926).

The dihydrohydnocarpic acid was produced by an analogous series of reactions. (a) Cyclopentylmagnesium bromide VI was treated with formaldehyde, thus yielding cyclopentyl carbinol XI which was then converted to the corresponding bromide, cyclopentyl-methyl bromide XII. (b) Cyclopentyl-methylmagnesium bromide and methyl θ-aldehydo nonanoate XIII[6] yielded methyl-κ-cyclopentyl-ι-hydroxy-undecanoate XIV. (c) This hydroxy ester was converted to the corresponding saturated acid by a series of reactions similar to that used in synthesizing dihydrochaulmoogric acid, forming in succession, methyl κ-cyclopentyl-ι-bromo-undecanoate, the corresponding olefinic acid (probably a mixture), and finally κ-cyclopentyl-undecanoic acid V (dihydrohydnocarpic acid).



This product was proved to be identical with reduced hydnocarpic acid by melting point, mixed melting point and conversion into the same amide.

For the preparation of the hydroxy esters one molecular equivalent of Grignard reagent was added to a dry ether solution of the aldehyde ester. Upon decomposition in the usual way a good yield of crude reaction product was obtained. By distillation in a vacuum the yield of pure hydroxy ester in the reaction using cyclopentyl-methylmagnesium bromide[7] and methyl θ-aldehydo-nonanoate was only 7 to 10% and using cyclopentylmagnesium bromide and methyl λ-aldehydo-dodecanoate still less (about 5%); in fact by the procedure mentioned pure hydroxy ester in the latter case could not be obtained by fractionation. These yields are much lower than those observed in an analogous reaction previously described[6] where n-butylmagnesium bromide and methyl η-aldehydo-octanoate were employed. The results with the more complex Grignard reagents showed in each instance a large, low-boiling fraction and a non-volatile residue which did not appear with butylmagnesium bromide. A study of the low-boiling fraction from the reaction product of cyclopentylmagnesium bromide and methyl λ-aldehydo-dodecanoate was made. It solidified and after puri-

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[7] Other hydroxy esters to be reported later have been prepared from simple aliphatic bromides and aldehyde esters with yields higher than 35%.

fication proved to be methyl μ-hydroxy-tridecanoate XV formed merely by reduction of the aldehyde ester.

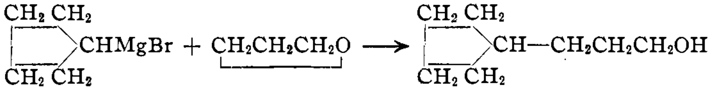
$$\underset{\text{XV}}{HOCH_2\text{-}(CH_2)_{11}\text{-}CO_2CH_3} \quad \underset{\text{XVI}}{CH_3O_2C\text{-}(CH_2)_{11}\text{-}CHOH\text{-}CHOH\text{-}(CH_2)_{11}\text{-}CO_2CH_3}$$

The non-volatile residue in the distillation did not solidify and could not be distilled without decomposition even under very low pressures. However, it could be completely saponified by alkali and as a consequence it can be concluded that none of the ester group in the original aldehyde ester had reacted with the Grignard reagent.

A procedure was found, however, by which a larger yield of pure condensation product could be obtained from the original reaction mixture. Instead of removing the ether and fractionally distilling the reaction product, the ether solution was cooled and two successive fractions of solid material were obtained. The first that separated was rather waxy in appearance and was probably impure reduction product of the aldehyde ester XV. The second solid fraction was more readily purified and proved to be an ester, which upon analysis and saponification gave constants which agreed with the pinacol XVI corresponding to the original aldehyde ester used. It seems probable that a large proportion of the non-volatile fraction when direct distillation was carried out consisted of this material or a decomposition product of it. The filtrate obtained from the two solid fractions just described was heated until the ether was removed. An oil remained which distilled under diminished pressure without decomposition and from which pure condensation product was obtained. It may be stated that from a consideration of recent work on the reaction products of aldehydes and Grignard reagents,[8] reduction products of the character found might have been anticipated when cyclopentylmagnesium bromide and cyclopentyl-methylmagnesium bromide were used. No attempt was made to isolate pure products from the high and low fractions of the other condensation reaction but it is probable that by-products similar to those just described would be found.

No difficulty was encountered in converting the hydroxy esters to the bromo esters, then to the olefinic acids and finally to the saturated acids.

