of white crystals, m. p. 86–87°. This material was identical with a sample prepared from the nitrile by the method of Schlenk and Bergmann.[6]

1-Phenyl-1-(2-biphenylyl)-ethylene (I) was prepared as described by Bergmann and Bondi[7] with the exception that the product of the reaction between methylmagnesium iodide and *o*-phenylbenzophenone was heated with potassium bisulfate for a half-hour before vacuum distillation. The fraction boiling at 201–202.5° (12 mm.) solidified to a white solid, m. p. 59–61°. The yields were 56–73%. A single attempt was made to prepare the olefin from the product of the reaction of acetophenone with 2-biphenylylmagnesium iodide. Upon distillation, a large fore-run of biphenyl and acetophenone was obtained, followed by a small amount (17.5%) of the desired olefin.

Oxidation of 1-Phenyl-1-(2-biphenylyl)-ethylene.—A solution of 27.9 g. of the olefin (I) was treated with an ethereal solution containing 20 g. of perbenzoic acid. After the solution had stood for three days, it gave a negative test for excess oxidant. The solution was washed free of acid with sodium bicarbonate solution and dried over sodium sulfate. Upon concentration of the solution and addition of petroleum ether, 14 g. (46%) of nearly colorless crystals was obtained, m. p. 107–109°. An analytical sample was prepared by repeated recrystallization, m. p. 111–112°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.32; H, 5.60. Found: C, 83.37; H, 5.68.

Dehydration of the "Dioxide" (III).—(a) By hydrobromic and acetic acids: one-half gram of the "dioxide" (III) was suspended in a boiling mixture containing 5 cc. of acetic and 5 cc. of 34% hydrobromic acids and the mixture refluxed for twenty-four hours. The product, once recrystallized from alcohol, was nearly white and melted at 139–141°; yield 0.33 g. (35%). In one case in which the "dioxide" had been heated previously for a few minutes at its boiling point (22 mm.) the yield was 56%.

(b) By the action of potassium bisulfate: one gram of the "dioxide" was heated at 170–180° for ten minutes with 2 g. of potassium bisulfate. The product was extracted with ether and recrystallized as above; yield 0.33 g. (35%).

(c) By the action of concentrated sulfuric acid: one-half gram of the "dioxide" was heated on the steam-bath for two minutes with 3 cc. of concentrated sulfuric acid. Poured into water and once recrystallized, it gave 0.30 g. (64%) of white needles, m. p. 141–143°.

The products obtained by all of these methods were shown to be identical by mixed melting point determinations.

Anal. Calcd. for $C_{20}H_{14}O$: C, 88.86; H, 5.22. Found: C, 88.94, 88.73; H, 5.30, 5.23.

The products were shown to be identical with a sample of 9-phenylphenanthrol-10 (V) prepared from (2-biphenylyl)-phenylacetic acid (VI) by the method of Koelsch.[6]

A crystalline derivative (m. p. 158–159.5°) was obtained by refluxing the cyclization product overnight with acetyl chloride.[10]

Summary

It has been demonstrated, in one case at least, that perbenzoic acid may bring about the addition of two atoms of oxygen to one mole of an olefin.

DURHAM, N. C. RECEIVED OCTOBER 4, 1943

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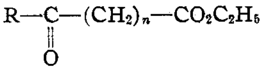
(10) This product is probably the acetate (m. p. 153–155°) prepared previously by Koelsch[6] by the action of acetic anhydride and sulfuric acid on 9-phenylphenanthrol-10.

[CONTRIBUTION FROM THE FURMAN CHEMICAL LABORATORY, VANDERBILT UNIVERSITY]

Branched-Chain Fatty Acids. II. Syntheses in the C_{19} and C_{25} Series. Preparation of Keto Esters

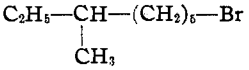
BY JAMES CASON AND FRANKLIN S. PROUT[1]

In continuation of the program of synthesizing methyloctadecanoic acids,[2] the 16-methyl isomer has been prepared by the general method used for synthesis of 17-methyloctadecanoic acid.[2] This procedure involves preparation of a keto ester (I) by reaction between a dialkylcadmium compound and an ω-carbethoxyalkoyl chloride, reduction of the keto ester by the Clemmensen method and hydrolysis of the reduced ester. For synthesis of 16-methyloctadecanoic acid the required alkyl halide is 1-bromo-6-methyloctane (II). This bromide has been prepared by Levene and Marker[3] from the corresponding alcohol which was obtained by reduction of ethyl 6-methyloctoate (IV). These workers prepared 6-methyloctoic acid[4] by extending the chain of 1-bromo-4-methylhexane by use of the malonic ester synthesis.



