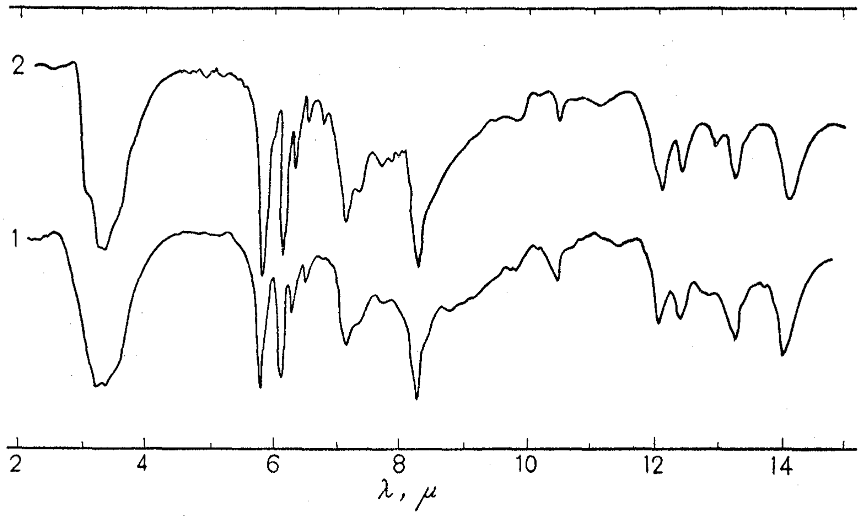

Fig. 2. Infrared Spectra of Terranaphthoic Acid in Dioxane
1. synthetic 2. natural

Summary

Terranaphthoic acid, a degradation product of oxytetracycline, was synthesized and the structure proposed by Hochstein, *et al*[5]. for this compound was thereby confirmed.

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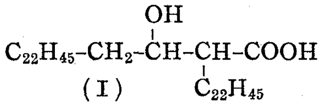
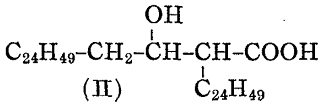
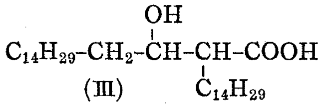
54. **Hikokichi Oura*** : Studies on Mycolic Acid and its Related Compounds. V.[1] Deuteration and Infrared Spectra of 2-Tetracosyl-3-hydroxyoctacosanoic Acid.

(*Pharmaceutical Faculty, University of Toyama*)

In the first paper of this series,[2] synthesis of 2-docosyl-3-hydroxyhexacosanoic acid (I) and 2-tetracosyl-3-hydroxyoctacosanoic acid (II), the characteristic structural portion of mycolic acid, was reported. Later, two substances from each of (I) and (II) were separated; α-compound, m.p. 91~92.5°, and β-compound, m.p. 86~88°, from (I), and α-compound, m.p. 92~92.5°, and β-compound, m.p. 87~89°, from (II). From their elementary analytical data, acetates, and infrared absorption spectra, it was assumed that these compounds are diastereoisomers.


$C_{22}H_{45}\text{-}CH_2\text{-}\overset{OH}{\overset{|}{C}H}\text{-}\underset{C_{22}H_{45}}{\underset{|}{C}H}\text{-}COOH$ (I)


$C_{24}H_{49}\text{-}CH_2\text{-}\overset{OH}{\overset{|}{C}H}\text{-}\underset{C_{24}H_{49}}{\underset{|}{C}H}\text{-}COOH$ (II)


$C_{14}H_{29}\text{-}CH_2\text{-}\overset{OH}{\overset{|}{C}H}\text{-}\underset{C_{14}H_{29}}{\underset{|}{C}H}\text{-}COOH$ (III)

In the present series of work, the α- and β-compounds of (II) were deuterated and their infrared absorption spectra were measured, by which some interesting observations were gained.

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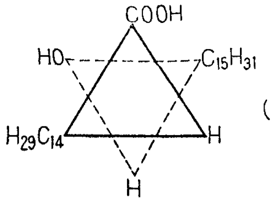
* Present address : University of Kyushu, Fukuoka(大浦彦吉).

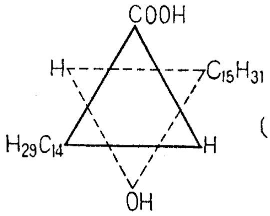
[1] Part IV : This Bulletin, **6**, 462(1958).