In the early work in this investigation an attempt was made to prepare γ-cyclopentyl-propanol XVII by the condensation of cyclopentylmagnesium bromide and trimethylene oxide. This proved to be successful, but the low yields led to the synthesis of the compounds desired by the methods described above.



XVII

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[8] Hess and Rheinboldt, *Ber.*, **54**, 2043 (1921). Hess, *Ann.*, **437**, 256 (1924). Meisenheimer, *Ann.*, **442**, 180 (1925). Rheinboldt, *J. prakt. Chem.*, **109**, 175 (1925). Marshall, *J. Chem. Soc.*, **105**, 527 (1914); **107**, 509 (1915); **127**, 2184 (1925).

Homologous acids of dihydrochaulmoogric and dihydrohydnocarpic acids are now being prepared by the methods used in this investigation and by other procedures commonly employed for building up molecules of this sort.

Experimental Part

Cyclopentanone.—Cyclopentanone was purified by being distilled twice over calcium oxide. In this way a product was obtained which boiled at 129° (corr.) and remained colorless on standing for long periods of time; n_D^{20}, 1.4370; d_4^{20}, 0.9502.

Cyclopentanol.[9]—A solution of 42 g. (0.5 mole) of cyclopentanone in 150 cc. of methyl alcohol was reduced with hydrogen in the presence of 1 g. of platinum-oxide platinum black catalyst[10] at 2 to 3 atmospheres. The calculated amount of hydrogen was absorbed after 9 to 12 hours. After the catalyst had been filtered off, the methyl alcohol was distilled through a long fractionating column and the residue fractionated. From 40 to 41 g. of product was obtained, boiling at 139–141° (93–95%). On redistillation it boiled at 139° (corr.); n_D^{20}, 1.4530; d_4^{20}, 0.9488.

It was noticeable that platinum oxide made from platinum salt that was not spectroscopically pure was more effective as a catalyst than that made from absolutely pure salt. When the platinum black was reworked too many times it also yielded an inactive catalyst.

Cyclopentyl Bromide.—In a 1-liter 3-neck flask fitted with a separatory funnel, mechanical stirrer, thermometer and calcium chloride tube was placed 172 g. (2 moles) of cyclopentanol. After this had been cooled in an ice-salt bath to 0°, 192 g. of redistilled phosphorus tribromide was added during stirring so that the temperature of the liquid did not rise above 0°. The addition of phosphorus tribromide required about an hour, after which the stirring was continued for two hours and the temperature was allowed to rise to about 20°. After the mixture had stood overnight at room temperature, water was added and the mixture steam distilled. The lower layer was separated, washed with 10% sodium carbonate solution, dried over calcium chloride and fractionated. From 232 to 250 g. of product boiling over 3° (78–84%) was obtained. On redistillation the product boiled at 135–136° (corr.); n_D^{20}, 1.4882; d_4^{20}, 1.3900.

The use of hydrobromic acid to prepare cyclopentyl bromide[11] led to the formation of considerable quantities of cyclopentene and consequent reduction of yield.

Cyclopentyl Carbinol, XI.—Previous investigators[12] have prepared cyclopentyl carbinol by the action of trioxymethylene on cyclopentylmagnesium bromide but this method gave at best yields of 15–20%. The good yields of alcohols reported by Wood and Scarf[13] using gaseous

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[9] Ref. 11 a. Godchot and Taboury, *Compt. rend.*, **152**, 881 (1911); **153**, 1010 (1911). Vavon, *ibid.*, **155**, 287 (1912); *Ann. chim.*, [9] **1**, 186 (1914). Auwers, *Ann.*, **415**, 143 (1918).

[10] Adams and Shriner, THIS JOURNAL, **45**, 2171 (1923). For further references where platinum-oxide platinum black has been used, see Tuley with Adams, *ibid.*, **47**, 3061 (1925).

[11] (a) Wislicenus and Hentschel, *Ann.*, **275**, 322 (1893). (b) Denjanow and Luschnikow, *J. Russ. phys.-chem. Ges.*, **35**, 26 (1903). (c) Borsche and Lange, *Ber.*, **40**, 2221 (1907).

[12] (a) Zelinsky, *Ber.*, **41**, 2629 (1908). (b) Nametkin, *J. Russ. phys.-chem. Ges.*, **43**, 1611 (1911). (c) Nametkin and Morosowa, *ibid.*, **47**, 1607 (1915).

[13] Wood and Scarf, *J. Soc. Chem. Ind.*, **42**, 13T (1923).

formaldehyde led to a procedure similar to theirs for the preparation of cyclopentyl carbinol.

