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Erylusamines, IL-6 Receptor Antagonists, from the Marine Sponge, *Erylus placenta*[1]

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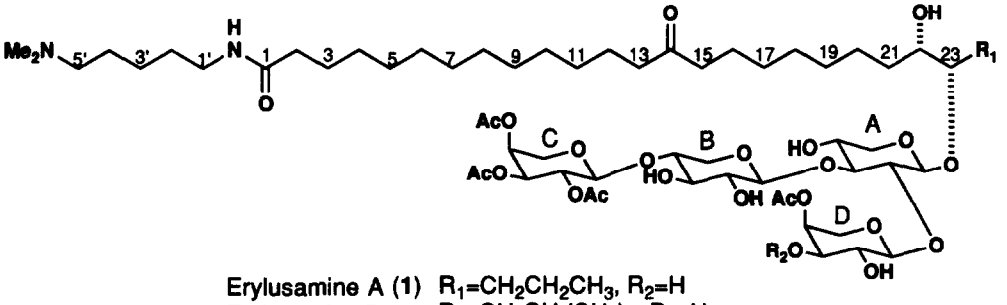
Abstract. Erylusamines A-E (**1-5**) have been isolated from the marine sponge *Erylus placenta*, as IL-6 receptor antagonists. Their gross structures were assigned by interpretation of 2D NMR and FABMS data as tetrasaccharides of long-chain dihydroxyketo-fatty acid amides formed with *N,N*-dimethyl-1,5-pentanediamine. Stereochemistry of **2** was established by spectroscopic and chemical methods.

Interleukin-6 (IL-6) is a multifunctional cytokine, which exhibits its function through binding with its specific receptor.[2] Abnormal production of IL-6 causes development of an autoimmune state such as rheumatoid arthritis or inflammation, whereas its constitutive production results in disease states of HTLV-1 or HIV infections. Therefore, inhibitors of IL-6 may be of potential therapeutical importance. In our screening for IL-6 antagonists from Japanese marine invertebrates, the extract of the sponge *Erylus placenta* collected off Hachijo-jima Island exhibited potent activity. The active fraction was comprised of a complex mixture of related metabolites from which we isolated erylusamines A-C (**1-3**). In addition, we obtained erylusamines C-E (**3-5**) from the same species collected in Miyazaki. In preliminary communication, we reported the structure of erylusamine B on the basis of spectral and chemical evidence.[3] The present paper deals with the isolation and gross structures of erylusamines A, C, D, and E, and the absolute stereochemistry of erylusamine B.



Erylusamine A (**1**) R_1=$CH_2CH_2CH_3$, R_2=H
Erylusamine B (**2**) R_1=$CH_2CH(CH_3)_2$, R_2=H
Erylusamine C (**3**) R_1=$CH_2CH(CH_3)_2$, R_2=Ac
Erylusamine D (**4**) R_1=$CH_2CH_2CH_2CH_3$, R_2=Ac
Erylusamine E (**5**) R_1=$CH_2CH_2CH_2CH_2CH_3$, R_2=Ac

A fraction rich in erylusamines, which was obtained from Sephadex LH-20 chromatography of the *n*-BuOH soluble portion of the alcoholic extract of *E. placenta*, gave multiple spots on silica gel TLC: spots with higher Rf values upon standing were converted to those with lower Rf values with decrease in the IL-6 binding inhibitory activity. Though the fraction gave broad spots with streaking on TLC when developed with neutral mobile phases, the spots became more discrete when NH_4OH was added to the mobile phase. Therefore, silica gel column chromatography was carried out with $CHCl_3$/MeOH/H_2O/conc. NH_4OH (8:2:0.1:0.1), followed by

quick work-up to obtain fractions giving a single spot on TLC, which were further purified by ODS HPLC with MeOH/H_2O/TFA (78:22:0.1) to yield erylusamines A (**1**, 1.0 x 10^{-5} % of wet sponge), B (**2**, 8.6 x 10^{-6} %), and C (**3**, 6.5 x 10^{-6} %). The Miyazaki collection was similarly processed to obtain erylusamines C (**3**, 5.3 x 10^{-6} %), D (**4**, 4.0 x 10^{-6} %), and E (**5**, 1.3 x 10^{-5} %).

