Summary

Terramycin and Achromycin form chelate compounds with various metals, especially stable compounds with zirconium and thorium, as previously reported with Aureomycin. Their molar ratio is 1:1 in thorium chelates and 1:2 in zirconium chelates. Further investigations on the chelate formation of Apoterramycin and Isoaureomycin showed that phenolic β-diketone in tetracycline structure was very important as the chelating group, as was indicated in the previous paper. It is also suggested that the chelation of tetracylines must further involve the 12–1 bond.

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2. **Koiti Kimura and Akira Tanaka** : Anodic Synthesis of Fatty Acids. II.[1)] The Syntheses of 3,3-Dimethylated Branched Acids.

(*Pharmaceutical Institute, Medical Faculty, University of Kyoto**)

There have been numerous data concerning the properties of pure synthetic branched acids, but those of 3,3-dimethylated branched acids have not been reported as a series.

Table I.

$RCH_2C(CH_3)_2CH_2COOH$						m.p. (°C)	
Compd. No.	R	Formula	b.p. or m.p. (°C)	d_{25}	n_D^{25}	S-Benzylthiuronium salt	p-Bromophenacyl ester
(I)	CH_3	$C_7H_{14}O_2$	b.p. 203~204[a]	0.9348	1.4280	162.0	54.8
(II)	C_2H_5	$C_8H_{16}O_2$	b.p. 208~210	0.9009	1.4278	144.0	66.2
(III)	C_3H_7	$C_9H_{18}O_2$	b.p. 217~218[b]	0.9102[b]	1.4329[b]	136.0	
(IV)	C_4H_9	$C_{10}H_{20}O_2$	b.p. 242~244	0.9129	1.4346	123.0	
(V)	C_5H_{11}	$C_{11}H_{22}O_2$	b.p$_5$ 130~133	0.8995	1.4370	131.0	
(VI)	C_6H_{13}	$C_{12}H_{24}O_2$	b.b$_3$ 124~125	0.8954	1.4398	124.5	
(VII)	C_7H_{15}	$C_{13}H_{26}O_2$	b.p$_7$ 154~157	0.8827	1.4415	125.5	42.0
(VIII)	C_8H_{17}	$C_{14}H_{28}O_2$	b.p$_3$ 141~145	0.8841	1.4420	118.0	
(IX)	C_9H_{19}	$C_{15}H_{30}O_2$	b.p$_3$ 157~158	0.8892	1.4450	126.5	41.5
(X)	$C_{10}H_{21}$	$C_{16}H_{32}O_2$	b.p$_4$ 162~164[c]		n_D^{30} 1.4469	119.0	
(XI)	$C_{11}H_{23}$	$C_{17}H_{34}O_2$	b.p$_4$ 186~189 (m.p. 29.0)			126.0	50.5
(XII)	$C_{12}H_{25}$	$C_{18}H_{36}O_2$	b.p$_2$ 164~166 (m.p. 33.0)			123.5	47.5
(XIII)	$C_{13}H_{27}$	$C_{19}H_{38}O_2$	m.p. 40.5~41.0			123.5	54.0
(XIV)	$C_{14}H_{29}$	$C_{20}H_{40}O_2$	m.p. 44.0~44.8[d]			121.2	58.5
(XV)	$C_{15}H_{31}$	$C_{21}H_{42}O_2$	m.p. 47.5~48.0			121.3	62.0
(XVI)	$C_{16}H_{33}$	$C_{22}H_{44}O_2$	m.p. 53.5~54.0			121.5	60.5
(XVII)	$C_{17}H_{35}$	$C_{23}H_{46}O_2$	m.p. 57.0~57.3			120.0	66.0

All melting points are not corrected.

a) b.p. 209~210° by A. W. Crossley, W. H. Perkin, Jr. (J. Chem. Soc., **73**, 18, 35(1898)); b.p$_{778}$ 213°, anilide, m.p. 105.5~106.0° by N. L. Drake, G. W. Kline, W. G. Rose (J. Am. Chem. Soc., **56**, 2078(1934)); b.p. 201~202° by L. Schmerling (*Ibid.*, **67**, 1154(1945)).

b) b.p$_{18}$ 133~134°, d_{25} 0.9059, n_D^{25} 1.4319, by F. S. Prout (J. Am. Chem. Soc., **76**, 1913 (1954)).

c) b.p$_{10}$ 195°, m.p. 15°, by A. G. Birch, R. Robinson (J. Chem. Soc., **1942**, 494); m.p. 21~22.5° by G. Gustbée, E. Stenhagen (Chem. Zentr., **1943**, 1769).

d) m.p. 44.0~44.8° by J. Cason, *et al.* (J. Org. Chem., **15**, 855(1950)).

