The mass spectrum does not allow a distinction between the proposed structure and one in which rings A and D are interchanged and in which the methylene bridge is at the α position. Our proposed structure (I) possesses 6 conjugated double bonds in the conjugated chain. This alternate structure would have a conjugated bond chain of only 5 bonds and would be expected (see below) to have absorption maxima at shorter wavelengths. We have, therefore, assigned biladiene a, b isomer structure (I) to mesobilirhodin dimethyl ester.

The structure proposed here is identical to that proposed for mesobilirhodin prepared from i-Urobilin[4,5]. This establishes that mesobilirhodin prepared by alkaline isomerization of i-Urobilin and $FeCl_3$ oxidation of mesobilirubinogen are identical[14].

Zusammenfassung. Für das Pigment Mesobilirhodin wird aufgrund von massenspektrometrischen Daten und der NMR-Spektren eine neue Struktur abgeleitet.

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Isolation of Maridomycins and Structure of Maridomycin II

Maridomycins, a new group of macrolide antibiotics, were obtained from *Streptomyces hygroscopicus*[1], and named as maridomycin I, II, III, IV, V and VI, respectively, and characterized as follows:

All of these antibiotics show nothing but ultraviolet end absorption in methanol. They are classified as macrolide antibiotics from their physico-chemical, chemical and microbiological properties. The structure of maridomycin II was elucidated as shown in the chart.

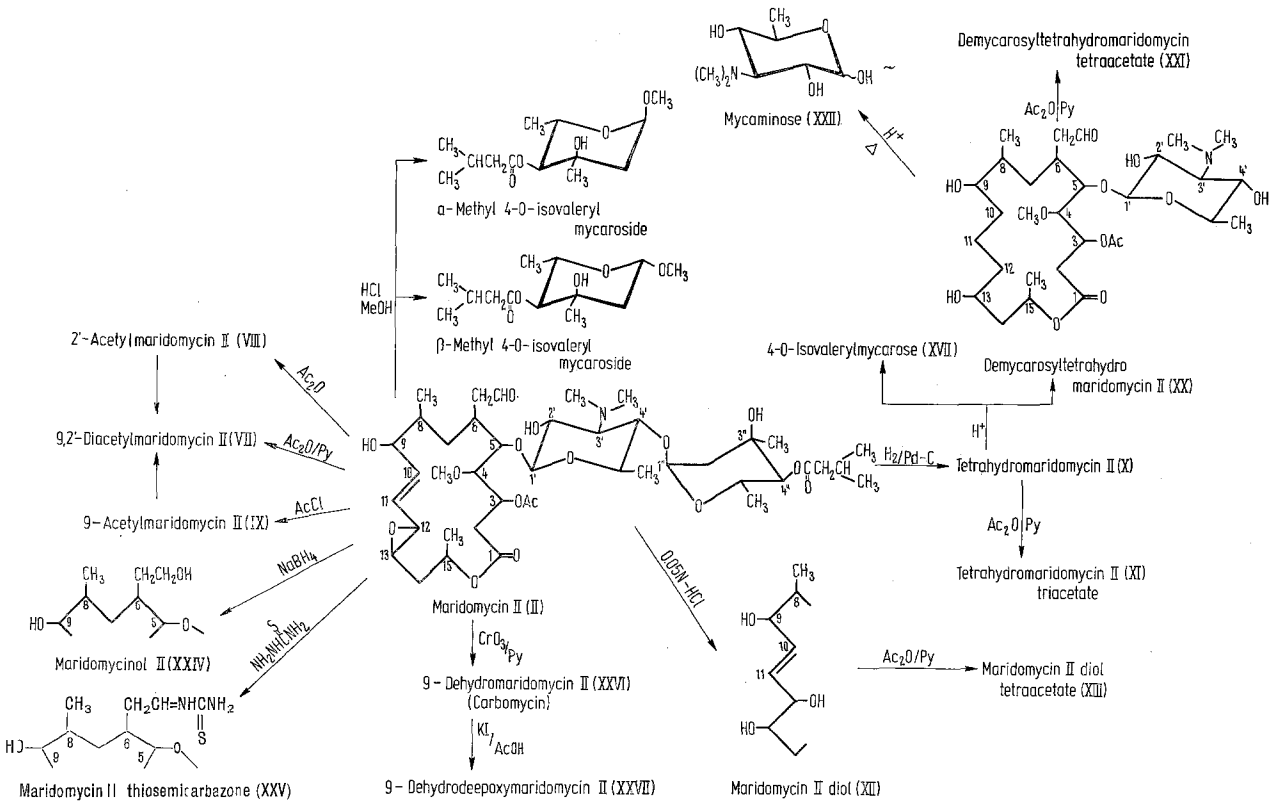
Maridomycin II (II) was obtained as colorless prisms, pKa′ 6.9, IR[2]: 1740 (–O–CO–), 1235 (–OAc), 2730 (–CHO), NMR[3]: 1.01 (9H, *d*, –CH–$(CH_3)_2$, –CH–CH_3), 2.25 (3H, *s*, –O*Ac*), 2.54 (6H, *s*, –N$(CH_3)_2$), 3.56 (3H, *s*, –OCH_3), 5.66 (1H, *dd*, >C=C<), 6.10 (1H, *dd*, >C=C<), 9.65 (1H, *s*, –*CH*O); (in d_6-Me_2CO), 3.96 (1H, *q*, HO–C–*H*, J = 9, 2.5 Hz), 6.04 (1H, *dd*, >C=C<, *J* = 16, 9 Hz), 5.49 (1H, *dd*, >C=C<, *J* = 16, 9 Hz), 3.10 (1H, *dd*?, –O–*H*). NMR inspection and spin decoupling experiments of II showed that the compound contains HO–C(H)–C(H)=C–C(O)–C– group.

