[Contribution from the Chemical Laboratory of the University of California]

BRANCHED-CHAIN FATTY ACIDS. XII. SYNTHESES IN THE METHYLOCTADECANOIC ACID SERIES

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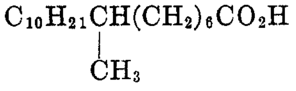
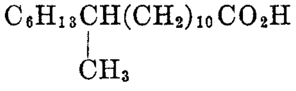
In continuation of the program of synthesis of all the monomethyloctadecanoic acids, four additional members of this series have been prepared. These are 8-methyl- (I), 12-methyl- (II), 13-methyl- (III), and 14-methyl-octadecanoic acid (IV).



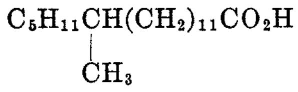
$C_{10}H_{21}\underset{\underset{CH_3}{|}}{CH}(CH_2)_6CO_2H$

I



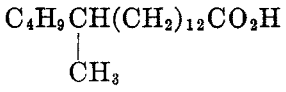
$C_6H_{13}\underset{\underset{CH_3}{|}}{CH}(CH_2)_{10}CO_2H$

II



$C_5H_{11}\underset{\underset{CH_3}{|}}{CH}(CH_2)_{11}CO_2H$

III

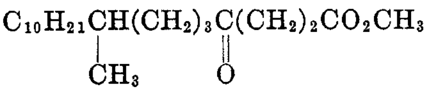


$C_4H_9\underset{\underset{CH_3}{|}}{CH}(CH_2)_{12}CO_2H$

IV

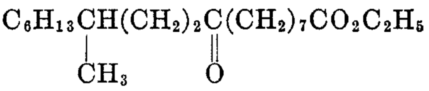
Of these, the 14-methyl isomer has previously been prepared by Ställberg-Stenhagen (1), and the properties of our acid and amide are in good agreement with those reported.

These acids were prepared by Clemmensen or Wolff-Kishner reduction of the keto esters V–VIII, and the keto esters were prepared by the previously-used (2) reaction between a dialkylcadmium reagent and an ester acid chloride. 1-Bromo-4-methyletradecane, used for the preparation of keto ester V, was available from previous work (3). 1-Bromo-4-methylnonane and 1-bromo-4-methyloctane, for the preparation of esters VII and VIII, were prepared from the corresponding alcohols which have been previously reported (4). 1-Chloro-4-methylnonane (4) gave about the same yield in the cadmium reaction as was obtained with the



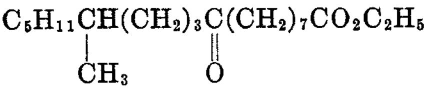
$C_{10}H_{21}\underset{\underset{CH_3}{|}}{CH}(CH_2)_3\underset{\underset{O}{\|}}{C}(CH_2)_2CO_2CH_3$

V



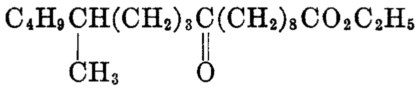
$C_6H_{13}\underset{\underset{CH_3}{|}}{CH}(CH_2)_2\underset{\underset{O}{\|}}{C}(CH_2)_7CO_2C_2H_5$

VI



$C_5H_{11}\underset{\underset{CH_3}{|}}{CH}(CH_2)_3\underset{\underset{O}{\|}}{C}(CH_2)_7CO_2C_2H_5$

VII



$C_4H_9\underset{\underset{CH_3}{|}}{CH}(CH_2)_3\underset{\underset{O}{\|}}{C}(CH_2)_8CO_2C_2H_5$

VIII

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corresponding bromide. This is in contrast with the somewhat lower yield obtained with the chloride in the case of the *n*-butyl halides (5).

The starting point for the preparation of 1-bromo-3-methylnonane, required for synthesis of ester VI, was a Reformatsky reaction between 2-octanone and ethyl bromoacetate. The resultant ethyl 3-hydroxy-3-methylnonanoate was dehydrated, then hydrogenated at high pressure with copper chromite catalyst to yield 3-methyl-1-nonanol, and this alcohol was converted to the desired bromide.

TABLE I

KETO ESTERS

ESTER	B.P., °C.	MM.	n_D^{20}	YIELD,[a] %	ANALYSIS[b]	
					C	H
V	193–195	2.5	1.4520	38	73.21	11.52
VI	216–220	5	[c]	43		
VII	198–202	3	1.4505	46	73.74	12.37
VIII	189–190	2	1.4506	54	74.06	11.46

[a] Based on alkyl halide, the more valuable reagent. [b] Calc'd for methyl ester, $C_{20}H_{38}O_3$: C, 73.57; H, 11.73. Calc'd for ethyl ester, $C_{21}H_{40}O_3$: C, 74.07; H, 11.84. [c] Not characterized but reduced directly to the desired acid.

TABLE II

KETO ACIDS

KETO ACID FROM	SOLVENT FOR CRYST.	M.P., °C.	ANALYSIS[a]	
			C	H
Ester V	acetone	65.7–66.3	72.91	11.51
Ester VII	hexane	40.2–40.6	73.39	11.98
Ester VIII	methanol	37.4–40.4[b]		

[a] Calc'd for $C_{19}H_{36}O_3$: C, 73.03; H, 11.61.

[b] Re-m.p. 39.2–40.0°.

EXPERIMENTAL

All melting points are corrected, while all boiling points are uncorrected. Analyses are by the Microanalytical Division of the Department of Chemistry of the University of California. All distillations, unless otherwise specified, were through a half-meter Podbielniak type column with tantalum wire spiral and partial reflux head.

Ester acid chlorides were prepared by methods previously described (2), except that thionyl chloride was used instead of phosphorus pentachloride.