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* Yoshida-Konoe-cho, Sakyo-ku, Kyoto (木村康一, 田中 彰).

1) Part I: Yakugaku Zasshi, **76**, 960(1956).

It seems to be interesting to observe changes of physical properties caused by the introduction of 3,3-dimethyl groups into a corresponding normal fatty acid and to compare 3,3-dimethyl branched acids with other branched acids. On the other hand, it appears desirable to investigate uses of synthetic acids, for example, in perfumes or in bactericidal activity with chemical structure, etc.

We prepared 3,3-dimethylated branched acids by the electrolysis of mixed salts, a kind of Kolbe reaction. This is a very convenient synthetic method for fatty acids.

A mixture of methyl or ethyl hydrogen 3,3-dimethylglutarate and various straight-chain acids was electrolysed in methanol or ethanol, giving a mixture of a hydrocarbon, a diester, and a monoester. The last one is the desired cross-coupled product.

This reaction is formulated as follows :

$$RCOOH + HOOCCH_2C(CH_3)_2CH_2COOR' \longrightarrow$$

$$R\text{-}R + RCH_2C(CH_3)_2CH_2COOR' + R'OOCCH_2C(CH_3)_2(CH_2)_2C(CH_3)_2CH_2COOR'$$

The lower members of this series of acids (up to $C_{16}H_{32}O_2$, 3,3-dimethyltetradecanoic acid) are liquid, while acids ranging from $C_{17}H_{34}O_2$ to $C_{23}H_{46}O_2$ are solids. Physical constants for 3,3-dimethylated branched fatty acids are listed in Table I. They do not show alternation of melting points between odd and even members.

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Experimental

Apparatus—The apparatus consisted of a cell, a source of D. C. current, an ammeter, and a variable resistor, all connected in a circuit in series, and a voltmeter in parallel with the cell. The cell was made up of a cylindrical glass vessel of 50-cc. capacity. The temperature of the electrolyte was maintained at 40~60° by water-cooled condenser and external cooling.

Method—A mixture of the half-ester and monocarboxylic acid was electrolysed according to the general procedure of Linstead, *et al.*[2] After termination of the electrolysis, the methanolic

TABLE II.

