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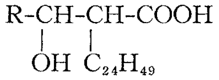
86. **Hikokichi Oura and Tokuko Makino:** Studies on Mycolic Acid and Related Compounds. II.[1] Syntheses of Analogous Componunds of Mycolic Acid.

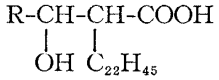
(*Pharmaceutical Faculty, University of Toyama**)

Synthesis of characteristic structure of mycolic acid, shown by the general formulae (A) and (B), had been carried out and 2-tetracosyl-3-hydroxyoctacosanoic acid (I) and 2-docosyl-3-hydroxyhexacosanoic acid (II) were obtained.[1]



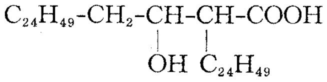
$$\text{R-}\underset{\text{OH}}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-COOH}$$

(A) R: $C_{60}H_{120}\pm5CH_2$



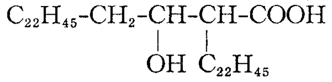
$$\text{R-}\underset{\text{OH}}{\text{CH}}\text{-}\underset{C_{22}H_{45}}{\text{CH}}\text{-COOH}$$

(B) R: $C_{58}H_{116}\pm5CH_2$



$$C_{24}H_{49}\text{-}CH_2\text{-}\underset{\text{OH}}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-COOH}$$

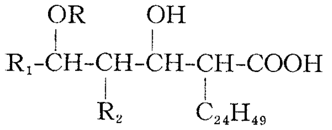
(I)



$$C_{22}H_{45}\text{-}CH_2\text{-}\underset{\text{OH}}{\text{CH}}\text{-}\underset{C_{22}H_{45}}{\text{CH}}\text{-COOH}$$

(II)

Partial structure (a) of α-mycolic acid (C, R: CH_3) of the Brěvannes strain of human-type tubercle bacilli proposed by Lederer and others,[2] and the partial structure (a) of (D) proposed recently by Polgar and others,[3] are both similar in structure, possessing a methoxyl group, and an attempt was made for the synthesis of 2-hexadecyl-3-methoxyeicosanoic acid (III) and 2-tetracosyl-3-methoxyoctacosanoic acid (IV).

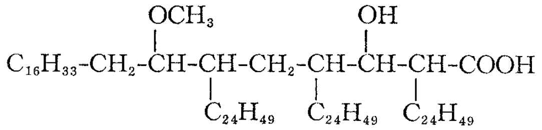


$$R_1\text{-}\overset{\text{OR}}{\text{CH}}\text{-}\underset{R_2}{\text{CH}}\text{-}\overset{\text{OH}}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-COOH}$$

(C)

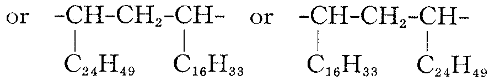
$R_1 + R_2$: $C_{58}H_{116}\pm5CH_2$

R = CH_3 or H

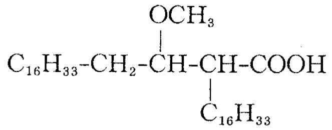


$$C_{16}H_{33}\text{-}CH_2\text{-}\overset{OCH_3}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-}CH_2\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-}\overset{\text{OH}}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-COOH}$$

(D)

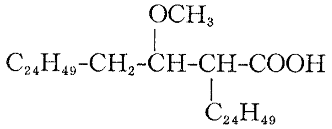


$$\text{or}\ \text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-}CH_2\text{-}\underset{C_{16}H_{33}}{\text{CH}}\text{-}\ \text{or}\ \text{-}\underset{C_{16}H_{33}}{\text{CH}}\text{-}CH_2\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-}$$



$$C_{16}H_{33}\text{-}CH_2\text{-}\overset{OCH_3}{\text{CH}}\text{-}\underset{C_{16}H_{33}}{\text{CH}}\text{-COOH}$$

(III)



$$C_{24}H_{49}\text{-}CH_2\text{-}\overset{OCH_3}{\text{CH}}\text{-}\underset{C_{24}H_{49}}{\text{CH}}\text{-COOH}$$

(IV)

Higher fatty acids possessing a methoxyl group in the β-position have not been reported in any literature as having been synthesized, as far as the authors' investigations are concerned. Two methods of forming this methoxyl can be considered; one of deriving a hydroxyl to a methoxyl, -CH(OH)- → -CH(OCH_3)-, and the other of building it up from a carbonyl, -CO-

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* 5 Okuda, Toyama (大浦彥吉, 牧野得子).