When II was acetylated with one mole of acetic anhydride, the 2′-monoacetate (VIII), $C_{44}H_{71}NO_{17}$, pKa′ 4.7, MS: *m/e* 885 (M^+), NMR: 2.06 (3H, *s*, –OAc), 4.02 (1H, *q*, HO–C–*H*) was obtained. An alternative acetylation of II with one mole of acetyl chloride gave the 9-monoacetate (IX), pKa′ 6.6, MS: *m/e* 885 (M^+).

Acetylation of VIII and IX led to the same diacetate $C_{46}H_{73}NO_{18}$ (VII), $[\alpha]_D^{29}$ –81.4° (c = 0.5 in EtOH), pKa′ 4.7, MS: *m/e* 927 (M^+), IR ($CHCl_3$): 3480 (–C–OH), 1240 (–OAc), NMR: 2.02, 2.04 (each 3H, *s*, –OAc).

On catalytic hydrogenation II gave tetrahydro II (X), $C_{42}H_{73}NO_{16}$, NMR: disappearance of olefinic protons of II at 5.5–6.3 ppm, and on acetylation X afforded the triacetate (XI), $C_{48}H_{79}NO_{19}$, IR ($CHCl_3$): 3500 (–C–OH), 1240 (–OAc), NMR: 2.00, 2.02, 2.06 (each 3H, *s*, –OAc).

Name		m.p. (decomp.)	$[\alpha]_D^{23}$ (c = 1.0 in EtOH)	MW[2] (VPO in EtOAc)	MS[2] *m/e* M^+	Mol. Formula	MIC[2] (mcg/ml)
Maridomycin I	(I)	129–132°	–72.3°	910	857	$C_{43}H_{71}NO_{16}$	0.5
Maridomycin II	(II)	134–136°	–71.9°	881	843	$C_{42}H_{69}NO_{16}$	0.5
Maridomycin III	(III)	135–138°	–76.0°	911	829	$C_{41}H_{67}NO_{16}$	1.0
Maridomycin IV	(IV)	143–146°	–76.2°	896	815	$C_{40}H_{65}NO_{16}$	2.0
Maridomycin V	(V)	144–149°	–73.6°	882	815	$C_{40}H_{65}NO_{16}$	5.0
Maridomycin VI	(VI)	149–154°	–77.7°	864	801	$C_{39}H_{63}NO_{16}$	5.0