Half-ester $(CH_3)_2C<{CH_2CO_2R' \atop CH_2CO_2H}$		Monobasic acid RCOOH		Crude monoester $RCH_2C(CH_3)_2CH_2\cdot CO_2R'$		MeOH	Current	Period	Product	Yield of acid[b]
	(g.)		(g.)	(°C)	(g.)	(cc.)	(A)	(hrs.)	(g.)	(%)
$R'=C_2H_5$	9.4	$R=CH_3$	18.0	[c]	5.0	25	1.2~1.6	4.5	2.0	30.4
〃	9.4	$R=C_2H_5$	15.0	b.p. 166~167	4.8	(EtOH)35	1.0	7.5	2.0	27.8
〃	9.4	$R=C_3H_7$	14.0	b.p. 195~204	5.0	23	0.6	9.0	2.0	25.3
$R'=CH_3$	8.7	〃	17.6	b.p. 189~193	1.4	35	1.0	7.5	1.0	12.7
〃	8.7	$R=C_4H_9$	10.0	[c]	7.0	45	1.0	6.5	2.8	32.6
〃	8.7	$R=C_5H_{11}$	11.6	b.p. 200~228	4.0	40	0.8~1.0	5.5	2.3	24.7
〃	8.7	$R=C_6H_{13}$	13.1	[c]	11.0	35	1.0	6.5	3.6	36.7
〃	8.7	$R=C_7H_{15}$	14.4	[c]	12.0	40	1.0	5.0	2.7	25.2
〃	8.7	$R=C_8H_{17}$	15.8	[c]	18.0	40	0.6~0.8	8.0	0.7	6.2
〃	6.0	$R=C_9H_{19}$	9.6	$b.p_5$ 140~160	9.0	40	1.0	5.5	2.7	32.2
〃	5.8	$R=C_{10}H_{21}$	9.3	[c]	11.0	40	1.0	4.5	1.2	14.1
$R'=C_2H_5$	4.8	$R=C_{11}H_{23}$	10.0	$b.p_3$ 140~167	9.0	40	0.8~1.0	4.5	2.7	40.0
$R'=CH_3$	4.8	$R=C_{12}H_{25}$	10.7	$b.p_2$ 165~182	1.9	40	0.8	4.5	0.8	10.3
〃	4.4	$R=C_{12}H_{25}$	8.2	$b.p_2$ 125~160	3.4	40	1.0	5.0	1.5	9.4
〃	5.0	$R=C_{13}H_{27}$	6.0	$b.p_2$ 125~172	3.0	30	1.0	2.0	0.7	5.6
〃	3.6	$R=C_{14}H_{29}$	4.0	$b.p_3$ 155~215	0.6	45	1.0	2.0	0.5	8.9
〃	5.5	$R=C_{15}H_{31}$	5.0	$b.p_2$ 136~176	0.8	40	0.8	4.0	0.6	5.8
〃	3.5	$R=C_{16}H_{33}$	5.4	$b.p_2$ 135~179	1.6	45	1.0	11.0	0.8	11.8
〃	3.5	$R=C_{17}H_{35}$	5.0	$b.p_3$ 127~187	1.5	50[a]	0.6~1.0	4.0	0.2	2.9

a) Tetrahydrofuran was used as a solubilization agent.
b) The yield was calculated on the half-ester present.
c) Crude oils were hydrolysed without distillation.

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2) R. P. Linstead, *et al.* : J. Chem. Soc., **1950**, 3326.

Table III. 3,3-Dimethylated Branched Acids

$RCH_2C(CH_3)_2CH_2COOH$

Compd. No.	R	Formula	Analyses (%) Calcd. C	Calcd. H	Found C	Found H
(I)	CH_3	$C_7H_{14}O_2$	64.58	10.84	64.76	11.16
(II)	C_2H_5	$C_8H_{16}O_2$	66.63	11.18	66.39	10.96
(III)	C_3H_7	$C_9H_{18}O_2$	68.31	11.47	68.61	11.44
(IV)	C_4H_9	$C_{10}H_{20}O_2$	69.72	11.70	69.58	12.00
(V)	C_5H_{11}	$C_{11}H_{22}O_2$	70.92	11.90	71.16	11.85
(VI)	C_6H_{13}	$C_{12}H_{24}O_2$	71.95	12.08	72.18	12.12
(VII)	C_7H_{15}	$C_{13}H_{26}O_2$	72.84	12.23	72.59	12.25
(VIII)	C_8H_{17}	$C_{14}H_{28}O_2$	73.63	12.36	73.77	12.41
(IX)	C_9H_{19}	$C_{15}H_{30}O_2$	74.32	12.48	74.37	12.68
(X)	$C_{10}H_{21}$	$C_{16}H_{32}O_2$	74.94	12.58	74.95	12.86
(XI)	$C_{11}H_{23}$	$C_{17}H_{34}O_2$	75.50	12.67	75.25	12.40
(XII)	$C_{12}H_{25}$	$C_{18}H_{36}O_2$	75.99	12.76	76.19	12.76
(XIII)	$C_{13}H_{27}$	$C_{19}H_{38}O_2$	76.45	12.83	76.40	12.78
(XIV)	$C_{14}H_{29}$	$C_{20}H_{40}O_2$	76.86	12.90	76.89	12.76
(XV)	$C_{15}H_{31}$	$C_{21}H_{42}O_2$	77.23	12.96	76.93	12.84
(XVI)	$C_{16}H_{33}$	$C_{22}H_{44}O_2$	77.58	13.02	77.47	12.83
(XVII)	$C_{17}H_{35}$	$C_{23}H_{46}O_2$	77.90	13.08	77.68	12.89