A solution of cyclopentylmagnesium bromide was prepared in a 3-necked flask fitted with stirrer and condenser, from 149 g. (1 mole) of cyclopentyl bromide and 24 g. of magnesium in 450 cc. of absolute ether. Paraformaldehyde was dried for two days in a vacuum desiccator over phosphorus pentoxide and 45 g. of the dried product placed in a 500cc. round-bottom flask from which a wide tube led into the 3-necked flask and dipped beneath the surface of the ether solution. When the paraformaldehyde was heated in an oil-bath to 160–190° depolymerization took place and the steady stream of formaldehyde was passed into the ether solution during stirring until practically all of the paraformaldehyde had been depolymerized. The reaction mixture was then refluxed for one-half hour and allowed to stand overnight. The ether was distilled until the volume was reduced about one-half, the residue decomposed with 500 g. of cracked ice, the magnesium hydroxide dissolved by the addition of hydrochloric acid and the mixture steam distilled. The alcohol layer was separated, the aqueous layer extracted with ether and the combined upper layers were washed with 10% sodium hydroxide solution and with water, and dried over potassium carbonate. Fractional distillation gave 62–64 g. (62–64%) of cyclopentyl carbinol boiling at 160–165°. Heating on the steam cone with a small amount of calcium oxide and redistillation gave a product boiling at 162–162.5° (corr.); n^{20}_{D}, 1.4579; d^{20}_{4}, 0.9313.

When too much ether was distilled, a violent reaction took place which could not be controlled. Likewise, it was necessary to add the ice as rapidly as possible to keep the decomposition from becoming too vigorous.

Cyclopentyl-methyl Bromide, XII.—Preparation of this compound from cyclopentyl carbinol by the use of hydrobromic acid has been shown to give mixtures of cyclopentyl-methyl bromide and cyclohexyl bromide.[12c] Since heat in the presence of hydrobromic acid apparently causes the rearrangement, phosphorus tribromide was used in the preparation of cyclopentyl-methyl bromide.

To 50 g. (0.5 mole) of cyclopentyl carbinol placed in a 3-necked flask and cooled to —15° was added through a separatory funnel during stirring, 50 g. of redistilled phosphorus tribromide at such a rate that the temperature did not rise above —5°. After all was added, the mixture was stirred for two hours at 0° and three hours at 25°. The crude reaction mixture was extracted with petroleum ether (40–50°) in which the phosphorous esters were insoluble, twice with 50cc. portions and thrice with 25cc. portions. The combined petroleum ether extractions were washed thoroughly with water, dil. sodium hydroxide solution and water again, and dried over anhydrous magnesium sulfate. After the petroleum ether had been distilled the product was fractionated under diminished pressure, giving 40 g. of product boiling at 56–57° (17 mm.). A small amount of alcohol was still present in this material but it gave satisfactory results in forming the Grignard reagent.

Trimethylene Oxide, $\underline{CH_2CH_2CH_2O}$.—The trimethylene oxide was prepared according to the method of Derick and Bissell[14] with the difference that stirring was used during the reaction and purification of the crude distillate accomplished merely by drying over potassium carbonate and fractionating. In this way yields of 32–33% of product boiling at 45–50° were obtained. Drying over fused potassium hydroxide and redistillation gave a product boiling at 45.8–46.4° (corr.).

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[14] Derick and Bissell, THIS JOURNAL, **38**, 2478 (1916).

γ-Cyclopentyl-propanol, XVII.—To a solution of cyclopentylmagnesium bromide prepared from 74.5 g. (0.5 mole) of cylcopentyl bromide and 12 g. of magnesium in 250 cc. of ether, was slowly added 29 g. of trimethylene oxide. The mixture was then refluxed for four hours, 150 cc. of dry benzene added and the ether distilled until the temperature of the vapors reached 70°. The residue was refluxed for three hours, during which time the whole mass became pasty. It was then decomposed with 200 g. of cracked ice and 100 g. of ammonium chloride to dissolve the magnesium hydroxide. This mixture was steam distilled, the alcohol separated, and after combining with the ether extract of the aqueous layer, dried over potassium carbonate and fractionated. After three fractional distillations, two distinct fractions were obtained: (1) about 7 g., b. p. 152–157°; (2) about 6 g., b. p. 202–208°. The low-boiling fraction was not investigated. The high-boiling fraction was warmed on the steam-bath with calcium oxide to remove a trace of halogen, and distilled under diminished pressure. About 3 g. of product boiling at 85–86° (6 mm.) (corr.) was obtained; n_D^{20}, 1.4590; d_4^{20}, 0.9137.