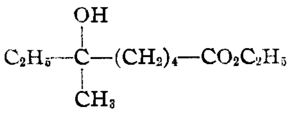
$$R{-}\underset{\underset{O}{\|}}{C}{-}(CH_2)_n{-}CO_2C_2H_5$$

I



$$C_2H_5{-}\underset{\underset{CH_3}{|}}{CH}{-}(CH_2)_5{-}Br$$

II



$$C_2H_5{-}\overset{\overset{OH}{|}}{\underset{\underset{CH_3}{|}}{C}}{-}(CH_2)_4{-}CO_2C_2H_5$$

V

Our preparation of 1-bromo-6-methyloctane also utilizes ethyl 6-methyloctoate, which was first prepared by us as in the scheme shown. It was hoped that the small amount of isoamyl alcohol present in the *s*-butylcarbinol[5] used as starting material would not interfere with obtaining a pure product in the final stages of the synthesis; however, such was not the case. Reduction of the keto ester, III, by the Clemmensen method proved more difficult than reduction of the 7-methyl isomer[2]; therefore, the concentration of the undesired 7-methyl isomer, arising from isoamyl bromide, was considerably increased at this step. 16-Methyloctadecanoic

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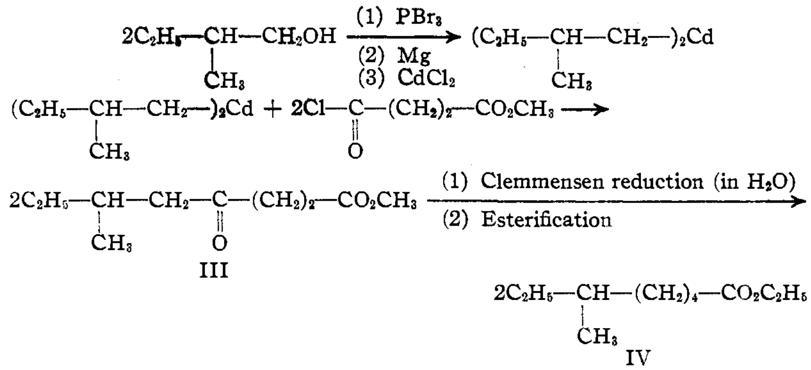
(1) Taken in part from the M.S. thesis of Franklin S. Prout.

(2) Cason, THIS JOURNAL, **64**, 1106 (1942).

(3) Levene and Marker, *J. Biol. Chem.*, **103**, 299 (1933).

(4) Levene and Marker, *ibid.*, **95**, 153 (1932).

(5) Fractionated through a 3-foot packed column, b. p. 127.5 128.5°.



$$2C_2H_5-\underset{CH_3}{\underset{|}{CH}}-CH_2OH \xrightarrow[(2)\ Mg\quad (3)\ CdCl_2]{(1)\ PBr_3} (C_2H_5-\underset{CH_3}{\underset{|}{CH}}-CH_2-)_2Cd$$

$$(C_2H_5-\underset{CH_3}{\underset{|}{CH}}-CH_2-)_2Cd + 2Cl-\underset{O}{\underset{\|}{C}}-(CH_2)_2-CO_2CH_3 \longrightarrow$$

$$2C_2H_5-\underset{CH_3}{\underset{|}{CH}}-CH_2-\underset{O}{\underset{\|}{C}}-(CH_2)_2-CO_2CH_3 \xrightarrow[(2)\ \text{Esterification}]{(1)\ \text{Clemmensen reduction (in } H_2O)}$$

III

$$2C_2H_5-\underset{CH_3}{\underset{|}{CH}}-(CH_2)_4-CO_2C_2H_5$$

IV

acid obtained from 1-bromo-6-methyloctane prepared by this route was contaminated with the less soluble 17-methyloctadecanoic acid and could not be isolated in a pure state.

Ethyl 6-methyloctoate was next synthesized by a method involving no branched-chain starting materials. The procedure used, which has been employed by Schneider and Spielman[6] for synthesis of several 10-methyl acids, depends on the reaction of a Grignard reagent with a keto ester to give a hydroxy ester. By use of ethylmagnesium iodide and ethyl 6-ketoheptoate in this reaction, there was obtained ethyl 6-hydroxy-6-methyloctoate (V). The crude hydroxy ester was dehydrated by heating with iodine and the unsaturated ester was hydrogenated to the desired ethyl 6-methyloctoate. The over-all yield from ethyl 6-ketoheptoate was 19–30%. When 1-bromo-6-methyloctane prepared from this ester was used in the synthesis of 16-methyloctadecanoic acid a readily purified product was obtained. 16-Methyloctadecanoic acid melts at 49.9–50.6°, about seventeen degrees below the 17-methyl isomer.