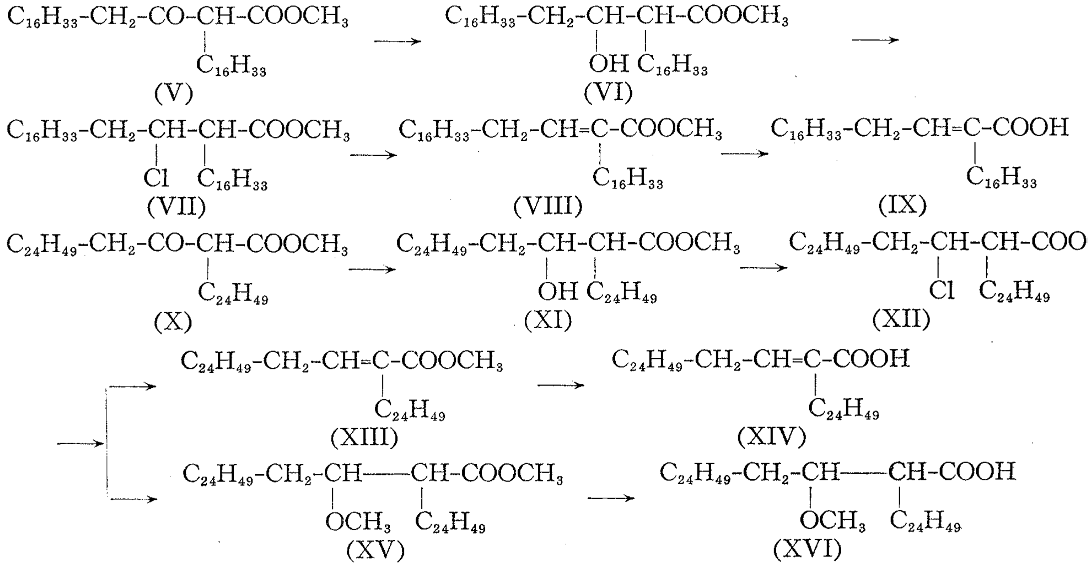
[1] Part I: Yakugaku Zasshi, **78**, 141(1958).

[2] A. Aebi, M. E. Vilkas, E. Lederer: Bull. soc. chim. France, **1954**, 79.

[3] E. D. Morgan, N. Polgar: J. Chem. Soc., **1957**, 3779.

→ -CH(OCH_3)-. The first reaction should be effected (1) by the usual method often used for sugars with methyl iodide and silver oxide (Purdie's reagent),[4] (2) the method recently used by Woodward[5] employing methyl iodide, silver oxide, and dimethylformamide, or (3) substitution with a halogen atom followed by reaction with sodium methoxide. For the second reaction, derivation to a ketal and dealcoholation can be considered. The methods (1) and (2) for the first reaction and the one for the second reaction were all tried but ended in the recovery of the starting materials.

However, method (3) for the first reaction offered an interesting result. Methyl 2-hexadecyl-3-oxoeicosanate (V), obtained by the method of Hansley,[7] or methyl 2-tetracosyl-3-oxoöctacosanate (X), reported in a preceding paper,[1] was reduced in methanol-dioxane with sodium borohydride and the product obtained was purified by chromatography through Florisil or Brockmann's alumina. The product obtained from (V) was methyl 2-hexadecyl-3-hydroxyeicosanate[8] (VI) and that from (X) was methyl 2-tetracosyl-3-hydroxyoctacosanate (XI). Further recrystallization and chromatographic purification of (VI) separated it into two isomers, respectively melting at 74~75° and 59~61°, which were designated as (VIa) and (VIb). (XI) was also separated into two isomers by chromatography and recrystallizations as (XIa), m.p. 86.5~88°, and (XIb), m.p. 77~78°. They were all identified as hydroxy acids.



