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Caprazamycins, Novel Lipo-nucleoside Antibiotics, from *Streptomyces* sp.

II. Structure Elucidation of Caprazamycins

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Abstract Novel antibiotics, active against acid-fast bacteria, caprazamycins, were isolated from the culture broth of *Streptomyces* sp. MK730-62F2. The planar structures of the compounds were determined by 2D NMR spectroscopic study. Furthermore, the absolute structure of caprazamycin B (**2**) was established by NMR spectroscopy and X-ray crystallography of its degradation products and by total synthesis of the 5-amino-5-deoxy-D-ribose moiety. In the course of degradation studies of **2** under alkaline and acidic conditions, we obtained the two core components, caprazene (**11**) and caprazol (**14**), respectively, in high yield.

Structurally, caprazamycins belong to a family of lipo-uridyl antibiotics, which have been discovered as specific inhibitors of a bacterial translocase.

Keywords caprazamycin, antituberculous antibiotics, absolute structure, caprazol, caprazen

Introduction

Caprazamycins (CPZs, Fig. 1) are novel lipo-nucleoside antibiotics, produced by *Streptomyces* sp. MK730-62F2.

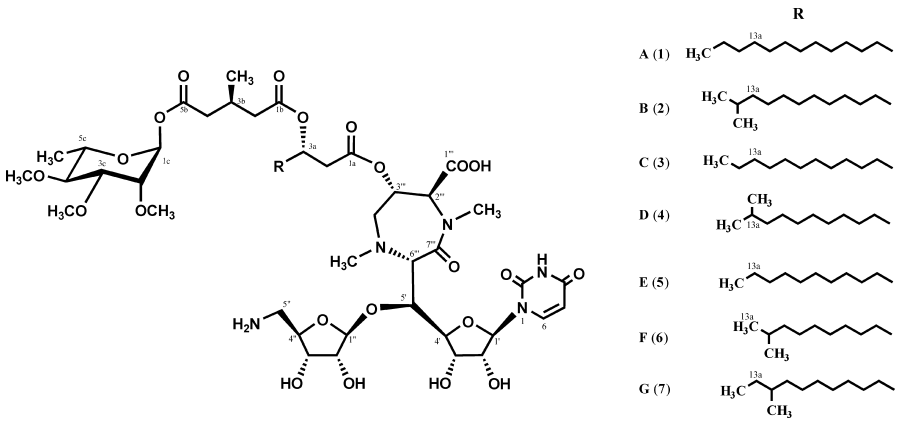

Fig. 1 Structures of caprazamycins.

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They show activity against acid-fast bacteria including *Mycobacterium tuberculosis* and *M. avium* complex (MAC). A taxonomic study and fermentation of the producing strain together with the isolation and biological activities of CPZs have been reported in the preceding papers [1～3].

In this paper, we report the physico-chemical properties, degradation studies and structural elucidation of CPZs. Anti-*M. tuberculosis* activities, anti-MAC activities and therapeutic efficacy of the compounds in a murine pulmonary tuberculosis model will be described in a separate paper [4].

Results and Discussion

Structure Determination

The physico-chemical properties of CPZ-A, B, C, D, E, F and G (**1**, **2**, **3**, **4**, **5**, **6** and **7**) are summarized in Table 1. The molecular formulae of **1**, **2**, **3**, **4**, **5**, **6** and **7** were established as $C_{53}H_{87}N_5O_{22}$, $C_{53}H_{87}N_5O_{22}$, $C_{52}H_{85}N_5O_{22}$, $C_{52}H_{85}N_5O_{22}$, $C_{51}H_{83}N_5O_{22}$, $C_{51}H_{83}N_5O_{22}$ and $C_{52}H_{85}N_5O_{22}$, respectively, on the basis of HR-FAB-MS and NMR spectral analyses. The characteristic UV absorptions at 261～262 nm in methanol and the NMR spectra of CPZs suggested the presence of uridyl moiety in the molecules. The ^{13}C NMR data of CPZs are shown in Table 2. The multiplicity of carbon signals was determined by DEPT experiments. The ^{1}H and ^{13}C NMR spectra of CPZs showed similar signal patterns, except for those of the acylated side chain moiety. The DEPT and HMQC (heteronuclear multiple quantum coherence) spectra of **2** revealed the presence of nine methyl, fourteen methylene, twenty two methine groups and seven carbonyl carbons. Of the twenty two methine groups, two were presumed to be olefinic and three anomeric. The ^{1}H and ^{13}C NMR data (Table 3) of **2** were similar to those of liposidomycins [5] except for signals assigned to the sugar portion.