Erylusamine A (**1**) was obtained as a colorless oil. The molecular formula of $C_{61}H_{106}N_2O_{24}$ was established by ^{13}C NMR and HRFABMS data. The only difference between the ^1H NMR spectra of **1** and **2** lay in the methyl signals: two doublets (δ 0.85 and 0.87) in **2** were replaced by a triplet (δ 0.83, J= 7.2 Hz) in **1**. The ^{13}C NMR spectrum revealed signals for an *n*-propyl unit (δ 34.2 t, 17.6 t, and 13.9 q) instead of an isobutyl unit (δ 42.0 t, 23.5 d, 21.5 q, and 21.5 q) in **2**. Therefore, erylusamine A was likely a C27-nor derivative of **2**. Interpretation of the COSY and HOHAHA spectra allowed assignments of four pentose units and an pentanediamine group. HMBC data further disclosed not only connectivities of 4 pentose units but also their linkage to an oxygenated methine (C-23, δ_C 84.5 d, δ_H 3.32 m). The chemical shifts and coupling constants suggested that the structure of the tetrasaccharide moiety in **1** was identical with that in **2**. The presence of an *N,N*-dimethyl-1,5-pentanediamine amide unit was also corroborated by HMBC data. The positions of a ketone and two oxygenated methines were deduced by positive FABMS data. Because of the presence of a dimethylamino group at the end of a long aliphatic chain, charge-remote fragmentations were observed in the FAB mass spectrum.[4] There was a large fragment ion at *m/z* 555 corresponding to the aglycone, together with prominent ions at *m/z* 481 and 325 which indicated the presence of 22,23-diol and 14-keto groups, respectively.

Erylusamine C (**3**) was obtained as a colorless oil with a molecular formula of $C_{64}H_{110}N_2O_{25}$ as determined by HRFABMS. The ^1H and ^{13}C NMR spectra were almost superimposable on those of **2** except for the presence of an additional acetyl group [δ_C 20.1 and 171.5; δ_H 2.01 (3H, s)] and a down-field shift of an oxygenated methine proton [δ 4.81 (dd, J=3.5, 10.3 Hz) vs. 3.61 (dd, J= 3.7, 9.8 Hz) in **2**]. This acetyl group was readily placed at C3 in sugar D by interpretation of the COSY and HOHAHA spectra. The structure of the rest of the molecule was confirmed from HMQC, HMBC, and FABMS data.

Erylusamine D (**4**) had a molecular formula of $C_{64}H_{110}N_2O_{25}$ as revealed by HRFABMS and NMR data. The ^1H NMR spectrum was very similar to that of **3** except for the presence of a primary methyl signal [δ 0.90 (3H, t, J=7.2 Hz)] instead of two secondary methyl signals, indicating that **4** was an isomer of **3** with a different alkyl terminal structure. The positions of a ketone and the two vicinal oxygenated methines were deduced from interpretation of fragment ions in the FABMS, whereas other structural features were confirmed by COSY data.

Erylusamine E (**5**) had a molecular formula of $C_{65}H_{112}N_2O_{25}$ as revealed by HRFABMS and NMR data. The ^1H NMR spectrum was very similar to that of **4**. The pseudomolecular ion of **5** was observed at *m/z* 1321 in the FAB mass spectrum, indicating that **5** was a homolog of **4** with a different alkyl chain at C23. The positions of a ketone and the two vicinal oxygenated methines were deduced from interpretation of fragment ions in the FABMS, whereas other structural features were confirmed by COSY, HOHAHA, HMQC, and HMBC data.

Stereochemistry of erylusamine B was determined as follows. Detailed analysis of ^1H-^1H coupling constants of the tetrasaccharide portion was carried out by proton non-decoupled HMQC [5] and decoupling difference experiments. All coupling constants except that between H3 and H4 in xylose A were determined. Although the two protons were in a crowded region, they exhibited coupling constants of 9.8 Hz and 8.9 Hz with other adjacent protons, thereby revealing that both protons were axial. Absolute stereochemistry of the sugars was determined by chiral GC analysis of the acid hydrolysate. The hydrolysate was converted to their