Mild acid hydrolysis (0.05 $N \cdot HCl$) of II yielded (XII), $C_{42}H_{71}NO_{17}$, and acetylation of XII gave the tetraacetate (XIII), $C_{50}H_{79}NO_{21}$, NMR: 2.02, 2.06 (each 6H, *s*, —OAc), 5.6–6.1 (2H, *m*, $>C=C<^{H}_{H}$). On catalytic hydrogenation, XII took up one molar equivalent of hydrogen and the dihydro XII (XIV), $C_{42}H_{73}NO_{17}$, NMR: disappearance of olefinic protons, was obtained.

The existence of an aldehyde group in II was suggested from its NMR and was ascertained from the formation of the alcohol (XXIV) by $NaBH_4$ reduction, and the thiosemicarbazone (XXV), UV: λ^{EtOH}_{max} 270 nm, IR: 1595 (NH_2), 1520 (—C(=S)—N), NMR: 7.44 (1H, *t*, $-CH_2-CH=N-$).

Hydrolysis of II with 1 N KOH afforded one mole each of acetic and isovaleric acids. Hydrolysis of II with 0.5 N·HCl gave a lipophilic neutral sugar which was identified as 4—*O*—isovaleryl mycarose[4] (XVII) by comparison with authentic sample obtained from leucomycin A_3.

Methanolysis of II with MeOH—HCl yielded neutral sugars, which were further separated into α-methyl 4-*O*-isovaleryl-L-mycaroside[5] (XIX), MS: *m/e* 260 (M^+), $[\alpha]_D^{21}$ –151° (c=1.0 in $CHCl_3$) and β-methyl 4-*O*-isovaleryl-L-mycaroside[5] (XVIII), MS: *m/e* 260 (M^+), $[\alpha]_D^{21}$ +8.6° (c = 1.5 in $CHCl_3$). Both compounds were identified with authentic samples obtained from leucomycin A_3.

Acid hydrolysis of (X) under mild conditions gave demycarosyl tetrahydro II (XX), $C_{30}H_{53}NO_{12}$, $[\alpha]_D$ –19.9° (c = 1.0 in EtOH), NMR: 2.30 (3H, *s*, OAc), 2.50 (6H, *s*, $-N(CH_3)_2$), 3.55 (3H, *s*, $-OCH_3$), 3.90 (1H, *q*, —O—C—*H*), 4.44 (1H, *d*, H_1'a, J = 7Hz), 5.35 (1H, *m*, AcO—C_3—*H*), 9.62 (1H, *s*, —*CH*O).

Acetylation of XX afforded tetraacetyl demycarosyltetrahydro II (XXI), $C_{38}H_{61}NO_{16}$, MS: *m/e* 787 (M^+), NMR: 2.01 (9H, *s*, OAc), 2.04, (3H, *s*, OAc), IR ($CHCl_3$): absence of OH group.

Acid hydrolysis under vigorous condition (2N · HCl, reflux) of XX gave an aminosugar, mycaminose[6] (XXII), m.p. 113–115°, which was identical with an authentic sample obtained from leucomycin A_3.

Maridomycin II (II) was oxidized with CrO_3-pyridine complex or MnO_2 to dehydromaridomycin II (XXVI), m.p. 206–207 °C (decomp.), which was identical with authentic sample of carbomycin[7] in UV-, IR-, MS-, NMR-spectra, specific rotation and Rf values on TLC.

[1] Detailed microbiological and isolation studies will be published in J. Antibiotics (Tokyo).

[2] MW, molecular weight; VPO, vapour pressure osmometry in ethyl acetate; MS, mass spectrum; MIC, minimum inhibitory concentration against *Staphylococcus aureus* (mcg/ml); NMR, nuclear magnetic resonance spectrum in $CDCl_3$ (δ (ppm)); IR, infrared spectrum (KBr, cm^{-1}); UV, ultraviolet spectrum; TLC, thin layer chromatography (SiO_2).