The ^{1}H-^{1}H COSY and HMBC (hetero nuclear multiple bond correlation) spectra suggested that **2** contained five partial structures (**a**, **b**, **c**, **d** and **e**) and two *N*-CH_3 groups as shown in Fig. 2. The ^{13}C-^{1}H couplings of ^{2}J and ^{3}J observed in the HMBC experiments gave the following evidence. The cross peaks from δ 8.07 (6-H) to δ 150.7 (C-2), δ 163.9 (C-4) and δ 90.2 (C-1′), from δ 4.15 (6″-H) to δ 170.8 (C-7‴) supported partial structure **a**. The cross peak from δ 5.62 (1″-H) to δ 79.1 (C-4″) supported partial structure **b**. The cross peak from δ 4.94 (2‴-H) to δ 170.8 (C-1‴) supported partial structure **c**. The cross peaks from δ 5.48 (3a-H) to δ 169.7 (C-1a) and δ 171.7 (C-1b), from δ 2.62 (2b-H) to δ 171.7 (C-1b), and from δ 2.64 and 2.47 (4b-H) to δ 171.0 (C-5b) supported partial structure **d**. Moreover, the cross peaks from δ 6.34 (1c-H) to δ 70.2 (C-5c), from δ 3.50 (2c-OCH_3) to δ 76.0 (C-2c), from δ 3.53 (3c-OCH_3) to δ 80.9 (C-3c) and from δ 3.56 (4c-OCH_3) to δ 81.6 (C-4c) supported partial structure **e**.

The connections between the five partial structures (**a**, **b**, **c**, **d** and **e**) and two *N*-CH_3 groups were revealed by the HMBC spectrum as shown in Fig. 3. The anomeric proton at δ 5.62 (1″-H) was coupled with the methine carbon bearing an oxgen atom at δ 76.2 (C-5′). The methine proton bearing an oxgen atom at δ 5.75 (3‴-H) was coupled with the carbonyl carbon at δ 169.7 (C-1a). The anomeric proton at δ 6.34 (1c-H) of the sugar moiety **e** was coupled with the carbonyl carbon at δ 171.0 (C-5b). The *N*-methyl protons at δ 2.72 (5‴-*N*CH_3) were coupled with the methine carbon at δ 63.8 (C-6‴) and the methylene carbon at δ 57.1 (C-4‴). Moreover, the *N*-methyl protons at δ 3.35 (8‴-*N*CH_3) were coupled with the methine carbon at δ 63.9 (C-2‴) and the carbonyl carbon at δ 170.8 (C-7‴). Based on the above observations, the planar structure of caprazamycin B (**2**) was elucidated as shown in Fig. 3.

Stereochemistry of Caprazamycin B

The absolute structure of **2** was determined by NMR spectroscopy and X-ray crystallography of its degradation products, including the two core components.

Acid hydrolysis of **2** with 80% trifluoroacetic acid in methanol at room temperature gave the aglycone, designated as caprazamycin B1 (**8**) and 2,3,4-tri-*O*-methyl-L-rhamnose (**9**) in high yield, respectively (Scheme 1). To ascertain the L-rhamnose structure of **9**, the sugar was converted to the known methyl glycosides. Treatment of **9** with acidic methanol at 50°C gave a mixture of the α-glycoside, methyl 2,3,4-tri-*O*-methyl-α-L-rhamnopyranoside (**10a**), and its β-anomer **10b**. Isolation of the anomeric mixture by column chromatography gave **10a** as a syrup, of which the physico-chemical properties were identical with those of the authentic sample [6～8]. The glycosidic linkage of L-rhamnose to caprazamycin B (**2**) was deduced from the ^{13}C-NMR spectra. The $^{1}J_{C-H}$ coupling constant (167 Hz) of the anomeric carbon of α-glycoside **10a** was larger than those of the β-anomer **10b** ($^{1}J_{C-H}$=153 Hz). On the other hand, the anomeric carbon of 2,3,4-tri-*O*-methylated rhamnose in **2** showed a larger value ($^{1}J_{C1c-H1c}$=174 Hz, in dimethylsulfoxide-d_6). Because it is known that introduction of an acyl group instead of a methoxyl group at an anomeric position increases the $^{1}J_{C-H}$ values to some extent [9], the mode of sugar linkage in **2** is regarded as α.