Since 6-methyl- and 10-methyltetracosanoic acids were desired for biological testing,[7] they have been prepared by the general method of Schneider and Spielman,[6] as described above for preparation of ethyl 6-methyloctoate. The reaction between myristylmagnesium bromide and ethyl 10-ketohendecanoate was carried out essentially as described by Schneider and Spielman; however, the resulting hydroxy ester was used for dehydration, rather than the acid, as used by the above authors. The unsaturated ester was hydrogenated over platinum and, in order to insure as pure a product as possible, the saturated C_{25} ester was distilled through an 18-inch Vigreux type column. The over-all yield of recrystallized 10-methyltetracosanoic acid, obtained after saponification of the ester, was 39%. Schneider and Spielman obtained this acid in 34% yield. 6-Methyltetracosanoic acid was obtained by a similar procedure, starting with octadecyl bromide and ethyl 6-ketoheptoate, in an over-all yield of 26%.

The keto esters prepared in the course of the syntheses described above were obtained by the reaction between a dialkylcadmium compound and an ω-carbethoxyalkoyl chloride. The method of Cason[2] has been improved so that yields of 75–85% were obtained, and this procedure now appears to be the most efficient yet devised for synthesis of aliphatic keto esters. The improvement was effected by removing as much ether as possible from the reaction mixture after preparation of the dialkylcadmium compound from the corresponding Grignard reagent. This process greatly reduces the yield of di-ester, arising from reaction of the ester acid chloride with ether, and the yield of keto ester is nearly doubled. If a dialkylcadmium derivative other than dimethylcadmium is used, the small amount of di-ester may be removed by fractional distillation; however, when dimethylcadmium is used the di-ester and keto ester have nearly identical boiling points. In this case, a pure product may be obtained by distillation of the keto acid.

When the above-described method of running the cadmium reaction was applied to a secondary bromide, 2-bromopentane, the reaction failed completely. However, when the cadmium derivative of 2-bromopentane was prepared in ether at −5 to −7° and allowed to react with β-carbomethoxypropionyl chloride at this temperature a 21.5% yield of methyl 4-keto-5-methyloctoate was obtained.

It has been previously reported[2] that when diisoamylcadmium is allowed to react with succinic anhydride in ether the yield of 4-keto-7-methyloctoic acid is only 5–10%. In a trial run, this reaction was carried out in boiling benzene solution, and a yield of 31% was obtained.

Experimental[8]

Keto Esters and Acids

Methyl 4-Keto-7-methyloctoate.[2]—The Grignard solution prepared in an atmosphere of nitrogen from 7.3 g. of magnesium and 45.3 g. of isoamyl bromide (b. p. 120.0–120.2°) in 150 cc. of ether was cooled in an ice-bath and 29.3 g. of dried C. P. cadmium chloride was added in one portion. After removal of the ice-bath the mixture was stirred for five minutes, then ether was distilled rapidly from the solution by heating on a steam-bath, while stirring was continued. Distillation was continued until a dark semi-solid residue remained, then 100 cc. of dry thiophene-free benzene was added and distillation resumed until benzene had practically ceased to distil. After 100 cc. of benzene had been added to the residue the mixture was stirred and refluxed until the cake had been broken up and dispersed through the mixture. There was then added during ten minutes a solution of 36.1 g. of β-carbomethoxypropionyl chloride[9] in 50 cc. of benzene. After the exo-

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[6] Schneider and Spielman, *J. Biol. Chem.*, **142**, 345 (1942).

[7] These acids were prepared at the request of Dr. Bruno Gerstl of the Yale University Medical School and are being tested by him for biological activity.

[8] All melting points corrected.

[9] Ruggli and Maeder, *Helv. Chim. Acta*, **25**, 943 (1943).

thermic reaction had subsided the mixture was refluxed with stirring for one hour.

The organometallic complex was decomposed with ice and sulfuric acid, and the water was separated and extracted twice with benzene. The benzene extracts were washed with water, 5% sodium carbonate solution, water and saturated sodium chloride solution, then filtered through a layer of anhydrous sodium sulfate. After the solvent had been flashed off, the residue was distilled through an 18-inch Podbielniak type column, and the following fractions were obtained

Fraction	B. p. (8 mm.), °C.	Weight, g.
Methyl ethyl succinate[2]	82–89	1.44
Intermediate fraction	89–116.5	0.98
Methyl 4-keto-7-methyloctoate	116.5–117	32.74

The yield of keto ester is 73.5% of theory based on ester acid chloride or 58.8% based on isoamyl bromide.