Anal. Subs., 0.1679: CO_2, 0.4588; H_2O, 0.1899. Calcd. for $C_8H_{16}O$: C, 74.94; H, 12.57. Found: C, 74.53; H, 12.57.

PHENYLURETHAN.—Upon treatment with phenylisocyanate, the compound gave a phenylurethan which after crystallization from dil. methyl alcohol and then from petroleum ether (40–50°) melted at 55–55.4° (corr.).

Anal. Subs., 0.3512: 18.0 cc. of N (16.2°, 740 mm.). Calcd. for $C_{15}H_{21}O_2N$: N, 5.66. Found: 5.79.

Condensation of Cyclopentylmagnesium Bromide and Cyclopentylmethylmagnesium Bromide with Aldehyde Esters.—The general procedure for the condensations was that described in a previous paper[6] with butylmagnesium bromide.

Methyl μ-Cyclopentyl-μ-hydroxy-tridecanoate, VIII. *Distillation Procedure.*—By careful fractionation of the product from 37.3 g. of cyclopentyl bromide and 60.5 g. of methyl λ-aldehydo-dodecanoate,[6] only 4.5 g. (5.8%) yield of a product boiling at 190–195° (3 mm.) could be obtained. This was shown to be the impure hydroxy ester desired. The low-boiling fraction, amounting to 13 g. and boiling from 160° to 185° (3 mm.), solidified on cooling. It proved to be methyl μ-hydroxy-tridecanoate XV. A small high-boiling fraction of about 2 g. was obtained and a large residue amounting to 18 g. which could not be distilled at all. This residue could be completely saponified by alcoholic sodium hydroxide but no pure acid was obtained from it.

Fractionation Procedure.—A procedure involving crystallization made it possible to obtain pure methyl μ-cyclopentyl-μ-hydroxy-tridecanoate. The dried ether solution of the condensation product obtained from 76.5 g. of methyl λ-aldehydo-dodecanoate was evaporated to a volume of 100 cc. and cooled in an ice-salt bath. A slimy precipitate formed which was filtered off with suction. Cooling of the filtrate gave another crop which was less slimy but still waxy in appearance. The two crops weighed about 30 g. By repeating the cooling and filtering process twice, two more crops of crystals were obtained, this time white and dry and melting, respectively, at 40–41° and 48–52°. Evaporation of a portion of the ether from the last filtrate, and cooling, gave only a slight precipitate. When this was filtered off and the remainder of the ether allowed to evaporate by standing in the air a solid separated which after being washed twice with cold ether melted at 56–69°. Washing of the fractions, m. p. 40–44 and 48–52°, with cold ether raised the melting points to 50–52° and 57–60°. The three fractions amounted to 15 g. The filtrate from the product melting at 56–59° on evaporation of the ether gave 16 g. of an oily residue. This whole process was then repeated on the first waxy portion of 30 g. which gave 11 g. of waxy product, 4 g. more of product corresponding to the second fraction and 12 g. more of oily residue.

The combined oily residues amounting to 28 g. were then fractionally distilled under diminished pressure. After three fractionations there was obtained 8.2 g. boiling at 205–210 (4 mm.). This solidified at room temperature and on recrystallization from petroleum ether (40–50°) melted at 29–29.5° (corr.).

Anal. Subs., 0.1427: CO_2, 0.3834; H, 0.1492. Calcd. for $C_{19}H_{36}O_3$: C, 73.01; H, 11.62. Found: C, 73.27; H, 11.62.

μ-Cyclopentyl-μ-hydroxy-tridecanoic Acid.—By the action of alcoholic potassium hydroxide on the ester, the acid was obtained melting, after purification from acetone, at 70.5–71° (corr.).

Anal. Subs., 0.1670, 0.4761: CO_2, 0.4449; H_2O, 0.1724; 17.2 cc. of 0.0930 *N* KOH. Calcd. for $C_{18}H_{34}O_3$: C, 72.41; H, 11.50; neut. equiv., 298.2. Found: C,7 2.65; H, 11.47; neut. equiv., 297.7.