[3] *s* = singlet, *d* = doublet; *dd* = double doublet; *t* = triplet; *q* = quartet; *oct* = octet; *m* = multiplet; J = coupling constant.

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[7] The authors are greatly indebted to Dr. F. A. Hochstein of Chas Phizer & Co., Inc., for valuable gifts of carbomycin and carbomycin B.

The structure of carbomycin has been elucidated by WOODWARD et al.[8].

From these findings, the structure of maridomycin II was determined to be II. Its absolute configuration, except for the C_9-hydroxyl group, was also clarified. Further treatment of XXVI with KI in AcOH yielded dehydrodeepoxymaridomycin II which was identical with carbomycin B[7] in all respects.

Zusammenfassung. Das aus *Streptomyces hygroscopicus* isolierte neue Makrolid Maridomycin II lässt sich mit Säure Mycarcose und Mycaminose spalten. Auf Grund der Oxidation ins Carbomycin sowie der spektroskopischen Daten wurde die Struktur als II erklärt.

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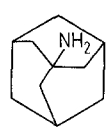
The Dissociation Constant of the 1-Aminoadamantane Cation

The pK value of 1-aminoadamantane (I) has not previously been reported. This omission is surprising in view of the unusual, diamond-like structure of this base and of the widespread interest in 1-aminoadamantane and its derivatives as antiviral and antitumour agents. From measurements of the enthalpy of sublimation, BRATTON and SZILARD[1] concluded that the structure of adamantane leads to a low strain energy, and this appears to be supported by the similarity of pK_a values for adamantane-1-carboxylic acid (6.81[2]) and cyclohexanecarboxylic acid (6.40[3]), measured in aqueous 50% ethanol at 25°.



(I)

On this basis, 1-aminoadamantane should be similar in strength to the corresponding alkyl analogues[4], 2-amino-2-methylpropane (pK_a = 10.68[5] at 25°) and 3-amino-3-ethylpentane (pK_a = 10.59[5]).

Solutions 0.005M in 1-aminoadamantane hydrochloride (Fluka *purum*, recrystallized from ethanol/ethyl ether) were titrated potentiometrically with 1M carbonate-free potassium hydroxide under nitrogen, using the procedure of ALBERT and SERJEANT[6]. The ionic strengths of the solutions were varied from 0.005 to 0.105 by adding potassium nitrate. Free hydroxyl ion concentrations were calculated from the measured pH values, using the ionic product of water and DAVIES' equation[7] to approximate the required activity coefficients at the specified ionic strengths. At each temperature and ionic strength, 9 points were taken covering the range from $^1/_{10}$ to $^9/_{10}$ neutralization, and the pK'_a values calculated for these points were averaged. (The maximum range in any set was within ±0.05 pH unit.) The resulting 'practical' pK_a values for 20° and 37° are given in the Table.

Extrapolation to zero ionic strength afforded thermodynamic pK_a values of 10.71±0.01 at 20° and 10.14±0.02 at 37°. For intermediate temperatures, values were 10.58 at 25°, 10.39 at 30° and 10.25 at 35°. A linear plot gave $-d(\mathrm{p}K_a)/dT = 0.034$, in good agreement with a predicted[8] value of 0.032.

The near-identity of pK_a values of 1-adamantane and 3-amino-3-ethylpentane supports the conclusion that there is little strain in this alicyclic molecule. Similar agreement is found for quinuclidine (10.58[9] or 10.95[10] at 25°) and its analogue, triethylamine (10.67[11] or 10.75[12] at 25°).

pKa' values

I =	0.005	0.010	0.015	0.030	0.055	0.105
20°	10.74	10.77	10.79	10.80	10.84	10.92
37°	10.12	10.21	10.23	10.26	10.30	10.34

Zusammenfassung. Der pK_a-Wert des 1-Aminoadamantan zwischen 20° und 37° wurde durch potentiometrische Messungen bestimmt.

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