When this reaction was run as above except that only 29.3 g. of β-carbomethoxypropionyl chloride was used the yield of keto ester was 74–76% based on ester acid chloride or 48.3–49.5% based on isoamyl bromide. When the reaction was carried out in ether, using the above quantities (29.3 g. of acid chloride), there were obtained 3.70 g. of methyl ethyl succinate and 15.40 g. (42.5% based on ester acid chloride) of methyl 4-keto-7-methyloctoate.

4-Keto-7-methyloctoic Acid.[2]—A solution of diisoamylcadmium in 200 cc. of benzene was prepared from 0.3 mole of isoamyl bromide as described in the preparation of methyl 4-keto-7-methyloctoate. After addition of 22.5 g. of succinic anhydride, which had been ground and washed with carbon bisulfide and ether,[9] the mixture was stirred under reflux for four hours. The reaction mixture was decomposed with ice and sulfuric acid, and the benzene phase was separated and extracted with 300 cc. of 5% sodium carbonate solution in four portions. The material obtained from the carbonate extract after acidification was distilled from a Claisen flask at 4 mm. pressure. The entire distillate, consisting of 4-keto-7-methyloctoic acid, boiled at 152–153° and crystallized rapidly in the receiver; yield, 11.9 g. (30.8%).

On working up the benzene solution containing the neutral material from this reaction only 2.0 g. of material was obtained. This yielded, on distillation at 4 mm. pressure, 0.94 g. boiling at 100–110° and 0.93 g. boiling at 147–150°. These fractions were not further investigated.

Ethyl 10-keto-13-methyltetradecanoate was prepared in a 0.3-mole run from isoamyl bromide and ω-carbethoxynonoyl chloride[2,10] by the procedure described for methyl 4-keto-7-methyloctoate, except that the ester acid chloride was added in 100 cc. of benzene. This keto ester was obtained in a yield of 58.2 g. (85% based on acid chloride); b. p. 180–182° (3 mm.).

Anal. Calcd. for $C_{17}H_{32}O_3$: C, 71.80; H, 11.34. Found: C, 71.76; H, 11.66.

Ethyl 6-ketoheptoate,[11] b. p. 143–145° (33 mm.), and **ethyl 10-ketohendecanoate,**[6,12] b. p. 137–138° (2 mm.), were prepared by the procedure described for methyl 4-keto-7-methyloctoate. In both cases the yields in 1.0-mole runs were 76%. Since some dimethylcadmium is lost by volatilization during distillation of benzene and since it is desirable to reduce di-ester formation to a minimum in these cases, only 0.5 mole equivalent of ω-carbethoxyvaleryl chloride[13] and of ω-carbethoxynonoyl chloride were used for these preparations. The purity of these keto esters was indicated to be 80–90% by conversion to semicarbazones. From ethyl 6-ketoheptoate there was obtained an 86.5% yield of **semicarbazone**, m. p. 100.2–104.2°. After recrystallization from aqueous alcohol and from benzene the m. p. was 104.8–107.0° (Blaise and Koehler[11a] reported this m. p. as 107°). The **semicarbazone** of ethyl 10-ketohendecanoate was obtained in 89.6% yield (m. p. 90.2–99.4°). After three crystallizations from benzene very fine crystals melting at 110.7–112.8° were obtained.

Anal. Calcd. for $C_{14}H_{27}O_2N_2$: C, 58.92; H, 9.54. Found: C, 59.35; H, 9.70.

A 30-g. sample of ethyl 10-ketohendecanoate was saponified and the product was distilled through an 18-inch Podbielniak type column. There were obtained 1.5 g. of fore-run, b. p. 143–145° (2 mm.); 19.7 g. (75%) of 10-ketohendecanoic acid, b. p. 168–169° (1 mm.), m. p. 52–59°; and 3.2 g. of residue. After one crystallization from ether-petroleum ether the keto acid melted at 58–60°. This substance appears to be polymorphic, for it melts at once when placed in a bath at 59°, partially resolidifies and melts completely at 60°. It has been reported as melting at 57.5°,[6] 58.5–59.5°,[14] 53–55°.[15]

The residue (3.2 g.) from the above distillation was extracted with 200 cc. of boiling water, and after considerable salve-like material had been removed by filtration the clear filtrate was concentrated to 100 cc. On cooling there crystallized 0.99 g. of sebacic acid, m. p. 121–129°. After one crystallization from acetone-benzene, this product melted at 131.5–132.5° and gave no depression on mixing with pure sebacic acid of the same melting point. If this weight of sebacic acid is increased by 0.10 g. to allow for that remaining in the mother liquor, it corresponds to 1.4 g. or 4.7% of diethyl sebacate in the sample of keto ester.