Further hydrolysis of **8** with 80% aqueous acetic acid at 70°C gave the unsaturated compound **11**, designated as

Table 1 Physico-chemical properties of CPZs

	Caprazamycin A (**1**)	Caprazamycin B (**2**)	Caprazamycin C (**3**)	Caprazamycin D (**4**)
Appearance	colorless powder	colorless powder	colorless powder	colorless powder
Molecular formula	$C_{53}H_{87}N_5O_{22}$ [obsd. 1146.5933 $(M+H)^+$, error +1.2]	$C_{53}H_{87}N_5O_{22}$ [obsd. 1144.5750 $(M-H)^-$, error −1.4]	$C_{52}H_{85}N_5O_{22}$ [obsd. 1132.5747 $(M+H)^+$,error −1.7]	$C_{52}H_{85}N_5O_{22}$ [obsd. 1132.5747 $(M+H)^+$, error −1.7]
FAB-MS (*m/z*)	1146 $(M+H)^+$ 1144 $(M-H)^-$	1146 $(M+H)^+$ 1144 $(M-H)^-$	1132 $(M+H)^+$ 1130 $(M-H)^-$	1132 $(M+H)^+$ 1130 $(M-H)^-$
$[\alpha]_D^{23}$	−1.4 (*c* 0.83, DMSO)	−2.6 (*c* 0.91, DMSO)	−1.1 (*c* 1.33, DMSO)	−3.0 (*c* 1, MeOH)
UV λ_{max}^{MeOH} nm(ε)	261 (7,400)	262 (8,000)	261 (8,300)	262 (9,200)
0.03 M HCl-MeOH	260 (7,200)	262 (7,800)	261 (8,200)	261 (8,900)
0.03 M NaOH-MeOH	261 (5,600)	262 (6,400)	260 (6,400)	260 (7,300)
IR ν_{max} (KBr) cm^{-1}	3421, 2925, 2854, 1740, 1697 (sh), 1675, 1635 (sh), 1269, 1466, 1387, 1268, 1124, 1103	3400, 2925, 2854, 1739, 1701 (sh), 1674, 1635 (sh),1467, 1386, 1193, 1126, 1001	3421, 2925, 2854, 1739, 1697 (sh), 1675, 1637 (sh), 1465, 1386, 1268, 1124, 1103	3426, 2925, 1736 (sh), 1677, 1641 (sh), 1466, 1389, 1203, 1192, 1132, 1103, 1009
Color reaction positive:	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid
Silica gel TLC	Rf 0.19* Rf 0.04** Rf 0.44***	Rf 0.19* Rf 0.04** Rf 0.44***	Rf 0.19* Rf 0.04** Rf 0.44***	Rf 0.19* Rf 0.04** Rf 0.44***

	Caprazamycin E (**5**)	Caprazamycin F (**6**)	Caprazamycin G (**7**)
Appearance	colorless powder	colorless powder	colorless powder
Molecular formula	$C_{51}H_{83}N_5O_{22}$ [obsd. 1118.5613 $(M+H)^+$, error +0.5]	$C_{51}H_{83}N_5O_{22}$ [obsd. 1118.5615 $(M+H)^+$, error +0.7]	$C_{52}H_{85}N_5O_{22}$ [obsd. 1132.5747 $(M+H)^+$, error −1.7]
FAB-MS (*m/z*)	1118 $(M+H)^+$ 1116 $(M-H)^-$	1118 $(M+H)^+$ 1116 $(M-H)^-$	1132 $(M+H)^+$ 1130 $(M-H)^-$
$[\alpha]_D^{23}$	−5.1 (*c* 0.83, DMSO)	−4.7 (*c* 0.90, DMSO)	−4.2 (*c* 1, MeOH)
UV λ_{max}^{MeOH} nm (ε)	262 (7,700)	262 (7,600)	262 (9,000)
0.03 M HCl-MeOH	262 (7,500)	262 (7,400)	261 (8,600)
0.03 M NaOH-MeOH	261 (5,900)	261 (5,800)	260 (7,000)
IR ν_{max} (KBr) cm^{-1}	3421, 2925, 2854, 1739, 1697, 1675 (sh), 1629, 1465, 1386, 1268, 1124, 1103	3450, 2929, 2856, 1737, 1704, 1631, 1465, 1386, 1268, 1122, 11031	3423, 2929, 2854, 1738, 1680, 1637 (sh), 1466, 1392, 1271, 1203, 1184, 1132, 1009
Color reaction positive:	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid	I_2, vanillin-sulfuric acid molybdophosphoric acid-sulfuric acid
Silica gel TLC	Rf 0.19* Rf 0.04** Rf 0.44***	Rf 0.19* Rf 0.04** Rf 0.44***	Rf 0.19* Rf 0.04** Rf 0.44***