Table 1. ^{1}H NMR Data for Erylusamines A, B, C, and E

	Erylusamine A[a),c)]	Erylusamine B[b)]	Erylusamine C[a)]	Erylusamine E[b)]
2	2.12 (t, 7.7)	2.13 (t, 7.6)	2.11 (t, 7.2)	2.13 (t, 7.6)
3	1.55 m	1.56 m	1.53 m	1.55 m
4-11	1.23 brs	1.25 brs	1.24 brs	1.26 brs
12	1.50 m	1.52 m	1.49 m	1.51 (quint, 7.3)
13	2.36 (t, 7.4)	2.38 (t, 7.4)	2.36 (t, 7.2)	2.39 (t, 7.4)
15	2.36 (t, 7.4)	2.38 (t, 7.4)	2.36 (t, 7.2)	2.39 (t, 7.4)
16	1.50 m	1.52 m	1.49 m	1.51 (quint, 7.3)
17-20	1.23 brs	1.25 brs	1.24 brs	1.26 brs
21	1.30m	1.46 m	1.40 m	1.42 (q, 6.8)
22	3.34 m	3.35 m	3.30 m	3.41 (q, 6.3)
23	3.32 m	3.41 m	3.39 m	3.35 (q, 5.4)
24	1.47 m	1.19 m, 1.45 m	1.40 m, 1.16 m	1.53 m
25	1.34 m	1.80 m	1.70 m	1.26 brs
26	0.83 (t, 7.2)	0.85 (d, 6.5)	0.82 (d, 6.8)	1.26 brs
27		0.87 (d, 6.5)	0.85 (d, 6.8)	1.26 brs
28				0.85 (t, 7.2)
1'	3.14 (t, 7.2)	3.50 (t, 7.0)	3.16 (t, 6.8)	3.15 (t, 7.0)
2'	1.50 m	1.52 m	1.48 m	1.51 m
3'	1.34 m	1.38 m	1.34 m	1.35 m
4'	1.69 m	1.70 m	1.70 m	1.79 (quint, 7.9)
5'	3.00 (ddd, 8.4,5.9,1.8)	3.03 (ddd, 8.2,5.5,2.7)	3.00 (ddd, 8.0,5.1,1.0)	3.03 (t, 8.1)
5'NMeX2	2.80 s	2.81 s	2.80 s	2.82 s
1A	4.40 (d, 8.1)	4.40 (d, 7.1)	4.43 (d, 7.2)	4.41 (d, 7.3)
2A	3.54 m	3.57 (dd, 9.8, 7.1)	3.54 m	3.53 (dd, 9.0, 7.3)
3A	3.46 m	3.52 m	3.47 (t, 8.5)	3.54 (dd, 9.0, 9.0)
4A	3.55 m	3.64 m	3.57 m	3.57 m
5A	3.12 m	3.14 (dd, 11.8, 8.9)	3.12 m	3.15 m
	3.93 m	3.92 (dd, 11.9, 5.3)	3.92 m	3.94 (dd, 11.7, 5.4)
1B	4.46 (d,7.8)	4.52 (d, 7.8)	4.45 (d, 7.5)	4.50 (d, 7.1)
2B	3.31 (dd, 7.8, 9.0)	3.32 (dd, 9.2, 7.8)	3.33 m	3.32 (dd, 9.0, 7.1)
3B	3.41 (dd, 9.0, 9.0)	3.44 (dd, 9.0, 9.0)	3.45 (t, 8.5)	3.94 (dd, 9.0, 9.0)
4B	3.61 m	3.65 m	3.64 m	3.72 m
5B	3.94 (dd, 11.6, 5.5)	3.25 (dd, 11.6, 10.4)	3.24 (dd, 11.2, 4.0)	3.24 (dd, 11.3, 10.7)
	3.22 (dd, 11.6, 1.0)	3.98 (dd, 11.6, 5.4)	3.92 m	3.97 (dd, 11.3, 5.4)
1C	4.49 (d, 7.2)	4.57 (d, 7.4)	4.49 (d, 7.2)	4.56 (d, 7.1)
2C	5.09 (dd, 9.9, 7.2)	5.08 (dd, 9.8, 7.4)	5.08 (dd, 10.0, 7.2)	5.08 (dd, 9.8, 7.1)
3C	4.99 (dd, 9.9, 2.9)	5.03 (dd, 9.8, 3.5)	4.99 (dd, 10.0, 3.5)	5.02 (dd, 9.8, 3.2)
4C	5.23 brs	5.25 (ddd, 3.5,1.6,2.8)	5.23 brs	5.24 m
5C	3.69 (dd, 13.3, 1.5)	3.73 (dd, 13.3, 1.6)	3.68 m	3.72 (d, 12.9)
	4.03 (dd, 13.3, 2.6)	4.03 (dd, 13.3, 2.8)	4.02 (dd, 13.4, 2.4)	4.03 (dd, 12.9, 2.7)
1D	4.55 (d, 7.8)	4.60 (d, 7.7)	4.67 (d, 7.8)	4.71 (d, 7.9)
2D	3.52 (dd, 9.8, 7.8)	3.52 (dd, 9.8, 7.8)	3.65 m	3.66 (dd, 10.3, 7.9)
3D	3.57 (dd, 9.8, 4.0)	3.61 (dd, 9.8, 3.7)	4.81 (dd, 10.3, 3.5)	4.82 (dd, 10.3, 3.5)
4D	4.98 brs	4.98 (ddd, 3.7,2.2,1.8)	5.15 brs	5.16 m
5D	3.52 m	3.55 (dd, 13.3, 1.8)	3.63 m	3.64 (d, 13.2)
	3.94 m	3.94 (dd, 13.3, 2.2)	3.93 m	3.93 (dd,13.2, 1.9)
Ac	1.97 s	1.97s	1.98 s	1.96 s
Ac	2.03 s	2.03s	2.01 s	2.02 s
Ac	2.10 s	2.10s	2.03 s	2.05 s
Ac	2.11 s	2.10s	2.11 s	2.11 s
Ac			2.12 s	2.11 s