The fore-run (1.5 g.) from 10-ketohendecanoic acid solidified when cooled in ice and salt, so it was recrystallized from petroleum ether (b. p. 30–40°). After three crystallizations there was obtained 30 mg. of a substance crystallizing as clusters of feathery needles and melting at 67.4–67.8°. It reacts with 2,4-dinitrophenylhydrazine and the analytical figures suggest that it is **dodecanedione-2,11**. This would arise from reaction of dimethylcadmium with the ester group of ethyl 10-ketohendecanoate.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.71; H, 11.19. Found: C, 72.48; H, 11.28.

Methyl 4-keto-5-methyloctoate could not be obtained by the procedure described above for preparing keto esters, presumably due to the instability of di-(2-amyl)-cadmium. For preparation of this keto ester, the Grignard reagent from 0.3 mole of 2-bromopentane in 150 cc. of ether was cooled to −7° and treated with 29.3 g. of dried cadmium chloride at such a rate as to allow the temperature to remain below −5°. After the resultant mixture had been stirred for one and one-half hours at −5 to −7° a solution of 33.8 g. of β-carbomethoxypropionyl chloride in 75 cc. of ether was added during twenty minutes at −5 to −7°. After addition was complete the reaction mixture was stirred four hours at the same temperature. When the reaction was worked up as described for methyl 4-keto-7-methyloctoate there was obtained 8.07 g. (21.5% based on ester acid chloride) of methyl 4-keto-5-methyloctoate, b. p. 130.5–130.7° (21 mm.). No fraction corresponding to methyl ethyl succinate was obtained.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.50; H, 9.75. Found: C, 63.87; H, 9.93.

16-Methyloctadecanoic Acid

Methyl 4-keto-6-methyloctoate was prepared from 1-bromo-2-methylbutane (b. p. 119–121°) and *p*-carbomethoxypropionyl chloride in the manner described for preparation of methyl 4-keto-7-methyloctoate, except that only about half the ether was distilled after preparation of the cadmium compound; b. p. 132–134° (16 mm.); yield, 60%. When the preparation was carried out in ether solution the yield was only 24–27%.

Since this ester is contaminated with the 7-methyl iso-

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(10) By distilling this ester acid chloride at a pressure of 5 mm. or less a yield of 90–95% may be obtained.

(11) (a) Blaise and Koehler, *Bull. soc. chim.*, (4) **7**, 222 (1910); (b) Lease and McElvain, THIS JOURNAL, **55**, 806 (1933).

(12) Ruzicka and Stoll, *Helv. Chim. Acta*, **10**, 692 (1927).

(13) Prepared in same manner and in same yield as ω-carbethoxynonoyl chloride.

(14) Chuit, Boelsing, Hauser and Malet, *Helv. Chim. Acta*, **9**, 1074 (1926).

(15) Abraham, Morvat and Smith, *J. Chem. Soc.*, 948 (1937).

mer it was saponified, and the **semicarbazone** of the resultant 4-keto-6-methyloctoic acid was prepared. It crystallizes from 50% ethanol as thin blades, m. p. 137–138° (dec.). When this semicarbazone was mixed with that from 4-keto-7-methyloctoic acid the m. p. was depressed to 128–131°.

Anal. Calcd. for $C_{10}H_{19}O_3N_3$: C, 52.39; H, 8.35. Found: C, 52.64; H, 8.39.

6-Methyloctoic Acid.[4]—Clemmensen reduction of methyl 4-keto-6-methyloctoate in alcoholic solution[6] gave yields of only 10–16%; so reduction was accomplished in aqueous hydrochloric acid as has been described for the 7-methyl isomer.[2] When reduction of 45.2 g. of keto ester was continued for forty-eight hours there was obtained in the best run 22.4 g. (76.7%, based on keto ester consumed) of 6-methyloctoic acid, b. p. 98–105° (1–2 mm.) and 10.1 g. of 4-keto-6-methyloctoic acid, b. p. 125–129° (1–2 mm.).

6-Methyloctamide was prepared from a sample of pure acid recovered from reduction of the ester (see below). The method used was that previously described for 7-methyloctoic acid.[2] This amide crystallizes from benzene as small plates, m. p. 90.4–91.6°.

Anal. Calcd. for $C_9H_{19}ON$: C, 68.74; H, 12.18. Found: C, 68.52; H, 12.44.