* Kieselgel 60 F_{254}, art 5715, Merck ($CHCl_3$: MeOH : H_2O : formic acid=10 : 5 : 1 : 0.1), ** ($CHCl_3$: MeOH : H_2O : conc NH_4OH=10 : 5 : 1 : 0.1), *** (BuOH : MeOH : H_2O=4 : 1 : 2)

caprazene, and the diacid **12** in high yield, respectively. The core component **11** was also obtained quantitatively by direct hydrolysis of **2** under the same conditions. The two carboxyl groups of **12** were treated with 4-bromoaniline in the presence of bis(2-oxo-3-oxazolidinyl)phosphinic chloride (BOP-Cl) to give the bromoanilide **13** in 70% yield, which was crystallized from its acetone solution. The ORTEP drawing of **13** is shown in Fig. 4. On the basis of

Table 2 ^{13}C NMR data of CPZs (125 MHz)

1* δ	**2**** δ	**3*** δ	**4*** δ	**5**** δ	**6*** δ	**7*** δ
13.9 q	17.8 q	13.9 q	18.2 q	14.1 q	17.7 q	11.8 q
17.7 q	19.2 q	17.7 q	20.2 q	17.9 q	19.0 q	18.2 q
19.0 q	22.6 q	19.0 q	23.0 q	19.3 q	22.5 q	19.6 q
22.1 t	22.6 q	22.1 t	23.0 q	22.3 t	24.5 t	20.1 q
24.5 t	24.6 t	24.5 t	26.3 t	24.7 t	26.7 t	26.3 t
27.1 d	26.9 t	27.1 d	28.5 t	28.8 t	27.4 t	28.2 t
28.6 t	27.2 d	28.7 t	30.4 d	27.3 d	27.1 d	28.8 d
28.7 t	27.5 d	28.6 t	28.7 d	29.0 t	28.7 t	30.4 d
28.7 t	28.7 t	28.7 t	29.1 t	28.8 t	28.6 t	30.6 t
28.8 t	28.9 t	28.9 t	30.6 t	29.0 t	28.9 t	30.6 t
28.9 t	29.0 t	29.0 t	30.6 t	29.1 t	28.9 t	30.7 t
28.9 t	29.1 t	29.0 t	30.8 t	29.1 t	29.0 t	31.0 t
29.0 t	29.1 t	29.0 t	31.0 t	31.5 t	29.2 t	35.2 t
29.0 t	29.4 t	31.3 t	35.3 t	33.4 t	33.2 t	35.7 t
31.2 t	33.3 t	33.2 t	39.0 q	36.1 q	36.2 q	37.6 q
33.2 t	36.1 q	35.8 q	39.3 q	37.6 q	37.7 q	37.8 q
35.8 q	37.5 q	37.3 q	40.2 t	38.8 t	38.4 t	38.6 t
37.3 q	38.6 t	38.6 t	40.3 t	40.2 t	38.8 t	40.3 t
38.6 t	38.7 t	40.0 t	41.4 t	40.2 t	40.0 t	41.4 t
40.0 t	39.5 t	40.0 t	41.6 t	40.3 t	40.1 t	41.7 t
40.0 t	40.2 t	40.1 t	42.6 t	56.7 t	40.1 q	42.1 t
40.2 t	40.4 t	56.5 t	58.0 t	56.9 q	56.5 d	58.0 t
56.5 t	56.7 t	56.7 q	59.0 q	58.5 q	56.7 d	58.0 q
56.6 q	56.8 q	58.3 q	59.3 q	60.3 q	58.3 d	59.3 q
58.3 q	58.5 q	60.1 q	61.2 q	63.1 d	60.1 d	61.2 q
60.1 q	60.2 q	62.9 d	64.3 d	63.2 d	62.6 d	64.8 d
62.9 d	62.9 d	63.0 d	64.7 d	69.0 d	68.9 d	65.0 d
63.0 d	63.0 d	68.8 d	69.9 d	69.7 d	69.5 d	70.7 d
68.8 d	68.9 d	69.5 d	70.6 d	70.0 d	69.9 d	71.4 d
69.5 d	69.6 d	69.8 d	71.3 d	70.4 d	72.2 d	71.9 d
69.8 d	69.9 d	74.1 d	75.2 d	70.3 d	70.2 d	75.7 d
70.3 d	70.0 d	70.2 d	71.9 d	74.5 d	74.4 d	72.2 d
70.3 d	70.3 d	70.2 d	72.2 d	74.2 d	74.3 d	72.4 d
74.2 d	74.2 d	74.5 d	75.7 d	75.3 d	76.5 d	76.4 d
74.5 d	74.5 d	78.2 d	80.8 d	75.2 d	75.1 d	80.2 d
75.1 d	75.1 d	75.1 d	75.9 d	80.2 d	80.1 d	77.2 d
75.1 d	75.3 d	75.1 d	77.4 d	78.3 d	78.3 d	77.4 d
78.2 d	78.3 d	80.1 d	82.1 d	81.1 d	80.9 d	82.1 d
80.1 d	80.2 d	80.9 d	82.8 d	82.3 d	83.0 d	82.8 d
80.8 d	81.0 d	82.0 d	83.8 d	89.4 d	88.9 d	83.9 d
82.1 d	82.2 d	89.2 d	92.3 d	90.7 d	90.5 d	92.3 d
89.2 d	89.3 d	90.5 d	92.9 d	101.3 d	101.1 s	92.5 d
90.4 d	90.6 d	101.1 d	102.8 d	110.2 d	110.0 s	102.2 d
101.1 d	101.3 d	110.1 d	110.8 d	140.0 d	140.2 s	111.9 d
110.1 d	110.1 d	139.7 d	142.8 d	150.4 s	150.3 s	142.4 d
139.7 d	139.9 d	150.2 s	152.1 s	163.6 s	163.3 s	152.0 s
150.2 s	150.3 s	163.3 s	166.1 s	169.3 s	169.2 s	166.2 s
163.2 s	163.5 s	169.0 s	168.0 s	169.8 s	169.2 s	171.0 s
169.0 s	169.1 s	169.7 s	170.1 s	170.1 s	170.2 s	171.0 s
169.7 s	169.6 s	170.0 s	170.4 s	170.6 s	170.4 s	172.3 s
170.1 s	170.0 s	170.3 s	172.3 s	171.5 s	171.1 s	172.3 s
170.2 s	170.5 s	171.2 s	173.7 s	172.3 s		173.6 s
171.2 s	171.4 s					