$$\underset{\text{(V)}}{C_{16}H_{33}\text{-}CH_2\text{-}CO\text{-}\underset{\substack{|\\ C_{16}H_{33}}}{CH}\text{-}COOCH_3} \longrightarrow \underset{\text{(VI)}}{C_{16}H_{33}\text{-}CH_2\text{-}\underset{\substack{|\\ OH}}{CH}\text{-}\underset{\substack{|\\ C_{16}H_{33}}}{CH}\text{-}COOCH_3} \longrightarrow$$

$$\underset{\text{(VII)}}{C_{16}H_{33}\text{-}CH_2\text{-}\underset{\substack{|\\ Cl}}{CH}\text{-}\underset{\substack{|\\ C_{16}H_{33}}}{CH}\text{-}COOCH_3} \longrightarrow \underset{\text{(VIII)}}{C_{16}H_{33}\text{-}CH_2\text{-}CH{=}\underset{\substack{|\\ C_{16}H_{33}}}{C}\text{-}COOCH_3} \longrightarrow \underset{\text{(IX)}}{C_{16}H_{33}\text{-}CH_2\text{-}CH{=}\underset{\substack{|\\ C_{16}H_{33}}}{C}\text{-}COOH}$$

$$\underset{\text{(X)}}{C_{24}H_{49}\text{-}CH_2\text{-}CO\text{-}\underset{\substack{|\\ C_{24}H_{49}}}{CH}\text{-}COOCH_3} \longrightarrow \underset{\text{(XI)}}{C_{24}H_{49}\text{-}CH_2\text{-}\underset{\substack{|\\ OH}}{CH}\text{-}\underset{\substack{|\\ C_{24}H_{49}}}{CH}\text{-}COOCH_3} \longrightarrow \underset{\text{(XII)}}{C_{24}H_{49}\text{-}CH_2\text{-}\underset{\substack{|\\ Cl}}{CH}\text{-}\underset{\substack{|\\ C_{24}H_{49}}}{CH}\text{-}COOCH_3}$$

$$\longrightarrow \begin{cases} \longrightarrow \underset{\text{(XIII)}}{C_{24}H_{49}\text{-}CH_2\text{-}CH{=}\underset{\substack{|\\ C_{24}H_{49}}}{C}\text{-}COOCH_3} \longrightarrow \underset{\text{(XIV)}}{C_{24}H_{49}\text{-}CH_2\text{-}CH{=}\underset{\substack{|\\ C_{24}H_{49}}}{C}\text{-}COOH} \\ \longrightarrow \underset{\text{(XV)}}{C_{24}H_{49}\text{-}CH_2\text{-}\underset{\substack{|\\ OCH_3}}{CH}\text{—}\underset{\substack{|\\ C_{24}H_{49}}}{CH}\text{-}COOCH_3} \longrightarrow \underset{\text{(XVI)}}{C_{24}H_{49}\text{-}CH_2\text{-}\underset{\substack{|\\ OCH_3}}{CH}\text{—}\underset{\substack{|\\ C_{24}H_{49}}}{CH}\text{-}COOH} \end{cases}$$

(VI) and (XI) were each reacted with thionyl chloride and the products were purified by chromatography. (VIa) afforded two substances, (VIIa), m.p. 34~35°, and (VIIb), m.p. 50~51°, and (VIb) afforded (VIIb), m.p. 50~51°. Similarly, (XIIa), m.p. 61~61.5°, was obtained from (XIa), and (XIIb), m.p. 58.5°, from (XIb). The elemental analytical values of these compounds agreed respectively with those for methyl 2-hexadecyl-3-chloroeicosanate (VII) and methyl 2-tetracosyl-3-chloroöctacosanate (XII) that they were considered to be isomers.

Reaction of (VIIa) or (VIIb) with sodium methoxide in benzene failed to afford the desired methoxyl compound and the product so obtained was methyl 2-hexadecyl-2-eicosenate (VIII), m.p. 48~49°, assumed to have been formed by the elimination of hydrogen chloride. Similarly, (XIIa) and (XIIb) afforded methyl 2-tetracosyl-2-octacosanate (XIII), m.p. 60~60.5°. The ultraviolet spectra of (VIII) and (XIII) show absorptions at 222 and 266 mμ, and their infrared spectra indicated the presence of an ester (5.85 μ) and a double bond (6.10 μ).