Ethyl 6-Methyloctoate.[3]—A Grignard reagent was prepared from 23.4 g. of ethyl iodide (b. p. 72.5–72.9°) in 100 cc. of ether and forced from the flask under nitrogen pressure into a nitrogen-filled separatory funnel. This solution was added during one hour to a stirred solution of 21.5 g. of ethyl 6-ketoheptoate in 100 cc. of ether, which was cooled in an ice–salt mixture. After addition was complete the mixture was stirred for an additional hour with continued cooling. The Grignard complex was then decomposed in the usual way and the aqueous phase was extracted with two portions of ether. The extracts were washed with water, 5% sodium carbonate solution, water and saturated sodium chloride solution, then filtered through a layer of anhydrous sodium sulfate. The residue remaining after removal of solvent was heated for thirty minutes with a crystal of iodine at 180–190°, and the unsaturated ester was distilled from a Claisen flask, b. p. 83–100° (3 mm.). This ester was readily hydrogenated in 100 cc. of 95% ethanol in the presence of 0.3 g. of platinum oxide catalyst. The resulting ethyl 6-methyloctoate was distilled through an 18-inch Podbielniak type column at 36 mm. pressure; b. p. 125.5–127.5°; yield in the best run, 7.0 g. (30%). The average yield of several runs was 20%.

In an effort to improve the yield, the hydroxy ester was dehydrated by other methods: with phosphorus tribromide followed by alcoholic potassium hydroxide[16] the yield was 21%; with phosphorus pentachloride followed by alcoholic potassium hydroxide[17] the yield was 16%; with phosphorus oxychloride[18] the yield was 17%; and with acetic anhydride the yield was 20.5%. Since these processes are relatively more laborious the use of iodine was adopted as most satisfactory.

1-Bromo-6-methyloctane.[3]—6-Methyloctanol-1 was prepared by reduction of ethyl 6-methyloctoate with sodium and alcohol according to Manske.[19] From 25.9 g. of ester there was obtained 10.8 g. of 6-methyloctanol-1, b. p. 108–111° (22 mm.). Since 7.3 g. of 6-methyloctoic acid, b. p. 139–143° (17 mm.), was recovered the yield on the basis of acid consumed was 83%. By treating 14.5 g. of the alcohol with anhydrous hydrogen bromide[20] there was obtained 13.0 g. (62.5%) of bromide, b. p. 105–108° (21 mm.). There was 1.0 g. of lower-boiling material and 1.8 g. of higher-boiling material (distillation through 18-inch column).

Ethyl 10-keto-16-methyloctadecanoate, prepared by the general method described above for methyl 4-keto-7-methyloctoate, was distilled through an 18-inch Podbielniak type column, with no head and with the take-off just above the heating jacket. The keto ester, which was collected at 192–195° (2 mm.), weighed 11.5 g. (76.5% based on acid chloride, 53.7% based on bromide).

Anal. Calcd. for $C_{21}H_{40}O_3$: C, 74.07; H, 11.84. Found: C, 73.54; H, 12.30.

The fore-run from the keto ester consisted of 1.2 g. of material boiling at 71.5–73° (3 mm.) and 2.0 g. of material boiling almost entirely at 130° (2 mm.). The latter fraction was saponified and the product separated into neutral and acidic portions. After crystallization from water the acidic fraction weighed 0.44 g. and melted at 126–128°. After an additional crystallization from acetone–benzene it melted at 128–130.5° and gave no depression on mixing with pure sebacic acid. The liquid neutral fraction weighed 1.2 g. and was insoluble in concentrated sulfuric acid. The analysis corresponds to that of **3,14-dimethylhexadecane** (from coupling of the Grignard reagent).

Anal. Calcd. for $C_{18}H_{38}$: C, 84.95; H, 15.05. Found: C, 85.04; H, 15.20.

10-Keto-16-methyloctadecanoic acid was prepared by saponification of 0.68 g. of the ester according to the method described for the 17-methyl isomer.[2] The yield of material melting at 50.3–53.6° was 0.54 g. (86%). After three crystallizations from ligroin (b. p. 35–39°) this keto acid was obtained as fine feathery crystals melting at 52.7–54.1°.

Anal. Calcd. for $C_{19}H_{36}O_3$: C, 73.03; H, 11.62. Found: C, 73.06; H, 11.67.

Ethyl 16-methyloctadecanoate was prepared by Clemmensen reduction of the above-described keto ester in alcoholic solution.[6] From 10.7 g. of keto ester there was obtained, after distillation through the Podbielniak type column, 8.1 g. (78.6%) of reduced ester, b. p. 170–175° (1.5 mm.).

Anal. Calcd. for $C_{21}H_{42}O_2$: C, 77.24; H, 12.97. Found: C, 77.10; H, 13.11.