[2] H. Oura, T. Makino : Yakugaku Zasshi, **78**, 141(1958).

Previously, Lederer and others[3] isolated corynomycolic acid ((+)-2-tetradecyl-3-hydroxyoctadecanoic acid) (III), m.p. 70°, $[\alpha]_D$ +7.5°, from *Corynebacterium diphtheriae*. Later, he synthesized (III) and separated it into the α-compound, m.p. 73∼75°, and β-compound, m.p. 68∼69°.[4] The elementary analytical values and molecular weight of the three substances agreed with theoretical values, but their melting point, solubility, Debye-Scherrer pattern, X-ray diffraction pattern, infrared spectral data, and derivatives were all different, and Lederer therefore concluded that the two synthesized compounds are diastereoisomers. Later, Asselineau and Lederer[5] corrected the melting point of the α-compound to 76° and that of β-compound to 70°. Since the melting point of the β-compound agreed with that of natural corynomycolic acid, he presumed that it is the racemic compound of the natural acid. The α-compound is eluted first during chromatographic separation with ether containing glacial acetic acid and it was therefore assumed that it possessed a steric configuration which would effect facile hydrogen bonding[6] and had a higher melting point,[7] conforming to the structure (IV). The β-compound, which is eluted later, has a stronger affinity (because the carboxyl is free) and probably possessed a steric configuration which would make it difficult to form a hydrogen bonding. Since it has a low melting point, it was assumed to be the racemic compound of the natural acid, conforming to the structure (V).



(IV)



(V)

The infrared spectra of the α- and β-compounds of (II) synthesized by the present author failed to show a distinct absorption band for alcoholic hydroxyl around 3330 cm^{-1}, either as a KBr disk or in liquid state, and this was thought to be due to hydrogen bonding.[2] Under the assumption that there is a difference in the strength of hydrogen bonding between the α- and β-compounds, and that this might give a clue to elucidation of their steric configuration, (II) was deuterated and infrared spectrum of the deuterated (II) was measured. It was thereby learned that there is some difference in the ease of deuteration. First, 50 mg. each of the α- and β-compounds was mixed with 0.5 cc. of heavy water (99.86%) and the mixture was allowed to stand for three days in a sealed tube. During this time, the tube was heated in a water bath of 95° for a few hours each day and shaken occasionally. This procedure was repeated twice, heavy water was distilled off under a reduced pressure, and dried. This residue was submitted to infrared spectral measurement. The β-compound gave an absorption curve of a deuterated substance, as indicated in Fig. 1, but the α-compound showed a curve identical with that of the starting material. Therefore, the α-compound was further treated with heavy water for 5 days, heating in an oil bath at 100∼110° for consecutive days. This procedure was repeated three times, making a total of 15 days in contact with heavy water. As a result, the curve shown in Fig. 1 was obtained of the deuterated compound and this has clearly shown that there is a difference in the reaction velocity between the α- and β-compounds of (II) to deuteration.

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[3] E. Lederer, J. Pudles, S. Barbezat, J. J. Trillat: Bull. soc. chim. France, **1952**, 93.
[4] M. J. Polonsky, E. Lederer: *Ibid.*, **1954**, 504.
[5] J. Asselineau, E. Lederer: Ciba Foundation Symposium, Exptl. Tuberc. Bacillus and Host, **1955**, 14.
[6] H. Hoyer: Kolloid Z., **116**, 121(1950); Ber., **86**, 1016(1953).
[7] D. Swern, L. P. Wittnauer, H. B. Knight: J. Am. Chem. Soc., **74**, 1655(1952).

