Structures of Maridomycin I, III, IV, V and VI, Macrolide Antibiotics

The isolation of maridomycins (I, II, III, IV, V, VI) and the structure of maridomycin II have been reported in the preceding paper[1]. All of these components show similar physicochemical, chemical and biological properties. Each component gave the same color reactions with erythromycin test and Dragendorff reagent, and showed the same ultraviolet end absorption. The following functional groups were observed in the NMR-and IR-spectra of these compounds (Table I).

Alkali hydrolysis of maridomycin I (I), $C_{43}H_{71}NO_{16}$, III (III), $C_{41}H_{67}NO_{16}$, IV (IV), $C_{40}H_{65}NO_{16}$, V (V), $C_{40}H_{65}NO_{16}$, VI (VI) $C_{39}H_{63}NO_{16}$ gave 1 mole each of propionic acid and isovaleric acid, 2 moles of propionic acid, 1 mole each of acetic acid and propionic acid, 1 mole each of acetic acid and propionic acid, and 2 moles of acetic acid, respectively. Methanolysis of I afforded α- and β-methyl isovaleryl mycaroside. By the same treatment both III and IV gave α-methyl propionyl mycaroside (XXVIII)[2], $[\alpha]_D^{22}$ − 145.2 (c = 0.5 in $CHCl_3$), and its β-anomer (XXIX), $[\alpha]_D^{21}$ + 18.2 (c = 1.5, in $CHCl_3$), while V and VI yielded α and β-methyl acetyl mycaroside (XXX)[2] (Table II).

On mild acid hydrolysis of 9-dehydromaridomycins, 2 kinds of demycarosyl derivatives were obtained; one from 9-dehydro compounds of I, III, V and the other from

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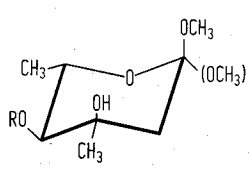
Table 1. NMR- and IR-spectra of maridomycins

Component / Group	I	II	III	IV	V	VI
C_4''–OAc	—	—	—	—	2.16	2.17
C_3–OAc	—	2.25	—	2.24	—	2.26
$-N(CH_3)_2$	2.54	2.54	2.52	2.54	2.55	2.55
$-OCH_3$	3.55	3.56	3.53	3.55	3.55	3.56
–O–C–*H*	3.91	3.92	3.89	3.91	3.91	3.93
HO–C_9–*H*	4.03	4.03	4.02	4.02	4.04	4.03
C_1'H	4.45	4.46	4.43	4.45	4.45	4.46
C_4''H	4.63	4.64	4.61	4.62	4.62	4.63
C_1''H	5.06	5.08	5.05	5.06	5.07	5.08
Olefine C_{11}H	5.69	5.66	5.67	5.65	5.69	5.67
Olefine C_{10}H	6.09	6.10	6.08	6.08	6.09	6.10
–CHO	9.63	9.65	9.62	9.64	9.64	9.64
	(δ ppm, 100 Mc, in $CDCl_3$)					
IR ν–C–O–Ac (KBr)	—	1235 cm^{-1}	—	1237 cm^{-1}	1242 cm^{-1}	1239 cm^{-1}

Table II. Fatty acid and neutral sugar moieties

Maridomycin	Alkali hydrolysis		Acid methanolysis
	Fatty acid		α- and β-Neutral sugar
I	$(CH_3)_2CHCH_2COOH$	CH_3CH_2COOH	$R=(CH_3)_2CHCH_2CO-$
II	$(CH_3)_2CHCH_2COOH$	CH_3COOH	$R=(CH_3)_2CHCH_2CO-$
III	CH_3CH_2COOH	CH_3CH_2COOH	$R=CH_3CH_2CO-$
IV	CH_3CH_2COOH	CH_3COOH	$R=CH_3CH_2CO-$
V	CH_3COOH	CH_3CH_2COOH	$R=CH_3CO-$
VI	CH_3COOH	CH_3COOH	$R=CH_3CO-$