Branched-chain alkyl bromides were prepared by the usual procedure (6) from the alcohols with anhydrous hydrogen bromide taken from a cylinder. 1-Bromo-3-methylnonane (7, 8), b.p. 121–122° (25 mm.), yield 86%. 1-Bromo-4-methylnonane (7), b.p. 113–114° (18 mm.), n_D^{28} 1.4538, yield 88%. 1-Bromo-4-methyloctane (7), b.p. 88–90° (12 mm.), n_D^{27} 1.4528, yield 84%.

3-Methyl-1-nonanol was prepared (with the assistance of Raylene E. Adams) by a method involving no secondary halides, in contrast to previously-reported methods (7, 8). To 18.3 g. (0.28 mole) of zinc foil (in small rolls), stirred and heated under reflux in 100 ml. of dry thiophene-free benzene, there was added during about one hour a mixture of 25.6 g. (0.2 mole) of redistilled 2-octanone, 50.1 g. (0.3 mole) of ethyl bromoacetate, and 100 ml. of benzene. After heating under reflux with stirring for an additional hour, the mixture was treated with ice and sulfuric acid; then the organic material was extracted with benzene. The extract was washed, the solvent was removed by distillation, and the residue was

TABLE III

Reduction of Keto Esters

ESTER REDUCED	REDUCED ESTER			
	YIELD,[a] %	B.P., °C.	MM.	n_D^{20}
V	36[b,c]	196–199	6	1.4480
VI	73[d]	183–185	2	1.4463
VII	66[b]	174–176	2	1.4459
VIII	88[d]	190–195	4	

[a] Esters V, VI, and VII were reduced by the modified Wolff-Kishner method (12), ester VIII by the modified Clemmensen method (10). [b] Methyl ester. [c] The low yields obtained in reduction of γ-keto esters is being further investigated, and this work will be reported in a later paper in this series. The modified Clemmensen reduction (10) fails almost completely with a γ-keto ester (14). [d] Ethyl ester.

TABLE IV

Branched-Chain Acids and Derivatives

ACID	M.P., °C.	M.P., °C. OF AMIDE	M.P., °C. OF TRIBROMOANILIDE
I	33.9–34.7	71.0–72.6[a]	96.2–96.6
		69.0	
II	27.6–28.2[a]	86.0–88.2[b]	94.2–95.2
	36.6–37.1	87.5	
III	29.4–31.6	77.2–78.7	98.2–99.6
IV	37.2–37.6	79.3–79.6	101.0–101.6
IV Ref. (1)	36.3–36.5	79.0–79.3	

[a] High-melting form crystallizes from acetone, low-melting form crystallizes from the melt. [b] Crystals obtained from solvents exhibit the broad m.p. If solidified melt is placed immediately in bath at 86.8° or higher, it re-melts completely at once. If solidified melt is placed in bath at 85°, it re-melts at 87.5°.

TABLE V

Analyses of Acids and Derivatives

ISOMER	ACID			AMIDE			TRIBROMOANILIDE		
	C	H	EQ. WT.	C	H	N	C	H	N
I	76.42	12.81	301.4	77.07	13.16				2.26
II	76.64	13.01	299.0	76.69	13.18				2.28
III	76.79	12.65	297.9			4.68			2.58
IV			297.7				49.14	6.50	
Calc'd	76.45	12.83	298.5	76.71	13.21	4.71	49.21	6.60	2.29

heated with a few crystals of iodine for about one hour at 190–200°. Distillation from a Claisen flask gave a 55–60% yield of ethyl 3-methylnonenoate, b.p. 100–105° (10 mm.).

The unsaturated ester was immediately hydrogenated at high pressure and 250° with a copper chromite catalyst (9). In a representative run using 73 g. of ester and 22 g. of catalyst, the initial pressure at 20° was 3490 p.s.i., the maximum pressure reached at 250° was 4700 p.s.i., and hydrogenation was complete in seven hours. Distillation of the product gave an 86% yield, b.p. 108–109° (11 mm.)

Keto esters were prepared by the general procedure described previously (2), using a ratio of 1 mole of bromide, 1 atom of magnesium, 0.54 mole of cadmium chloride, and 0.8 mole of ester acid chloride. The results are found in Table I. These yields are probably not maximum, in view of results obtained more recently in this laboratory with higher molecular weight dialkylcadmium reagents. These investigations will be reported in a later paper in this series.

The keto acids were obtained from esters V, VII, and VIII by saponification in alcoholic potassium hydroxide. Their properties are included in Table II.

Reduction of keto esters. The data in Table III show that the modified Clemmensen reduction (10) is capable of at least as good yields as the modified Wolff-Kishner reduction (11), but the modified Wolff-Kishner method is faster and probably less laborious. The yield of crude acid from the Wolff-Kishner reduction was usually nearly quantitative, as reported by other workers (13), but esterification of the crude acid and distillation through a column leaves considerable residue, and the yield of pure ester is rarely greater than 80%.

Branched-chain acids were obtained by saponification of the pure esters in alcoholic potassium hydroxide, and crystallization of the acids from acetone until a constant melting point was reached (usually two or three crystallizations).

Amides were prepared by the method previously described (15), and were crystallized from acetone, methanol, or 95% ethanol.

Tribromoanilides were made by the previously-described method (16) except that acid chlorides were prepared with thionyl chloride. Crystallization was from 95% ethanol.

Data on the acids and derivatives are found in Tables IV and V.

SUMMARY

There is reported the preparation of 8-methyl-, 12-methyl-, 13-methyl-, and 14-methyloctadecanoic acid, by reduction of the keto ester obtained from the appropriate ester acid chloride and dialkycadmium reagent.

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