a) $CDCl_3$-CD_3OD (3:1)

b) $CDCl_3$-CD_3OD (1:1)

c) Coupling constants were determined by a measurement in $CDCl_3$-CD_3OD (1:1).

Table 2. ^{13}C NMR Data for Erylusamines A, B, C, and E

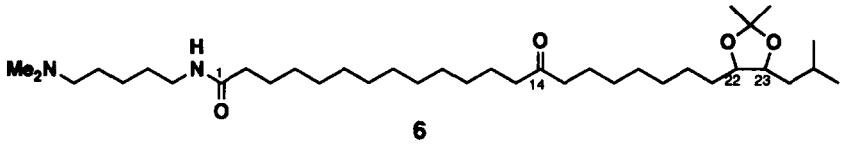
	Erylusamine A[a)]	Erylusamine B[b)]	Erylusamine C[a)]	Erylusamine E[b)]
1	174.8 s	173.0 s	174.8 s	176.0 s
2	36.1 t	37.0 t	36.2 t	37.0 t
3	25.6 t	25.0 t	25.6 t	26.7 t
4-11	29.0 t	29.0 t	29.0 t	30.0 t
12	23.5 t	22.5 t	23.5 t	24.5 t
13	42.6 t	43.5 t	42.5 t	43.3 t
14	213.0 s	212.0 t	212.8 s	214.1 s
15	42.6 t	43.5 t	42.5 t	43.3 t
16	23.5 t	22.5 t	23.5 t	24.5 t
17-20	29.0 t	29.0 t	29.0 t	30.0 t
21	32.0 t	33.0 t	33.0 t	33.5 t
22	73.2 d	74.1 d	74.2 d	74.1 d
23	84.5 d	85.4 d	82.5 d	85.7 d
24	34.2 t	42.0 t	41.8 t	26.4 t
25	17.6 t	23.5 d	23.0 d	30.0 t
26	13.9 q	21.5 q	20.0 q	30.0 t
27		21.5 q	21.5 q	30.0 t
28				14.3 q
1'	38.1 t	39.5 t	38.1 t	39.2 t
2'	29.0 t	29.0 t	28.0 t	30.0 t
3'	23.0 t	22.0 t	23.0 t	24.1 t
4'	23.5 t	23.0 t	23.5 t	25.0 t
5'	57.3 t	56.5 t	57.0 t	58.5 t
5'NMeX2	42.4 q	43.0 q	42.4 q	43.3 q
1A	103.6 d	104.0 d	103.3 d	104.5 d
2A	80.5 d	81.4 d	80.5 d	81.5 d
3A	86.1 d	86.8 d	86.0 d	86.8 d
4A	68.0 d	68.7 d	68.5 d	69.3 d
5A	64.9 t	65.7 t	65.0 t	65.8 t
1B	103.2 d	104.0 d	103.3 d	104.3 d
2B	73.0 d	73.0 d	73.0 d	74.3 d
3B	74.5 d	74.2 d	74.5 d	75.5 d
4B	78.0 d	77.9 d	77.0 d	79.5 d
5B	63.0 t	64.0 t	63.2 t	64.1 t
1C	100.4 d	101.0 t	100.9 d	101.0 d
2C	68.9 d	70.0 d	69.0 d	70.1 d
3C	70.0 d	71.2 d	70.1 d	71.3 d
4C	67.4 d	69.2 d	67.5 d	68.8 d
5C	62.7 t	64.5 t	63.9 t	64.4 t
1D	104.4 d	105.3 d	104.4 d	105.2 d
2D	72.0 d	72.9 d	69.5 d	70.5 d
3D	71.2 d	72.1 d	72.7 d	73.7 d
4D	70.6 d	71.9 d	63.5 d	69.5 d
5D	64.1 t	65.0 t	64.4 t	65.0 t
Ac	20.1 q, 170.0 s	20.9 q, 171.2 s	20.0 q, 170.6 s	21.9 q, 171.8 s
Ac	20.2 q, 169.5 s	20.9 q, 170.7 s	20.1 q, 171.5 s	22.0 q, 172.5 s
Ac	20.4 q, 170.0 s	21.0 q, 171.3 s	20.1 q, 168.0 s	22.0 q, 171.5 s
Ac	20.5 q, 171.2 s	21.0 q, 172.2 s	20.3 q, 172.8 s	22.1 q, 172.0 s
Ac			20.3 q, 174.0 s	22.1 q, 172.0 s