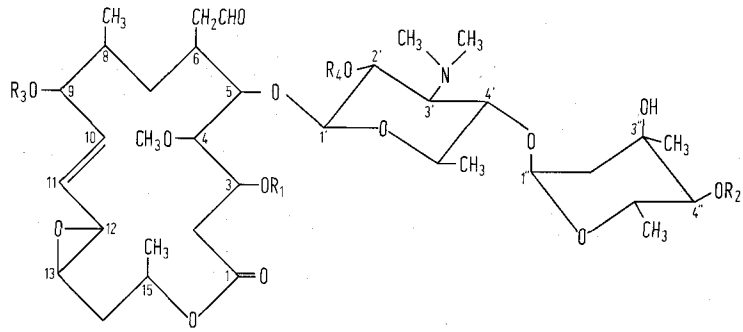
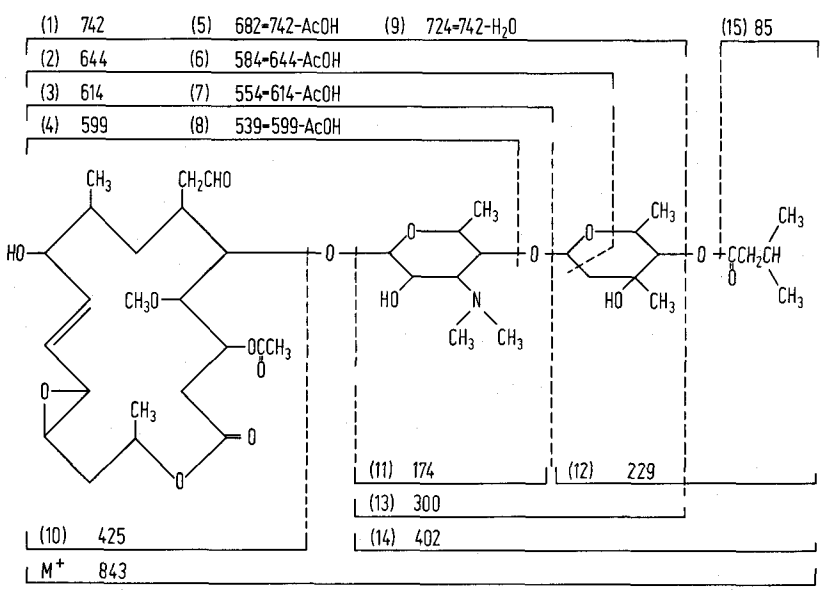


Fig. 1.

	R_1	R_2	R_3	R_4	pKa'
I	$COCH_2CH_3$	$COCH_2CH(CH_3)_2$	H	H	6.9
III[3]	$COCH_2CH_3$	$COCH_2CH_3$	H	H	6.9
IV	$COCH_3$	$COCH_2CH_3$	H	H	6.9
V	$COCH_2CH_3$	$COCH_3$	H	H	6.9
VI	$COCH_3$	$COCH_3$	H	H	6.9
XXXI	$COCH_2CH_3$	$COCH_2CH(CH_3)_2$	$COCH_3$	$COCH_3$	4.7
XXXII	$COCH_2CH_3$	$COCH_2CH(CH_3)_2$	$COCH_2CH_3$	$COCH_2CH_3$	4.7
XXXIII	$COCH_2CH_3$	$COCH_2CH(CH_3)_2$	$COCH_2CH_3$	H	6.6
XXXIV	$COCH_2CH_3$	$COCH_2CH(CH_3)_2$	H	$COCH_2CH_3$	4.7



Mass spectrum of maridomycin II

Table III.