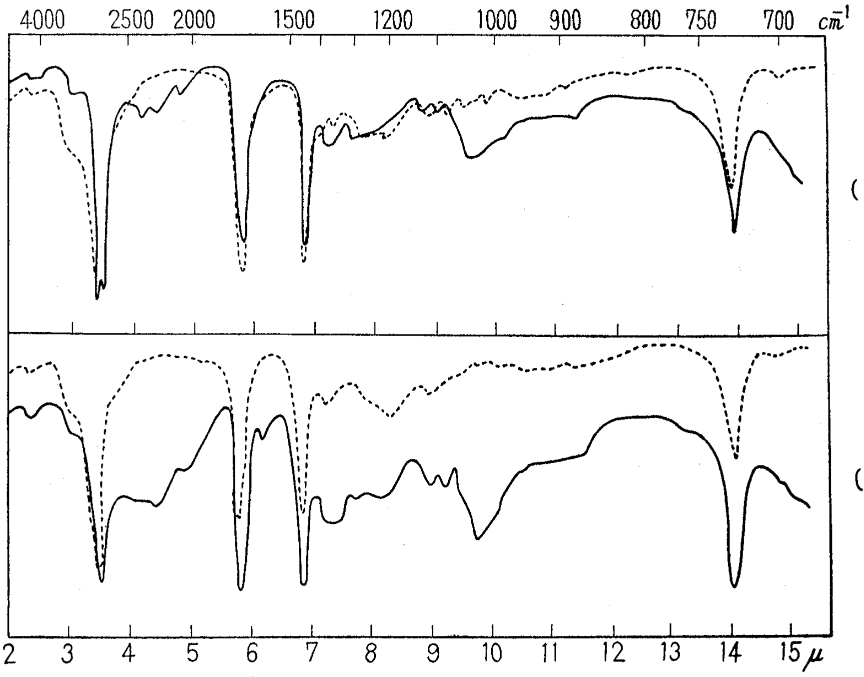

Fig. 1. Infrared Spectra (Perkin-Elmer Model-21, NaCl-prism)

(a) ------ 2-Tetracosyl-3-hydroxyoctacosanoic acid (IIα), m.p. 92∼93.5° (KBr-disk)
—— Deuterated 3-hydroxyoctacosanoic acid (IIα), m.p. 92∼93.5° (film)
(b) ------ 2-Tetracosyl-3-hydroxyoctacosanoic acid (IIβ), m.p. 87∼89° (KBr-disk)
—— Deuterated 3-hydroxyoctacosanoic acid (IIβ), m.p. 87∼89° (film)

In the infrared absorption spectra of these compounds, the region of O–H stretching vibration will be taken up first. The absorption around 3000 cm^{-1} is weak in both the α- and β-compounds, appearing like a shoulder, and it is difficult to determine the wave number correctly but it shifts when transiting from liquid to solid state; that of α-compound from 3400 to 3230 cm^{-1}, and of β-compound from 3400 to 3180 cm^{-1}. This is thought to originate in the O–H stretching vibration of the alcoholic hydroxyl. The O–H stretching vibration of the carboxyl-OH usually appears at 2700∼2500 cm^{-1},[8] but its position cannot be determined in both α- and β-compounds by overlapping with the strong absorption of the straight-chain C–H stretching vibration.

Deuteration causes appearance of a new absorption in the region of 2860∼2200 cm^{-1}. Since there was no absorption in this region in the non-deuterated compounds, it is clear that the newly appearing absorption is due to the O–D stretching vibration of the hydroxyl and carboxyl groups. It seems more appropriate to assign the absorption in the region of 2200∼2300 cm^{-1} to the O–D stretching vibration of the carboxyl,[9] and a band of this mode appears at 2250 (liquid) or 2240 (solid) cm^{-1} in the α-compound, and at 2250 (liquid) or 2220 (solid) cm^{-1} in the β-compound.

The absorption due to O–D stretching vibration of the hydroxyl might be assigned to the comparatively strong band remaining in this region and the bands which show shift in transiting from liquid to solid state appear at 2590 (liquid) or 2410 (solid) cm^{-1} in the α-compound, and at 2500 (liquid) or 2420 (solid) cm^{-1} in the β-compound.

The shift of a band when transiting from liquid to solid occurs due to hydrogen in both non-deuterated and deuterated compounds and according to this assignment, the larger shift of the hydroxyl O–D band than that of the carboxyl O–D band is char-

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[8] L. J. Bellamy: "The Infra-red Spectra of Complex Molecules," 140. Methuen & Co., Ltd., London.

[9] *Idem.*: *Ibid.*, 142; S. Bratoz, D. Hadži, N. Sheppard: Spectrochim. Acta, 8, 249(1956).

acteristic in these compounds. The region of 2400 cm^{-1}, considered to be the O–D stretching vibration of hydroxyl in the solid, corresponds to the foot of the strong band of CO_2 at 2350 cm^{-1} and sensitivity of a double-beam spectrometer falls in this region, so that it is difficult to determine the band position correctly, but it seems that the band positions of the α- and β-forms in the solid are in fair proximity. It is therefore considered that there is no great difference in the intensity of hydrogen bonding between these two forms.