a) $CDCl_3$-CD_3OD (3:1)

b) $CDCl_3$-CD_3OD (1:1)

pertrifluoroacetyl methyl glycoside derivatives after defatting with EtOAc. Chiral GC analysis of the reaction mixture revealed the presence of L-Ara and D-Xyl.[6]

The EtOAc phase was treated with 2,2-dimethoxypropane/*p*-TsOH to afford an acetonide **6**, in which H22 and H23 resonated at δ 3.47 (dt, *J*= 3.0, 8.5 Hz) and 3.58 (dt, *J*= 3.5, 8.5 Hz), respectively. The absence of an NOE between H22 and H23 as well as a vicinal coupling constant of 8.5 Hz between the two protons suggested that they were *anti*. This was consistent with an empirical rule for assigning the stereochemistry of 1,2-acetonides by chemical shifts of methyl groups: both methyls in the isopropylidene unit in **6** resonated at δ 1.27 ppm.[7] Absolute stereochemistry at C22 and C23 was assigned by CD spectroscopy in the presence of $Eu(fod)_3$.[8] A negative exciton split ($[\theta]_{311}$ +5800, $[\theta]_{278}$ -4800) indicated 22*S*, 23*S*-stereochemistry.



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The acid hydrolysis product of a mixture of erylusamines contained only D-Ara and L-Xyl as analyzed by chiral GC, indicating that the configuration of the component sugar units in **1**, **3**, **4**, and **5** was identical with that of **2**. Stereochemistry of C22 and C23 in **1**, **3**, **4**, and **5** have not been determined.

Erylusamines B, C, D, and E inhibited the binding of IL-6 to its receptor [9] with IC_{50}'s of 66, 33, 37, and 17 μg / mL, respectively.

Experimental Section

Infrared spectra were recorded on a JASCO IR-G spectrometer. Optical rotations were determined with a JASCO DIP-140 polarimeter. ^1H, ^{13}C, ^1H-^1H COSY, HMQC, HOHAHA, HMBC, and NOESY spectra were measured on either Bruker AM-600, Bruker AC-300, or JEOL GSX-500 NMR spectrometers. Chemical shifts were referenced to solvent peaks: δ_H 3.30 and δ_C 49.0 for CD_3OD, δ_H 2.49 and δ_C 39.5 for DMSO-d_6. Mass spectra were recorded on a JEOL SX-102 mass spectrometer. High resolution FAB mass spectra were measured using a dual target sample inlet probe. Glycerol was used as a matrix in the FAB and HRFAB mass spectra. HMBC and HMQC spectra were recorded essentially as described in the literature.[10]