	M^+	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)
I	857	756	658	628	613	682	584	554	539	738	439	174	229	300	402	85
II	843	742	644	614	599	682	584	554	539	724	425	174	229	300	402	85
III	829	756	658	628	613	682	584	554	539	738	439	174	201	300	374	57
IV	815	742	544	614	599	682	584	554	539	724	425	174	201	300	374	57
V	815	756	658	628	613	682	584	554	539	738	439	174	187	300	360	43
VI	801	742	644	614	599	682	584	554	539	724	425	174	187	300	360	43
VII	927	826	728	698	683	766	668	638	623		467	216	229	342	444	85
VIII	885	784	686	656	641	724	626	596	581		425	216	229	342	444	85
IX	885	784	686	656	641	724	626	596	581		467	174	229	300	402	85
XXVI	841	740	642	612	597	680	582	552	537		437	174	229	300	402	85
XXXI	941	840	742	712	697	766	688	638	623		481	216	229	342	444	85
XXXII	969	868	770	740	725	794	696	666	651		495	230	229	356	458	85
XXXIII	913	812	714	684	669	738	640	610	595		495	174	229	300	402	85
XXXIV	913	812	714	684	669	738	640	610	595		439	230	229	356	458	85

those of II, IV, VI. The difference between the 2 demycarosyl derivatives is assumed to come from the fatty acid moieties at carbon 3. And the differences among 9-dehydromaridomycin I, III, V and among 9-dehydromaridomycin II, IV, VI, all come from the fatty acid moieties at carbon 4″. On the basis of these findings, the structures of maridomycins were proposed as shown in the Figure.

To confirm the proposed structures, the mass fragmentation patterns[4] of each component and their derivatives were inspected (Table III).

Comparison of Maridomycin I and II; Maridomycin I shows molecular peak at 857, which is 14 mass unit greater than that of II. The fragments (1), (2), (3), (4), (9) and (10) correspond to aglycone moieties and show 1 methylene (*m/e* 14) difference between I and II.

The fragments (11), (12), (13) and (14) indicate that they have the same acylsugar moiety.

These mass patterns and the liberation of propionic acid from I with alkali hydrolysis suggest that the propionyl group is located at carbon 3 or 9. The NMR spin decoupling study excludes the possibility of carbon 9. The elimination mechanism of the propionic acid accounts for the fragments (5), (6), (7) and (8).

Thus it was concluded that I has propionyl group at carbon 3 instead of acetyl group at carbon 3 in II.

The mass spectra of I-diacetate (XXXI), I-dipropionate (XXXII), I-9-propionate (XXXIII) and I-2′-propionate (XXXIV) together with their NMR-spectra and *p*Ka′ values support the structure of I.

The structures of other maridomycin components were established analogously as shown in the figure[5].

Zusammenfassung. Strukturaufklärung einer Gruppe von Antibiotika aus der Reihe der Makrolide.

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Antimony Trichloride Catalyzed Reactions on Terpenoids, a Nucleophilic Addition Reaction on Khusinol

Unlike the well-known Lewis acids, aluminium chloride and boron trifluoride, which are extensively used in structural and synthetic organic chemistry, there is no similar record in the literature about the use of antimony trichloride. Limited use of antimony trichloride has, however, been made in the rearrangement of phenolic ethers[1], and as a spray reagent for the identification of isoprenoids[2]. We have recently observed that antimony trichloride, unlike aluminium chloride and boron trifluoride, uniquely catalyses some reactions on terpenoids. In the present communication, an interesting addition of CH_3OH to the methylenic double bond of Khusinol[3] (1) in the presence of catalytic amount of antimony trichloride is described.

Khusinol (I), on warming briefly on water bath with a methanolic solution of antimony trichloride, affords a pale yellow mobile liquid from which a compound was isolated in a pure form (TLC) by column chromatography over alumina, in 90% yield. Chemical and spectroscopic data presented in this paper shows that this compound represents a hydroxy ether (II, $C_{16}H_{28}O_2$). All compounds gave satisfactory elemental analysis.

The IR-spectrum of the compound showed intense bands at 3450 cm^{-1} (hydroxyl group), 1060 (methoxyl group) and at 810 cm^{-1} (trisubstituted double bond). The compound gave a positive tetranitromethane test and the presence of only 1 olefinic linkage was confrimed by

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