16-Methyloctadecanoic Acid.—From saponification of 8.0 g. of the ester there was obtained 7.3 g. (99%) of 16-methyloctadecanoic acid melting at 45.7–49.3°. After one crystallization from acetone and two from methanol there was obtained 5.22 g. of translucent blades melting at 49.9–50.6°, n^{70}D 1.4342, n^{65}D 1.4361, n^{60}D 1.4379, n^{55}D 1.4400.

Anal. Calcd. for $C_{19}H_{38}O_2$: C, 76.45; H, 12.83; mol. wt., 298.5. Found: C, 77.00; H, 12.73; mol. wt., 297.0.

When 16-methyloctadecanoic acid was prepared from 1-bromo-6-methyloctane obtained from *s*-butylcarbinol as starting material, the crude acid precipitated from the saponification mixture melted at 43–49°. After a 5.1-g. sample had been fractionally crystallized ten times there was obtained 0.25 g. of 17-methyloctadecanoic acid melting at 66.7–67.3°.

For preparation of the **amide,** the acid chloride from 1.54 g. of acid was dissolved in 15 cc. of dioxane and added with stirring to 25 cc. of cold concentrated ammonium hydroxide. The precipitated amide weighed 1.53 g. (99%) and melted at 89.4–91.8°. After three crystallizations from ligroin (b. p. 80–100°) there was obtained 1.23 g. of transparent blades melting at 92.5–93.0°.

Anal. Calcd. for $C_{19}H_{39}ON$: C, 76.71; H, 13.21. Found: C, 76.94; H, 13.52.

A 1.0-g. sample of this amide was saponified by refluxing for thirty-six hours with a mixture of 10 cc. of ethanol and 30 cc. of 10% aqueous sodium hydroxide, 20-cc. portions of 10% sodium hydroxide being added at twelve-hour intervals. On acidification there was obtained 0.99 g. of 16-methyloctadecanoic acid melting at 48.0–49.9°. After three crystallizations from acetone the constant m. p. of 49.9–50.6° was reached.

The **tribromoanilide** was prepared in 89% yield (m. p. 103.8–105.8°) from 0.51 g. of the acid, using the method previously described by one of us.[2] After three crystallizations from ligroin (b. p. 80–100°) the constant m. p. of 106.2–106.9° was reached.

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(16) Noller and Adams, THIS JOURNAL, **48,** 1074 (1926).

(17) Modification of the method of Noller and Adams.

(18) Butenandt and Schmidt-Thomé, *Ber.*, **71,** 1487 (1938); Butenandt and Peters, *ibid.*, **71,** 2688 (1938).

(19) Manske, *Org. Syn.*, **14,** 20 (1934).

(20) Reid, Ruhoff and Burnett, *ibid.*, **15,** 24 (1935).

Anal. Calcd. for $C_{25}H_{40}ONBr_3$: C, 49.21; H, 6.60. Found: C, 49.64; H, 6.91.

C_{25} Acids

6-Methyltetracosanoic Acid.—Octadecyl bromide was prepared from commercial octadecyl alcohol with anhydrous hydrogen bromide.[20] On distillation through an 18-inch Vigreux type column there was obtained an 81% yield of product boiling at 177.5–179° (3 mm.). The Grignard reagent prepared from 8.56 g. of this bromide in 50 cc. of ether was added during fifty minutes to a solution of 3.45 g. of ethyl 6-ketoheptoate in 50 cc. of ether. During addition the mixture was stirred at 0°, and after addition was complete the mixture was stirred under reflux for one hour. After decomposition of the organometallic complex with ice and sulfuric acid the ether layer was separated and filtered to remove 0.6 g. of suspended hexatriacontane (m. p. after crystallization from ligroin, 75.2–76.1°). The aqueous phase was extracted twice with ether and the ether extracts were washed with water, 5 % sodium carbonate solution, water and saturated sodium chloride solution, then filtered through a layer of anhydrous sodium sulfate. The total ether solution was concentrated to about 25 cc. and allowed to stand overnight in the refrigerator, whereupon a small additional amount of hexatriacontane separated. After removal of the hexatriacontane and distillation of the remaining solvent, the residual hydroxy ester was heated for thirty minutes at 180–190° with a crystal of iodine. The mixture was then heated to 150° under 1 mm. pressure to remove about 3 cc. of low-boiling material. The residue was treated with Norit in ether, then hydrogenated over platinum oxide in 100 cc. of alcohol. Hydrogenation was slow and several 0.1-g. portions of catalyst were required. The reduced ester was distilled through an 18-inch Podbielniak type column. After a forerun of 2.1 g., **ethyl 6-methyltetracosanoate** was collected at 211–214° (*ca.* 0.5 mm.); yield, 2.4 g. (29.2%).

Anal. Calcd. for $C_{27}H_{54}O_2$: C, 78.76; H, 13.47. Found: C, 79.33; H, 13.29.