Extraction and Isolation: The frozen sponge (1.3 kg wet weight) collected off Hachijo-jima Island was extracted with EtOH (3 L x 3). The combined extracts were concentrated, adjusted to pH 9 with 1N NH_4OH, and extracted with Et_2O followed by *n*-BuOH. The *n*-BuOH soluble portion was concentrated *in vacuo* to yield a brown oil (10 g) which was gel-filtered on a Sephadex LH-20 column [$CHCl_3$-MeOH (1:1) containing 1% AcOH]. Active fractions were then fractionated on silica gel [$CHCl_3$-MeOH-H_2O-25 % aq NH_4OH (8:2:0.1:0.1)] followed by HPLC on ODS [MeOH-H_2O-TFA (78:22:0.1)] to yield erylusamines A (14.5 mg), B (11.2 mg), and C (8.4 mg). The same species (1.0 kg) collected off Nichinan-Oshima Island, Miyazaki, 1650 km southwest of Tokyo, was extracted with EtOH (3 L x 3). The combined extracts were concentrated and extracted with Et_2O followed by *n*-BuOH. The MeOH soluble portion of the *n*-BuOH layer was gel-filtered on Sephadex LH-20 / MeOH: active fractions were purified on silica gel [$CHCl_3$-MeOH-H_2O-25 % aq NH_4OH (8:2:0.1:0.1)] followed by HPLC on ODS [MeOH-H_2O-TFA (80:20:0.05)] to afford erylusamines C (5.3 mg), D (4.0 mg), and E (13.6 mg).

Erylusamine A (1): colorless oil, $[\alpha]_D^{20}$ -3.5° (*c* 0.12, MeOH); IR (film) : ν_{max} 3350, 2920, 2885, 1740, 1670, 1450, 1365, 1225, 1195, 1170, 1125, 1080, 1050 cm^{-1}; FABMS : *m/z* 1251$(M+H)^+$, 555, 537, 481, 381, 353, 325, 311, 297, 283, 269, 259, 255, 157; HRFABMS : found $(M+H)^+$ *m/z* 1251.7209 $C_{61}H_{107}O_{24}N_2$ (Δ -0.4 mmu).

Erylusamine C (3): colorless oil, $[\alpha]_D^{20}$ -9.6° (*c* 0.33, MeOH); IR (film) : ν_{max} 3380, 2940, 2800, 1745, 1732, 1672, 1540, 1462, 1370, 1248, 1220, 1170, 1048, 1130, 1085, 1050 cm^{-1}; FABMS : *m/z* 1307 $(M+H)^+$, 569, 551, 481, 353, 325, 311, 297, 283, 269, 259, 255, 157; HRFABMS : found $(M+H)^+$ *m/z* 1307.7478 $C_{64}H_{111}O_{25}N_2$ (Δ +0.2 mmu).