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4) T. Purdie, J. C. Irvine: J. Chem. Soc., **83**, 1021(1903).
5) R. B. Woodward: Angew. Chem., **69**, 50(1957).
6) L. Claisen: Ber., **40**, 3906(1907).
7) V. L. Hansley: U. S. Pat. 2,158,071(1938), 2,218,026(1940).
8) M. J. Polonsky, E. Lederer: Bull. soc. chim. France, **1954**, 504.

exhibiting the absorption for an ester carbonyl conjugated to a double bond, thereby confirming these structures. Further saponification gave the corresponding acids, 2-hexadecyl-2-eicosenic acid (IX), m.p. 74∼74.5°, and 2-tetracosyl-2-octacosenic acid (XIV), m.p. 90∼90.5°.

In the above methoxylation, 100∼300 mg. of the starting compound was used in all cases.

Next, 1.9 g. of the racemic compound of (XII) was heated in a sealed tube with sodium methoxide at 110∼120° for 3 hours and the product was submitted to chromatographic separation, based on elemental analytical values, ultraviolet spectra, and the Beilstein reaction. Although in a poor yield (6.8%), the desired methyl 2-tetracosyl-3-methoxyoctacosanate (XV), m.p. 59∼59.5°, was obtained. Further saponification gave the corresponding acid, 2-tetracosyl-3-methoxyoctacosanoic acid (XVI), m.p. 80∼82°. Separation of (XV) should be carried out cautiously, using a large amount of alumina, since the adsorbability and melting points of (XII) and (XIII) are very similar. Further examinations should also be made on the yield from this reaction.

The authors express their sincere gratitude to Dr. Yokota, the Dean of this Faculty, and to Prof. T. Ishiguro of the University of Kyoto for their kind guidance and encouragement, and to Prof. Y. Yamamura of the University of Kyushu for valuable advices. The authors are indebted to Miss T. Morita and Messrs. M. Itoh and T. Hasegawa for technical help, to Dr. K. Okawa, Science Faculty, University of Osaka, for infrared spectral analysis, and to Miss M. Honda of this Faculty for elemental analyses.

Experimental (All m.p.s uncorrected)

Methyl 2-Hexadecyl-3-hydroxyeicosanate (VI)—According to the method of Polonsky and others[8]) methyl 2-hexadecyl-3-oxoeicosanate (V), m.p. 60∼62°, was reduced with $NaBH_4$ and the product was recrystallized from Et_2O, affording crystals of m.p. 71∼73°, and colorless granules, m.p. 58∼60°, from its mother liquor. These data agreed with those values given in the literature.

Further purification of the substance of m.p. 71∼73° by chromatography over Florisil raised the melting point to 74∼75°. *Anal.* Calcd. for $C_{37}H_{74}O_3$ (VIa) : C, 78.38 ; H, 13.16. Found : C, 78.19 ; H, 13.00.

Saponification of this substance with 10% methanolic KOH and recrystallization from AcOEt gave colorless crystalline powder, m.p. 79∼80° (m.p. 78∼79° given by Polonsky[8])). *Anal.* Calcd. for $C_{36}H_{72}O_3$: C, 78.19 : H, 13.13. Found : C, 78.30 ; H, 13.01.

Similar chromatographic purification of the substance of m.p. 58∼60° afforded (VIb), m.p. 59∼61°. *Anal.* Calcd. for $C_{37}H_{74}O_3$: C, 78.38 ; H, 13.16. Found : C, 78.28 ; H, 13.39.

The acid obtained by saponification of (VIb) melted at 74∼75° (the literature[8]) records m.p. 72∼74°). *Anal.* Calcd. for $C_{36}H_{72}O_3$: C, 78.19 ; H, 13.13. Found : C, 78.40 ; H, 12.96.

Methyl 2-Hexadecyl-3-chloroeicosanate (VII)—i) A mixture of 0.5 g. of (VIa), 0.1 cc. of dehyd. pyridine, and 0.2 cc. of $SOCl_2$ was heated at 80∼90° for 3 hrs., excess $SOCl_2$ was distilled off under a reduced pressure, and the residue was extracted with Et_2O. The extract was washed with water, dried, and Et_2O was evaporated. The residue was submitted to chromatography over 20 g. of Florisil (Table I-A) and the fraction Nos. 4, 5, and 6 were combined to be submitted to rechromatography. The column was eluted with petr. ether-Et_2O (0.1%) and 173 mg. of its residue was recrystallized from acetone to colorless microgranules (VIIa), m.p. 34∼35°. Beilstein test, positive. *Anal.* Calcd. for $C_{37}H_{73}O_2Cl$: C, 75.91 ; H, 12.57. Found : C, 76.34 ; H, 12.54.