According to the infrared spectrum of the solid in the whole region of NaCl prism indicated in Fig. 2, there are new absorptions at 1035 and 890 cm^{-1} in the α-compound, and at 1037 and 888 cm^{-1} in the β-compound on deuteration, which are not present in the spectra of non-deuterated compounds. These originate in the deformation vibration of hydroxyl-OD$^{10)}$ and there should be a difference in the shift of these bands according to the intensity of hydrogen bond. However, the values are close in the α- and β-compounds and even these facts indicate that there is no great difference in the hydrogen bonding of α- and β-compounds in the solid.

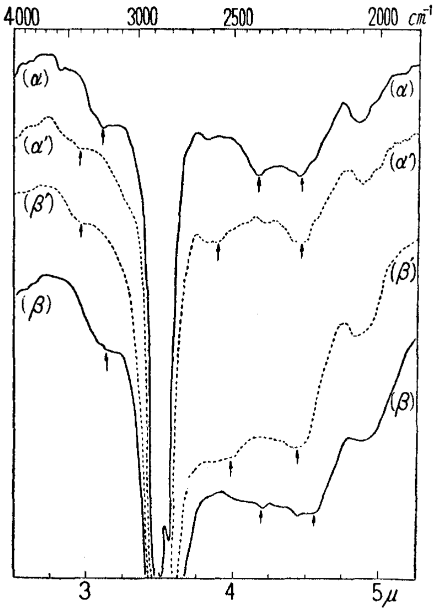

Fig. 2. Infrared Spectra (Perkin-Elmer Model-21, NaCl-prism)

(α) Deuterated 2-tetracosyl-3-hydroxyoctacosanoic acid (IIα), m.p. 92∼93.5° (film)

(α') Deuterated 2-tetracosyl-3-hydroxyoctacosanoic acid (IIα), m.p. 92∼93.5° (liquid)

(β) Deuterated 2-tetracosyl-3-hydroxyoctacosanoic acid (IIβ), m.p. 87∼89° (film)

(β') Deuterated 2-tetracosyl-3-hydroxyoctacosanoic acid (IIβ), m.p. 87∼89° (liquid)

If the molecules of α- and β-isomers in the crystal take the *trans* form to the long carbon chain, the mode of hydrogen bond might be formulated as (VI) and (VII). In these substances, the intensity of hydrogen bond becomes comparable in (VI), in which an intramolecular hydrogen bonding may be considered, and (VII), in which an intermolecular hydrogen bonding is possible.

It would be still difficult to assign (VI) and (VII) respectively to α- and β-compounds solely from the foregoing results but this assignment seems to be rational enough considering that the α-compound was eluted before the β-compound in the chromatographic separation of these isomers in the present series of work. The result of chromatography and melting points observed in this work agree well with the results obtained by Asselineau and Lederer.$^{5)}$

Both α- and β-compounds are sparingly soluble in heavy water and the difference in the ease of deuteration is considered to have arisen through the difference in the size of sample crystal at the time of deuteration, consequently, difference in the area of contact with heavy water and difference of degree of diffusion of heavy water mole-

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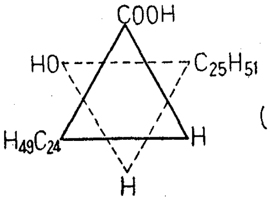
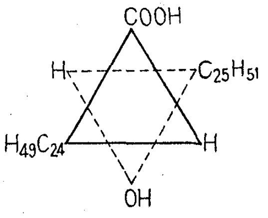
10) D. Hadži, N. Sheppard : Proc. Roy. Soc., A, **216**, 247(1953).

cules into the crystal according to different degree of packing of molecules in the crystal.[11]



(VI)



(VII)

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Summary

The α-compound, m.p. 92~93.5°, and β-compound, m.p. 87~89°, of 2-tetracosyl-3-hydroxyoctacosanoic acid was deuterated and their infrared spectra were measured. Attempt was made to elucidate the steric configuration of α- and β-compounds from difference in the strength of hydrogen bonds but there was no marked difference between the two isomers. Some difference, however, was found to exist between the α- and β-compounds in the velocity of deuteration.

(Received September 16, 1958)

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11) V. J. Frilette, J. Hanle, H. Mark: J. Am. Chem. Soc., **70**, 1107(1948); H. J. Marrinan, J. Mann: J. Appl. Chem., **4**, 204(1954).