* DMSO-d_6, ** DMSO-d_6 - D_2O (10 : 1)

X-ray structure analysis of **13**, the configurations at C-3a and C-3b of caprazamycin B (**2**) were determined to be *S* and *S*, respectively.

Alkaline degradation studies of **2** also gave another core component. Treatment of **2** with aqueous ammonia in *N*,*N*-dimethylformamide for **4** days at room temperature gave the deacylated compound **14** quantitatively, which was designated as caprazol (Scheme 2). Crystallization of **14** from aqueous methanol afforded prisms suitable for X-ray structure analysis. The ORTEP drawing of caprazol (**14**) is shown in Fig. 5. To elucidate the absolute structure of the ribose moiety of **2**, the reference methyl 5-amino-5-deoxy-α- and β-D-ribofuranosides (**18a** and **18b**) were prepared from 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribose (**15**) [10] in two steps (Scheme 3). Methanolysis of **15** in the presence of cation-exchange resin gave an anomeric mixture (1 : 2.9) of methyl glycosides (**16a** and **16b**) in 63% yield, along with methyl 5-azido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (**17**) [10, 11]. Treatment of a mixture of **16a** and **16b** with triphenylphospine in aqueous tetrahydrofuran gave an anomeric mixture of the free amino sugars (**18a** and **18b**), quantitatively. Separation of these anomers was successfully performed by silica gel column chromatography.

On the other hand, caprazene (**11**) was solvolyzed in boiling methanol in the presence of cation-exchange resin for 14 hours to give a mixture (1 : 2.2) of **18a** and **18b** in 51% yield. The β-glycoside **18b** isolated, was in all respects identical with the reference sample prepared from **15**. The agreement on the specific rotation value between the both compounds proved that the 5-amino-5-deoxy-ribose moiety in caprazamycin B (**2**) is the D-sugar.