Table IV. S-Benzylthiuronium Salts of 3,3-Dimethylated Branched Acids

Compd. No.	Formula	Analyses (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
(I_1)	$C_{15}H_{24}O_2N_2S$	60.79	8.16	9.45	60.60	7.96	9.47
(II_1)	$C_{16}H_{26}O_2N_2S$	61.91	8.44	9.03	62.03	8.26	9.33
(III_1)	$C_{17}H_{28}O_2N_2S$	62.94	8.70	8.64	62.71	8.67	8.89
(IV_1)	$C_{18}H_{30}O_2N_2S$	63.88	8.94	8.28	64.15	9.22	8.25
(V_1)	$C_{19}H_{32}O_2N_2S$	64.74	9.15	7.95	64.48	9.04	7.72
(VI_1)	$C_{20}H_{34}O_2N_2S$	65.54	9.35	7.64	65.32	9.54	7.71
(VII_1)	$C_{21}H_{36}O_2N_2S$	66.28	9.54	7.36	66.49	9.73	7.09
($VIII_1$)	$C_{22}H_{38}O_2N_2S$	66.97	9.71	7.10	66.90	9.85	7.00
(IX_1)	$C_{23}H_{40}O_2N_2S$	67.61	9.87	6.70	67.43	9.74	6.51
(X_1)	$C_{24}H_{42}O_2N_2S$	68.21	10.02	6.63	68.28	9.96	6.48
(XI_1)	$C_{25}H_{44}O_2N_2S$	68.77	10.16	6.42	68.52	10.34	6.20
(XII_1)	$C_{26}H_{46}O_2N_2S$	69.29	10.29	6.22	69.20	10.35	6.25
($XIII_1$)	$C_{27}H_{48}O_2N_2S$	69.79	10.41	6.03	69.53	10.62	5.86
(XIV_1)	$C_{28}H_{50}O_2N_2S$	70.25	10.53	5.85	69.96	10.68	5.62
(XV_1)	$C_{29}H_{52}O_2N_2S$	70.69	10.64	5.69	70.94	10.75	5.66
(XVI_1)	$C_{30}H_{54}O_2N_2S$	71.10	10.74	5.53	70.99	10.69	5.46
($XVII_1$)	$C_{31}H_{56}O_2N_2S$	71.49	10.84	5.38	71.22	10.70	5.43

Table V. *p*-Bromophenacyl Ester of 3,3-Dimethylated Branched Acids

Compd. No.	Formula	Analyses (%) Calcd. C	Calcd. H	Found C	Found H
(I_2)	$C_{15}H_{19}O_3Br$	55.05	5.85	54.97	5.91
(II_2)	$C_{16}H_{21}O_3Br$	56.30	6.16	56.10	6.15
(VII_2)	$C_{21}H_{31}O_3Br$	61.31	7.54	61.10	7.72
(IX_2)	$C_{23}H_{35}O_3Br$	62.79	8.02	62.56	8.02
(XI_2)	$C_{25}H_{39}O_3Br$	64.23	8.35	64.03	8.62
(XII_2)	$C_{26}H_{41}O_3Br$	64.84	8.58	64.69	8.57
($XIII_2$)	$C_{27}H_{43}O_3Br$	65.45	8.69	65.67	8.92
(XIV_2)	$C_{28}H_{45}O_3Br$	66.01	8.84	66.29	8.99
(XV_2)	$C_{29}H_{47}O_3Br$	66.52	9.05	66.24	8.76
(XVI_2)	$C_{30}H_{49}O_3Br$	67.04	9.13	66.80	9.04
($XVII_2$)	$C_{31}H_{51}O_3Br$	67.42	9.24	67.15	9.47

TABLE VI. Molecular Refractivity

Compd. No.	Formula	Mol. refraction	
		Calcd.	Found
(I)	$C_7H_{14}O_2$	35.1	35.1
(II)	$C_8H_{16}O_2$	40.6	40.5
(III)	$C_9H_{18}O_2$	45.3	44.8
(IV)	$C_{10}H_{20}O_2$	49.9	49.2
(V)	$C_{11}H_{22}O_2$	54.5	54.3
(VI)	$C_{12}H_{24}O_2$	59.2	58.9
(VII)	$C_{13}H_{26}O_2$	63.7	63.7
(VIII)	$C_{14}H_{28}O_2$	68.4	68.3
(IX)	$C_{15}H_{30}O_2$	73.0	72.6

reaction mixture was neutralised with glacial AcOH and extracted with ether or benzene. The extract solution was washed with K_2CO_3 solution and water, dried over $CaCl_2$, and evaporated.