Erylusamine D (4): colorless oil: $[\alpha]_D^{20}$ -6.0° (*c* 0.10, MeOH); ^{1}H NMR (CD_3OD) : 5.25 (1H, m, H-4C), 5.18 (1H, m, H-4D), 5.09 (1H, dd *J*=9.8 Hz, 3.3, H-3C), 5.06 (1H, dd, *J*=9.8, 6.9 Hz, H-2C), 4.86 (1H, dd, *J*=10.2, 3.5 Hz, H-3D), 4.81 (1H, brd, H-1D), 4.67 (1H, d, *J*=6.9 Hz, H-1C), 4.59 (1H, d, *J*=7.7 Hz, H-1B), 4.46 (1H, d, *J*=7.1 Hz, H-1A), 4.03 (1H, dd, *J*=11.8, 5.4 Hz, Heq-5B), 4.02 (1H, dd, *J*=12.5, 2.6 Hz, Ha-5C), 3.92 (1H, dd, *J*=13.5, 2.0 Hz, Ha-5D), 3.89 (1H, dd, *J*=12.4, 5.2 Hz, Heq-5A), 3.77 (1H, d, *J*=12.5 Hz, Hb-5C), 3.72 (1H, d, *J*=13.5 Hz, Hb-5D), 3.67 (1H, m, H-4B), 3.66 (1H, m, H-2D), 3.61 (1H, m, H-3A), 3.59 (1H, m, H-2A), 3.55 (1H, ddd, *J*=10.0, 9.5, 5.2 Hz, H-4A), 3.43 (1H, t, *J*=9.1 Hz, H-3B), 3.43 (1H, m, H-23), 3.29 (1H, m, H-22), 3.28 (1H, m, H-2B), 3.25 (1H, t, *J*=11.8 Hz, Hax-5B), 3.20 (1H, dd, *J*=12.4 Hz, 9.5, Hax-5A), 3.18 (2H, t, *J*=7.0 Hz, H-1'), 3.10 (2H, t, *J*=8.0 Hz, H-5'), 2.87 (6H, s, NMe2), 2.43 (4H, t *J*=7.3 Hz, H-13, H-15), 2.16 (2H, t, *J*=7.5 Hz, H-2), 2.10 (6H, s, acetyl), 2.04 (3H, s, acetyl), 2.02 (3H, s, acetyl), 1.96 (3H, s, acetyl), 1.73 (2H, quint, *J*=8.0 Hz, H-4'), 1.60 (2H, m, H-3), 1.56 (2H, m, H-2'), 1.55 (4H, quint, *J*=7.3 Hz, H-12, H-16), 1.48 (2H, m, H-24), 1.39 (2H, m, H-3'), 1.30 (2H, m, H-26), 1.28 (28H, br, H4-11, H-17-20, H-25-26), 0.90 (3H, t, *J*=7.2 Hz, H-27); FABMS : *m/z* 1307 $(M+H)^+$, 569, 481, 451, 437, 423, 409, 353, 325, 311, 297, 283, 269, 259, 255, 157; HRFABMS : found $(M+Na)^+$ *m/z* 1329.7358 $C_{64}H_{110}O_{25}N_2Na$ (Δ +6.3 mmu).

Erylusamine E (5): colorless oil; $[\alpha]_D^{20}$ -8.0° (*c* 0.19, MeOH); IR (film) : ν_{max} 3430, 2925, 2855, 1742, 1678, 1550, 1463, 1370, 1230, 1200, 1175, 1135, 1090, 1050, 835, 800, 720 cm^{-1}; FABMS : *m/z* 1321 $(M+H)^+$, 583, 481, 451, 437, 423, 409, 353, 325, 311, 297, 283, 269, 259, 255, 157; HRFABMS : found $(M+H)^+$ *m/z* 1321.7693 $C_{65}H_{113}O_{25}N_2$ (Δ +6.0mmu).

Acid hydrolysis of erylusamine B: A portion of erylusamine B (2.3 mg) was dissolved in 2N HCl (2 mL) and kept at 80°C for 2h. The reaction mixture was evaporated to dryness and partitioned between H_2O and EtOAc, both layers were evaporated to obtain a mixture of monosaccharides and the diol, respectively.

Chiral gas chromatography: A mixture of monosaccharides was methylated with MeOH containing 10% HCl (1 mL) at 100°C for 1h. After removal of the methanolic HCl *in vacuo*, ethyl trifluoroacetate (0.5 mL) and trifluoroacetic anhydride (0.3 mL) were added to the mixture which was heated at 100°C for 5 min. The reaction mixture was evaporated, dissolved in acetone (0.5 mL), and subjected to GC analysis. Chiral GC was carried out by using a Chirasil-L-Val capillary column (CHROMPACK, 0.25 mm x 25 m). Retention times (min): 8.3 (D-Xyl), 9.3 (L-Ara), 12.7 (D-Xyl), 13.2 (L-Ara).

Acetonide 6: The EtOAc layer of the acid hydrolysate (3.4 mg) containing the diol was converted to the HCl salt by lyophilization after being dissolved in 0.1N HCl (0.5 mL) and treated with 2,2-dimethoxypropane (2 ml) and *p*-TsOH (cat.). The reaction mixture was partitioned between H_2O and EtOAc; the EtOAc layer was purified by preparative TLC on silica gel ($CHCl_3$-MeOH-H_2O-25 % aq NH_4OH 8:2:0.1:0.1) to affored **6** (1.2 mg).

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