Finally, based on the results described above, the stereochemistry of **2** was established to be C-5′ (*S*), C-2‴ (*S*), C-3‴ (*S*), C-6‴ (*S*), C-3a (*S*) and C-3b (*S*) as shown in Fig. 1.

The CPZs are structurally related to lipo-uridyl antibiotics such as liposidomycins, muraymycins [12] and capuramycins [13～15], which have been shown to be specific inhibitors of a bacterial translocase. Liposidomycins are especially, close analogs of CPZs, differing in the absence of the tri-*O*-methyl-L-rhamnose moiety and the dissimilarity for configuration of the acylated side chain at the C-3a position [5]. These nucleoside antibiotics comprise a novel type of drugs having the inhibitory activity against bacterial cell wall biosynthesis.

In the degradation studies of caprazamycins, we obtained efficiently the two core components, caprazene (**11**) and caprazol (**14**). These compounds were considered to be attractive precursors for the synthesis of caprazamycin analogs. Semi-synthetic antibiotics derived from **11** or **14** and their biological activities will be reported later.

Table 3 ^{13}C and ^{1}H NMR data of caprazamycin B (**2**) in DMSO-d_6 - pyridine-d_5 - D_2O (5 : 5 : 1)

No.	δ_C*	δ_H**	*J* (Hz)	No.	δ_C*	δ_H**	*J* (Hz)
2	150.7 s			6a***	29.5 t	2.61 m	
4	163.9 s			7a***	29.5 t	2.61 m	
5	101.7 d	5.97 d	8	8a***	29.4 t	2.61 m	
6	140.0 d	8.07 d	8	9a***	29.4 t	2.61 m	
1′	90.2 d	5.84 d	1	10a***	29.2 t	2.61 m	
2′	75.4 d	4.32 dd	1, 4	11a	29.8 t	2.61 m	
3′	69.7 d	4.37 dd	4, 8	12a	27.3 t	1.26 m	
4′	83.0 d	4.77 dd	2, 4	13a	38.6 t	1.13 m	
5′	76.2 d	4.71 dd	2, 9	14a	27.8 d	1.48 m	
1″	111.1 d	5.62 s	~1	14a-Me	22.6 q	1.86 d	6
2″	75.1 d	4.43 d	4	15a	22.6 q	1.86 d	6
3″	71.0 d	4.65 dd	4, 8	1b	171.7 s		
4″	79.1 d	4.53 ddd	4, 4, 8	2b	40.5 t	2.62 m	
5″	40.5 t	3.49 m				2.4 dd	7, 14
1‴	170.8 s			3b	27.6 d	2.61 m	
2‴	63.9 d	4.94 d	4.5	3b-Me	19.4 q	1.11 d	5
3‴	71.4 d	5.75 m		4b	40.6 t	2.64 m	
4‴	57.1 t	3.83 m				2.47 dd	7, 14
		3.68 m		5b	171.0 s		
5‴-*N*Me	36.4 q	2.72 s		1c	91.2 d	6.34 d	2
6‴	63.8 d	4.15 d	9	2c	76.0 d	3.83 m	
7‴	170.8 s			2c-OMe	57.1 q	3.50 s	
8‴-*N*Me	37.9 q	3.35 s		3c	80.9 d	3.67 dd	3, 9
1a	169.7 s			3c-OMe	58.8 q	3.53 s	
2a	39.2 t	2.88 m		4c	81.6 d	3.33 dd	9, 9
3a	70.5 d	5.48 m		4c-OMe	60.5 q	3.56 s	
4a	33.9 t	1.75 m		5c	70.2 d	3.83 m	
5a	25.1 t	1.40 m		6c	18.0 q	1.32 d	6

* 125 MHz, chemical shifts in ppm, multiplicity. ** 500 MHz, chemical shifts in ppm, multiplicity.
*** Indistinguishable