The crude products thus obtained were either fractionally distilled or alternatively, hydrolysed with 10% EtOH-KOH and the neutral and acidic fractions were separated in the usual way. Cold petroleum ether was added to acidic products and cold petroleum ether-soluble product was crystallised from a suitable solvent. Petroleum ether-insoluble product was a dibasic acid. A monobasic acid of cross-coupled product was soluble in petroleum ether (b.p. 50~60°).

Intermediates—Methyl and ethyl hydrogen 3,3-dimethylglutarate³⁾ were prepared by semi-esterification of the corresponding anhydrides obtained by the oxidation of dimedone with NaOCl,⁴⁾ followed by dehydration of the resulting 3,3-dimethylglutaric acid with Ac_2O.

Methyl hydrogen 3,3-dimethylglutarate : b.p$_9$ 128~131°, n_D^{30} 1.4377.

Ethyl hydrogen 3,3-dimethylglutarate : b.p$_{10}$ 152~156°, n_D^{30} 1.4340.

Tridecanoic, pentadecanoic, and heptadecanoic acids were obtained by nitrile synthesis from the next lower homolog. Undecanoic acid was prepared by the catalytic reduction of undecenoic acid. Other monobasic acids were used after purifying commercial acids. Experimental conditions are shown in Table II and analytical values of these acids and their derivatives are given in Tables III, IV, and V. Molecular refractivities are presented in Table VI.

The liquid acids (I~XII) were purified after repeated distillation. Some of these esters were analysed before hydrolysis.

Methyl 3,3-Dimethylheptanoate—b.p. 191~193°. *Anal.* Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found : C, 69.56; H, 11.52.

Ethyl 3,3-Dimethylheptanoate—b.p. 203~304°. *Anal.* Calcd. for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found : C, 70.70; H, 11.85.

Methyl 3,3-Dimethylnonanoate—b.p. 220~221°. *Anal.* Calcd. for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found : C, 71.81; H, 12.05.

The acids ranging from $C_{19}H_{38}O_2$ to $C_{23}H_{46}O_2$ were purified through calcium or thiuronium salt, followed by decomposition with conc. HCl.

3,3,6,6-Tetramethylsuberic acid obtained as a by-product showed m.p. 162.0° (m.p. 165.2° (corr.)⁵⁾). *Anal.* Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found : C, 62.40; H, 9.85. *p*-Bromophenacyl ester, m.p. 130.0°. *Anal.* Calcd. for $C_{28}H_{32}O_6Br_2$: C, 53.86; H, 5.17. Found : C, 53.57; H, 5.19.

Summary

Seventeen kinds of 3,3-dimethylated branched fatty acids were prepared by anodic synthesis. Methyl or ethyl hydrogen 3,3-dimethylglutarate was used as the half-ester of dibasic acid. Cross-coupled products were obtained by crossing half-ester with monobasic acids. Platinum plates were used as the electrodes, and methanol or ethanol as the solvent. The lower members of the series (up to $C_{16}H_{32}O_2$) are liquid, while the higher members (up to $C_{23}H_{46}O_2$) are solid. No alternation was seen in the melting points of these acids.

(Received July 11, 1957)

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3) J. Cason, *et al.* : J. Org. Chem., **15**, 885(1950).

4) Org. Syntheses, **31**, 41(1951); Coll. Vol. **II**, 200(1948).

5) J. Walker and J. K. Wood (J. Chem. Soc., **1906**, 600) reported m.p. 164~165°; S. F. Birch, *et al.* (J. Chem. Soc., **1952**, 1363) reported m.p. 169.5°.