Methyl μ-Hydroxy-tridecanoate, XV.—A careful study was made of the low-boiling fraction obtained by the distillation procedure of the condensation product of cyclopentylmagnesium bromide and the methyl aldehydo-dodecanoate. It solidified at room temperature and after several crystallizations from petroleum ether (40–50°) a product was obtained which melted at 38–40° (corr.) and which proved from analyses, by saponification and by a condensation with phenylisocyanate to be methyl μ-hydroxy-tridecanoate.

Anal. Subs., 0.1666: CO_2, 0.4177; H_2O, 0.1730. Calcd. for $C_{14}H_{28}O_3$: C, 68.79; H, 11.51. Found: C, 68.38; H, 11.54.

PHENYLURETHAN DERIVATIVE.—This ester gave on treatment with phenylisocyanate in petroleum ether a phenylurethan which after crystallization from methyl alcohol melted at 73.5–74° (corr.).

Anal. Subs., 0.3708: 14.2 cc. of N (29°, 743 mm.). Calcd. for $C_{21}H_{33}O_4N$: N, 3.85. Found: 4.06.

μ-Hydroxy-tridecanoic Acid.—Saponification of the ester with alcoholic sodium hydroxide gave an acid which after crystallization from dil. alcohol (1:3) melted at 77-77.5° (corr.).

Anal. Subs., 0.1702, 0.4084: CO_2, 0.4247; H_2O, 0.1724; 19.17 cc. of 0.0930 *N* KOH. Calcd. for $C_{13}H_{26}O_3$: C, 67.83; H, 11.30; neut. equiv., 230.2. Found: C, 68.05; H, 11.22; neut. equiv., 229.7.

Pinacol of Methyl λ-Aldehydo-dodecanoate, XVI.—The second fraction amounting to 10–15 g. obtained in the fractional crystallization procedure for preparing methyl μ-cyclopentyl-μ-hydroxy-tridecanoate was recrystallized from ethyl ether until the melting point remained constant at 58–59.5° (corr.).

Anal. Subs., 0.1705, 0.5120: CO_2, 0.4326; H_2O, 0.1709; 18.97 cc. of 0.1117 *N* alc. NaOH. Calcd. for $C_{28}H_{54}O_6$: C, 69.08; H, 11.18; sap. equiv., 243.2. Found: C, 69.20; H, 11.14; sap. equiv., 241.6.

On saponification an acid was obtained which was very difficult to crystallize. When it was dissolved in dil. potassium hydroxide solution and cooled, a precipitate formed which was filtered off. When this was decomposed with dil. hydrochloric acid, filtered off and washed thoroughly, an acid was obtained which melted at 59–65°.

Neut. equiv. Subs., 0.2554: 11.8 cc. of 0.0930 *N* KOH. Calcd. for $C_{26}H_{50}O_6$: neut. equiv., 229.2. Found: 232.7.

Methyl κ-Cyclopentyl-ι-hydroxy-undecanoate, XIV.—By the general procedure using the Grignard reagent from 32.5 g. of cyclopentyl-methyl bromide and 40 g. of methyl θ-aldehydo-nonanoate there was obtained by fractional distillation 4.5 g. of methyl κ-cyclopentyl-ι-hydroxy-undecanoate; b. p., 175–180° (3 mm.). The low and high-boiling fractions were not investigated.

κ-Cyclopentyl-ι-hydroxy-undecanoic Acid.—By saponification of the ester with alcoholic potassium hydroxide and crystallization from acetone, the product formed white crystals melting at 60–60.5° (corr.).

Anal. Subs., 0.1443, 0.3817: CO_2, 0.3777; H_2O, 0.1458; 15.17 cc. of 0.0930 *N* KOH. Calcd. for $C_{16}H_{30}O_3$: C, 71.06; H, 11.18; neut. equiv., 270.2. Found: C, 71.38; H, 11.23; neut. equiv., 270.6.

μ-Cyclopentyl-tridecanoic Acid and κ-Cyclopentyl-undecanoic Acid.—These acids were prepared from the corresponding hydroxy esters by the procedure described in a previous paper[6] for converting methyl θ-hydroxy-tridecanoate into tridecanoic acid.

The μ-cyclopentyl-tridecanoic acid formed white crystals after crystallization from 70% alcohol and finally from petroleum ether, (b. p., 40–50°); m. p., 70–71° (corr.).

Anal. Subs., 0.1828: CO_2, 0.5141; H_2O, 0.2002. Calcd. for $C_{18}H_{34}O_2$: C, 76.51; H, 12.15. Found: C, 76.70; H, 12.17.