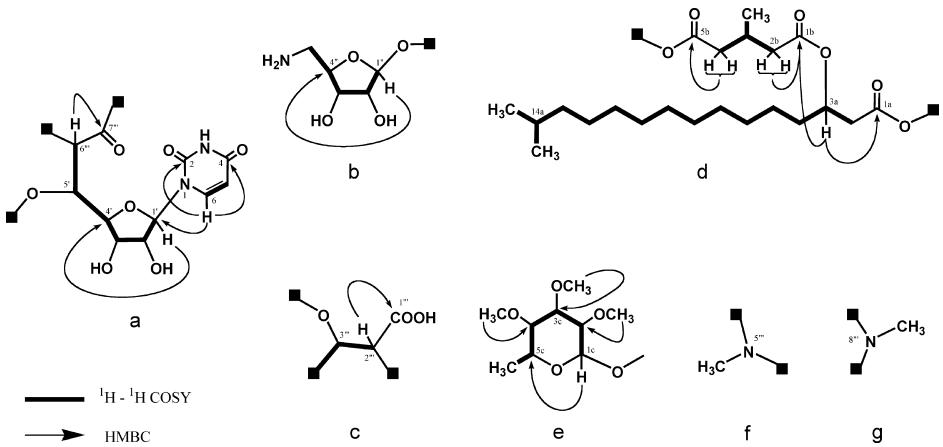


Fig. 2 Partial structures of caprazamycin B (**2**).

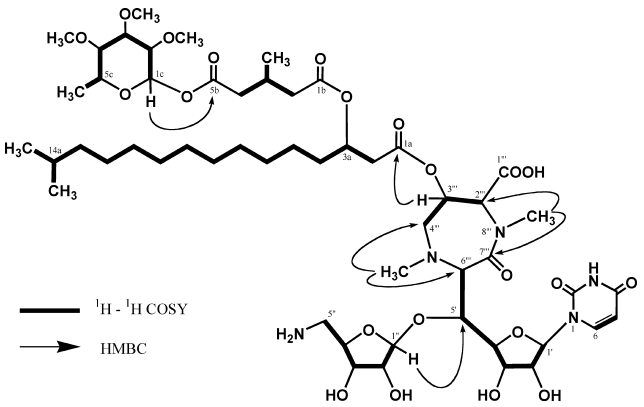


Fig. 3 HMBC correlations of caprazamycin B (**2**) in DMSO-d_6 - pyridine-d_5 - D_2O (5 : 5 : 1).

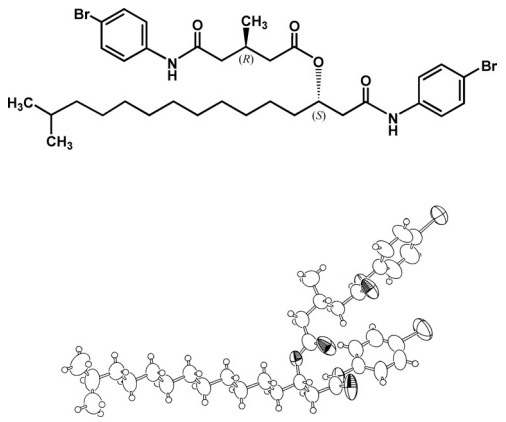
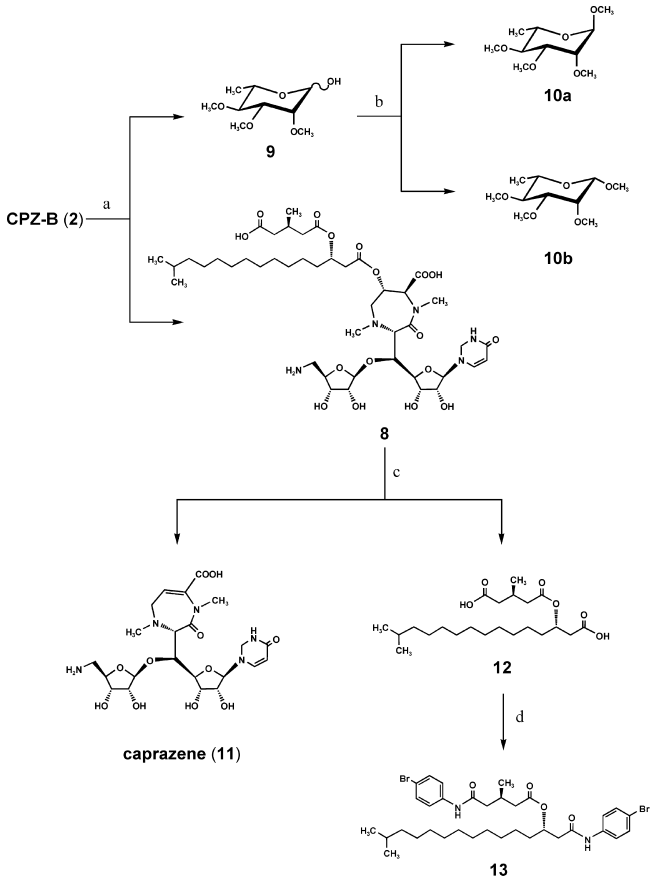
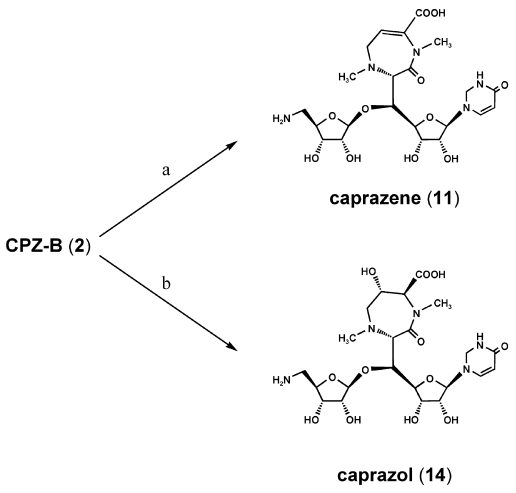