The residue (37 mg.) from the fraction eluted with petr. ether-Et_2O (1%) was recrystallized from acetone to colorless microgranules, (VIIb), m.p. 50∼51°. Beilstein test, positive. *Anal.* Calcd. for $C_{37}H_{73}O_2Cl$: C, 75.91 ; H, 12.57. Found : C, 75.87 ; H, 12.45.

Table I-A.

Fract. No.	Solvent system (cc.)	Residue (mg.)
1	Petr. ether* (50)	trace
2	— do —	〃
3	Petr. ether-Et_2O (1%)	1
4	— do —	207
5	— do —	122
6	— do —	17
7	Petr. ether-Et_2O (2%)	8
8	— do —	9
9	— do —	trace
	Total	364 mg.

Table I-B.

Fract. No.	Solvent system (cc.)	Residue (mg.)
1	Petr. ether* (100)	trace
2	Petr. ether-Et_2O (1%) (20)	3
3	— do —	5
4	— do —	30
5	— do —	225
6	— do —	50
7	— do —	16
8	— do —	10
9	— do —	3
	Total	342 mg.

* b. p. 35∼65°.

ii) Similar reaction of 0.5 g. of (VIb) and chromatographic purification over 20 g. of Florisil (Table I-B) were carried out. Residue from fraction No. 5 was recrystallized from AcOEt and (VIIb), m.p. 50∼51°, was obtained. Beilstein test, positive. *Anal.* Found : C, 75.76 ; H, 12.60.

Formation of (VIII) from Methyl 2-Hexadecyl-3-chloroeicosanate (VII)—i) To a solution of 200 mg. of (VIIa) dissolved in 10 cc. of dehyd. benzene, 1.5 moles of MeONa was added and the mixture was heated at 100° for 5 hrs. The cooled reaction mixture was acidified with dil. H_2SO_4, extracted with Et_2O, Et_2O was evaporated, and the residue was chromatographed over 15 g. of Al_2O_3 (Table II-C). The fractions 4 and 5 were combined and recrystallized first from Me_2CO and then from AcOEt to colorless microneedles, m.p. 48~49°. Beilstein test, negative. U. V. λ_{max}^{hexane} mμ (log ε): 222 (3.34), 266 (1.94). I. R. λ_{max}^{Nujol} μ: 5.85 (-C=C-COOR), 6.10 (-C=C-). *Anal.* Calcd. for $C_{37}H_{72}O_2$ (VIII): C, 80.95; H, 13.20. Found: C, 80.69; H, 13.31.

ii) The same result was obtained by treating 185 mg. of (VIIb) as above.

Table II-C.

Fract. No.	Solvent system	(cc.)	Residue (mg.)
1	Petr. ether	(50)	10
2	Petr. ether-Et_2O (0.1%)	(50)	4
3	Petr. ether-Et_2O (0.5%)	(50)	6
4	— do —		86
5	— do —		35
6	— do —	(20)	5
7	Petr. ether-Et_2O (1%)	(20)	17
8	Petr. ether-Et_2O (3%)	(20)	9
9	Petr. ether-Et_2O (5%)	(20)	4
	Total		176 mg.

Table II-D.

Fract. No.	Solvent system	(cc.)	Residue (mg.)
1	Benzene	(60)	160
2	Benzene-Et_2O (9:1)	(40)	780
3	— do —	(100)	235
4	— do —		73
5	— do —		30
6	Benzene-Et_2O (1:1)	(400)	212
7	Et_2O	(400)	149
8	Et_2O	(200)	52
9	Et_2O	(200)	29
	Total		1720 mg.