Saponification of 2.3 g. of the ester gave 1.92 g. (90%) of acid melting at 57.5–60.5°. After three crystallizations from ligroin (b. p. 72–80°), the constant m. p. of 55.8–56.6° was reached. Slightly impure samples usually melted higher than the pure substance.

Anal. Calcd. for $C_{25}H_{50}O_2$: C, 78.46; H, 13.17; mol. wt., 382.6. Found: C, 78.77; H, 13.35; mol. wt., 384.6.

In one run the unsaturated ester was saponified and the potassium salt of the acid was purified by washing with ether. The unsaturated acid was hydrogenated in acetic acid and the reduced acid was crystallized from acetic acid twice and from ligroin twice. The product obtained in this way melted at 55.2–56.4°. Crude samples of 6-methyltetracosanoic acid could not be purified by crystallization from acetone, methyl alcohol, acetic acid or petroleum ether (b. p. 30–40°).

The **amide,** prepared in 80% yield by the method described for 16-methyloctadecanoic acid, was crystallized four times from methanol and once from ligroin (b. p. 72–80°); m. p. 83.9–85.3°.

Anal. Calcd. for $C_{25}H_{51}ON$: C, 78.67; H, 13.47. Found: C, 78.56; H, 13.60.

The **tribromoanilide,** after crystallization from ligroin (b. p. 72–80°), acetone and ethanol, melted at 94.4–97.2°.

Anal. Calcd. for $C_{31}H_{52}ONBr_3$: C. 53.87; H, 7.58. Found: C, 54.00; H, 8.22.

6-Hydroxy-6-methyltetracosanoic Acid.—Ethyl 6-hydroxy-6-methyltetracosanoate was prepared from 17.1 g. of octadecyl bromide as described in the above section. The crude hydroxy ester was saponified with boiling alcoholic potassium hydroxide. After dilution of the alcoholic solution with hot water the soap was salted out with sodium chloride and, after filtration from the cooled solution, was washed well with saturated salt solution and ether. The crude hydroxy acid obtained by treating this soap with dilute hydrochloric acid weighed 5.19 g. (30.3%). After repeated crystallization from ligroin (b. p. 39–55°) this acid melted constantly at 46.0–47.3°.

Anal. Calcd. for $C_{25}H_{50}O_3$: C, 75.32; H, 12.64. Found: C, 75.46; H, 12.87.

10-Methyltetracosanoic Acid.—Myristyl bromide, prepared[20] from 100 g. of commercial myristyl alcohol (E. K. Co.), was distilled through an 18-inch Vigreux type column at 2 mm. pressure. There was obtained 4.4 g. of material boiling at 123–125°, 70.8 g. of myristyl bromide boiling at 135–137° and 24.8 g. of material boiling at 154–155°. Thus, the alcohol used apparently contained about 4% lauryl alcohol and 20% cetyl alcohol.

Starting with myristyl bromide and ethyl 10-ketohendecanoate, **ethyl 10-methyltetracosanoate** was prepared by the same general procedure described for the 6-methyl isomer; yield in a 0.15-mole run, 44.0%; b. p. 218–222° (*ca.* 0.5 mm.).

Anal. Calcd. for $C_{27}H_{54}O_2$: C, 78.76; H, 13.47. Found: C, 79.43; H, 13.25.

By saponification of the ester and crystallization of the crude acid from acetone an 89.5% yield of 10-methyltetracosanoic acid melting at 49.5–51.5° was obtained. After two additional crystallizations fine crystals were obtained which melted constantly at 50.5–51.5° (Schneider and Spielman,[6] 51.0–51.5°).

The **amide,** prepared in 96% yield, after crystallization from acetone, melted at 77.5–78.5° (literature,[6] 79–79.5°).

The **tribromoanilide,** prepared in 72% yield, crystallized from ethanol as fine white crystals, m. p. 84.2–84.8°.

Anal. Calcd. for $C_{31}H_{52}ONBr_3$: C, 53.87; H, 7.58. Found: C, 54.02; H, 8.18.

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Summary

16-Methyloctadecanoic acid has been synthesized from the intermediate ethyl 10-keto-16-methyloctadecanoate. This and four other keto esters were prepared in yields of 75–85% by the reaction between the appropriate ester acid chlorides and dialkylcadmium derivatives.

6-Methyltetracosanoic acid has been prepared from the corresponding 6-hydroxy acid. The ester of the hydroxy acid was prepared from octadecylmagnesium bromide and ethyl 6-ketoheptoate. Schneider and Spielman's synthesis of 10-methyltetracosanoic acid has been repeated and modified slightly.

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