The κ-cyclopentyl-undecanoic acid formed white crystals after crystallization from 70% alcohol and finally from petroleum ether, (b. p., 40–50°); m. p., 63–63.5° (corr.).

Anal. Subs., 0.1559: CO_2, 0.4333; H_2O, 0.1674. Calcd. for $C_{16}H_{30}O_2$: C, 75.53; H, 11.88. Found: C, 75.80; H, 11.93.

Mixed melting points taken on mixtures of μ-cyclopentyl-tridecanoic acid with dihydrochaulmoogric acid, m. p. 70–71° (corr.), prepared by the catalytic reduction of chaulmoogric acid, and of κ-cyclopentyl-undecanoic acid with dihydrohydnocarpic acid, m. p. 63–63.5° (corr.), prepared by the catalytic reduction of hydnocarpic acid showed no depression of the melting points.

Dihydrochaulmoogramide, μ-Cyclopentyl-tridecano-amide, Dihydrohydnocarpamide and κ-Cyclopentyl-undecano-amide.—To 1 g. of acid was added 10 cc. of ligroin (60–70°) and then 0.5 g. of phosphorus trichloride. The mixture was heated to boiling for ten minutes, cooled and poured into 50 cc. of concd. ammonium hydroxide cooled in an ice-salt bath. The resulting solid was filtered, washed and crystallized from 95% alcohol to a constant melting point.

Dihydrochaulmoogramide; m. p., 105–106° (corr.).

Anal. Subs., 0.3408: 15.7 cc. of N (28°, 747.6 mm.). Calcd. for $C_{18}H_{35}ON$: N_2, 4.98. Found: 4.95.

μ-Cyclopentyl-tridecano-amide; m. p., 105–106° (corr.). A mixed melting point with dihydrochaulmoogramide showed no depression.

Dihydrohydnocarpamide; m. p., 114.5–115.5° (corr.).

Anal. Subs., 0.0845: 4.5 cc. of N (26°, 742.6 mm.). Calcd. for $C_{16}H_{31}ON$: N, 5.53. Found: 5.74.

κ-Cyclopentyl-undecano-amide; m. p., 114–115° (corr.). A mixed melting point with dihydrohydnocarpamide showed no depression.

Summary

1. μ-Cyclopentyl-tridecanoic acid and κ-cyclopentyl-undecanoic acid have been synthesized and shown to be identical with dihydrochaulmoogric and dihydrohydnocarpic acids, respectively.

2. The amides of these synthesized acids were prepared and shown to be identical with the amides of dihydrochaulmoogric and dihydrohydnocarpic acids.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE SYNTHESIS OF HOMOLOGS OF DIHYDROCHAULMOOGRIC AND DIHYDROHYDNOCARPIC ACIDS CONTAINING A CYCLOHEXYL IN PLACE OF A CYCLOPENTYL GROUP. III

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The investigations of Dean and Wrenshall[2] have shown that ethyl dihydrochaulmoograte can be effectively used in the treatment of leprosy. Although the number of clinical cases tested was small, the results indicated that ethyl dihydrochaulmoograte was not far behind the ethyl esters of the mixed acids of chaulmoogra oil in effectiveness. Moreover, the former has the distinct advantage of not causing local irritation upon injection. It has been shown[3] that sodium dihydrochaulmoograte and sodium dihydrohydnocarpate are bactericidal toward *lepra* bacillus when tested *in vitro*, though relatively much less effective than the corresponding unsaturated compounds.

Since the straight-chained saturated and unsaturated aliphatic acids are not effective toward *lepra* bacillus but the dihydrochaulmoogric and dihydrohydnocarpic acids are effective, it may be concluded that the ring structure is at least one of the important groupings in the molecule and that the double bond which appears in chaulmoogric and hydnocarpic acids is not absolutely necessary, but merely enhances the effectiveness.[2b] The object of this research was to build up acids homologous to dihydrochaulmoogric and dihydrohydnocarpic acids containing a cyclohexyl ring in place of the cyclopentyl ring and to determine their effectiveness toward *lepra* bacillus.

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[1] This communication is an abstract of a portion of a thesis submitted by G. S. Hiers in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] (a) Dean and Wrenshall, *U. S. Pub. Health Bull.*, **141**, 7 (1924). (b) See also Schöbl, *Philippine J. Sci.*, **25**, 123, 135 (1924).

[3] Unpublished results from this Laboratory.