2-Hexadecyl-2-eicosenic Acid (IX)—(VIII) was saponified with 2*N* methanolic KOH and the product was chromatographed over alumina. The fraction eluted with Et_2O containing 0.3% glacial AcOH was recrystallized from AcOEt to colorless crystalline powder, m. p. 74~74.5°. U. V. λ_{max}^{hexane} mμ (log ε): 222 (3.35), 266 (1.82). I. R. λ_{max}^{Nujol} 5.95 μ (-C=C-COOH), 6.16 μ (-C=C-). *Anal.* Calcd. for $C_{36}H_{70}O_2$: C, 80.83; H, 13.19. Found: C, 80.46; H, 12.82.

Methyl 2-Tetracosyl-3-hydroxyoctacosanate (XI)—Methyl 2-tetracosyl-3-oxoöctacosanate[1] (X) was reduced with $NaBH_4$ and the product was recrystallized from AcOEt to crystals, m. p. 79~86°. Two grams of this product was submitted to chromatography over 60 g. of alumina (Table II-D). Fraction Nos. 2, 3, and 4 were combined and rechromatographed over 30 g. of alumina (Table III-E). Fraction No. 2 from this rechromatography was recrystallized twice from AcOEt to colorless microgranules, m.p. 86.5~88°. *Anal.* Calcd. for $C_{53}H_{106}O_3$ (XIa): C, 80.44: H, 13.50. Found: C, 80.48; H, 13.38.

Saponification of 100 mg. of this substance, purification of the product by chromatography over alumina, and recrystallization from AcOEt afforded the acid melting at 92~93°. *Anal.* Calcd. for $C_{52}H_{104}O_3$: C, 80.34; H, 13.49. Found: C, 80.16; H, 13.62.

The fraction No. 6 (Table II-D) was rechromatographed over 15 g. of alumina and the portion eluted with benzene-Et_2O (1:1) was recrystallized from AcOEt to colorless microgranules (XIb), m.p. 77~78°. *Anal.* Calcd. for $C_{53}H_{106}O_3$: C, 80.44; H, 13.50. Found: C, 80.33; H, 13.41.

Methyl 2-Tetracosyl-3-chlorooöctacosanate (XII)—i) The same procedure as above was carried out with 300 mg. of (XIa) and the product obtained was chromatographed over 20 g. of Florisil (Table III-F).

Table III-E.

Fract. No.	Solvent system	(cc.)	Residue (mg.)
1	Benzene	(200)	20
2	Benzene-Et_2O (9:1)	(100)	593
3	— do —		83
4	— do —		180
5	— do —		70
6	— do —		24
7	Benzene-Et_2O (1:1)	(200)	37
8	Et_2O	(200)	44
9	— do —		2
	Total		1053 mg.

Table III-F.

Fract. No.	Solvent system	(cc.)	Residue (mg.)
1	Petr. ether	(50)	10
2	— do —		2
3	— do —		trace
4	Petr. ether-Et_2O (9:1)	(50)	243
5	— do —		42
6	— do —		2
7	— do —		trace
	Total		299 mg.

Table III-G.

Fract. No.	Solvent system	(cc.)	Residue (mg.)
1	Petr. ether	(50)	8
2	Petr. ether-Et_2O (1%)	(20)	trace
3	— do —		55
4	Petr. ether-Et_2O (2%)	(20)	88
5	— do —		50
6	— do —		12
7	— do —		2
	Total		215 mg.

The fractions 4 and 5 (Table III-F) were combined, rechromatographed over 15 g. of alumina, and the fractions 3, 4, and 5 (Table III-G) were recrystallized from AcOEt to colorless microgranules (XIIa), m.p. 61～61.5°. Beilstein test, positive. *Anal.* Calcd. for $C_{53}H_{105}O_2Cl$: C, 78.60 ; H, 13.07. Found : C, 79.02 ; H, 12.98.

(ii) The same reaction of 200 mg. of (XIb) and chromatography of the product over 15 g. of alumina (Table IV-H) were carried out. Residue from the fraction No. 1 was recrystallized from AcOEt to colorless microgranules (XIIb), m. p. 58.5°. Beilstein test, positive. *Anal.* Calcd. for $C_{53}H_{105}O_2Cl$: C, 78.60 ; H, 13.07. Found : C, 78.65 ; H, 12.85.

Formation of (XIII) from (XII)—A solution of 200 mg. of (XIIa) dissolved in 5 cc. of benzene was submitted to the same treatment as in the case of the formation of (VIII) from (VII). The product of this reaction was chromatographed over alumina and its product was recrystallized from AcOEt to colorless micro-sandy crystals, m.p. 60～60.5°. Beilstein test, negative. U. V. $\lambda_{\max}^{\text{hexane}}$ mμ (log ε) : 222 (3.64), 266 (2.17). I. R. $\lambda_{\max}^{\text{Nujol}}$: 5.85 μ (-C=C-COOR), 6.10 μ (-C=C-). *Anal.* Calcd. for $C_{53}H_{104}O_2$ (XIII) : C, 82.31 ; H, 13.56. Found : C, 82.40 ; H, 13.43.

(XIII) was saponified with 2*N* KOH in MeOH-dioxane and the product was recrystallized from AcOEt to colorless crystalline powder. (XIV), m. p. 90～90.5°. *Anal.* Calcd. for $C_{52}H_{102}O_2$: C, 82.25 ; H, 13.54. Found : C, 81.95 ; H, 13.46.

Methyl 2-Tetracosyl-3-methoxyoctacosanate (XV)—A solution of 1.9 g. of the racemic compound of (XII) dissolved in 30 cc. of benzene was sealed in a tube with 1.1 moles of MeONa, the mixture was heated at 110～120° for 3 hrs., and the product was chromatographed over 50 g. of alumina (Table IV-I).

Table IV-H.

Fract. No.	Solvent system (cc.)		Residue (mg.)
1	Petr. ether	(60)	83
2	Petr. ether	(20)	10
3	— do —		5
4	— do —		2
5	Petr. ether·Et_2O (1%)	(20)	25
6	— do —		2
7	Petr. ether·Et_2O (2%)	(20)	trace
8	Petr. ether·Et_2O (5%)	(20)	3
	Total.		130 mg.

Table IV-I.

Fract. No.	Solvent system (cc.)		Residue (mg.)
1	Petr. ether	(100)	180
2	— do —		398
3	— do —		620
4	— do —		112
5	Petr. ether-benzene (10%)	(100)	13
6	Petr. ether-benzene (20%)	(200)	trace
7	Petr. ether-benzene (50%)	(200)	〃
	Total		1323 mg.

The fraction Nos. 3 and 4 (Table IV-I) were combined and rechromatographed over 75 g. of alumina.

Table V-J.

Fract. No.	Solvent system (cc.)		Residue (mg.)
1	Petr. ether	(200)	trace
2	— do —		15
3	Petr. ether-benzene (5%)	(100)	20
4	Petr. ether-benzene (10%)	(50)	18
5	— do —		8
6	Petr. ether-benzene (20%)	(50)	78
7	— do —		44
8	— do —		28
9	Petr. ether-benzene (50%)	(50)	82
10	— do —		39
11	Benzene	(50)	8
		Total	340 mg.

The fraction Nos. 6 and 7 were combined, the solvent evaporated, and the residue was recrystallized from AcOEt to colorless crystalline powder, m. p. 59～59.5°. Beilstein test, negative. U. V. $\lambda_{\max}^{\text{hexane}}$ 267 mμ (log ε 2.00). *Anal.* Calcd. for $C_{54}H_{108}O_3$: C, 80.92 ; H, 13.52. Found : C, 80.78 ; H, 13.46.

2-Tetracosyl-3-methoxyoctacosanoic Acid (XVI)—Saponification of (XV), chromatography of the product over alumina, and recrystallization of the residue from a portion eluted with Et_2O containing 0.2% of glacial AcOH afforded colorless crystalline powder, m. p. 80～82°. *Anal.* Calcd. for $C_{53}H_{106}O_3$: C, 80.43 ; H, 13.50 ; OCH_3, 3.92. Found : C, 80.38 ; H, 13.23 ; OCH_3, 3.69

Summary

Methylation of methyl 2-hexadecyl-3-hydroxyeicosanate and methyl 2-tetracosyl-3-hydroxyoctacosanate was examined. 2-Tetracosyl-3-methoxyoctacosanoic acid was obtained from this reaction followed by chlorination of its product, but not 2-hexadecyl-3-methoxyeicosanoic acid.

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