Fig. 4 Structure of **13** and its ORTEP.



Conditions: (a) 80% CF_3COOH, MeOH, rt, 1 hour, **8**: 99%, **9**: 97%; (b) H_2SO_4, MeOH, 50°C, 4 hours, **10a**+**10b** (5:1): 87%; (c) 80% aq AcOH, 70 °C, 2 hours, **11**: 99%, **12**: 92%; (d) 4-bromoaniline, BOP-Cl, Et_3N, THF, rt, 2 hours, 70%.

Scheme 1 Degradation study of caprazamycin B (**2**).



Conditions: (a) 80% aq AcOH, 70°C, 2 hours, 99%; (b) 28% aq NH_3, DMF, rt, 4 days, 99%.

Scheme 2 Synthesis of the core components of caprazamycins.

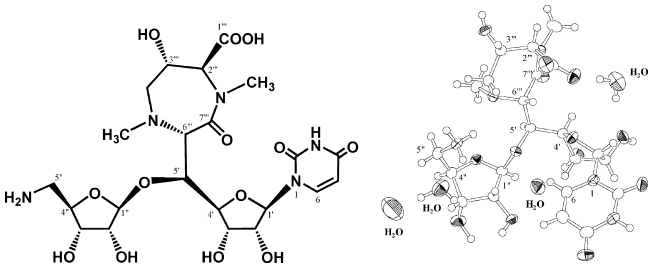
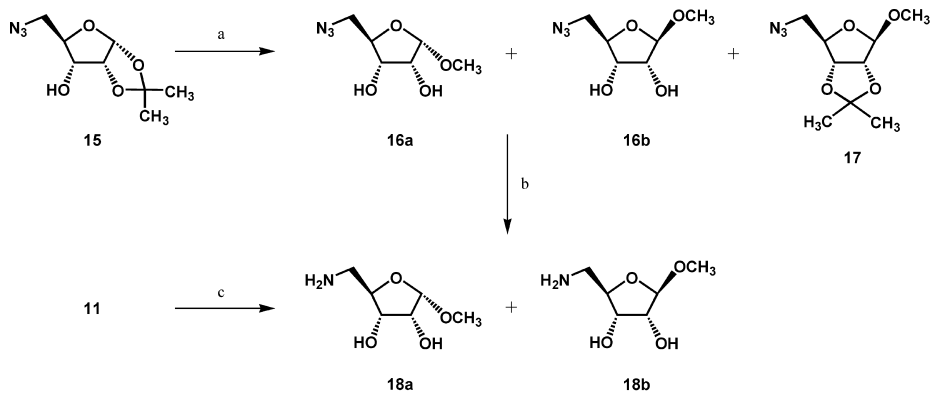


Fig. 5 Structure of caprazol (**14**) and its ORTEP.



Conditions: (a) Amberlite CG 120 (H^+), MeOH, reflux, 30 minutes, **16a**+**16b** (1:2.9): 63%, **17**: 22%; (b) Ph_3P, THF-H_2O, rt, overnight, 99%; (c) Amberlite CG 120 (H^+), MeOH, reflux, 14 hours, **18a**+**18b** (1:2.2): 51%.

Scheme 3 Synthesis of methyl 5-amino-5-deoxy-α- and β-D-ribofuranoside (**18a** and **18b**).

Experimental

General Methods

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. UV spectra were measured with a Hitachi 557 spectrophotometer. IR spectra were recorded on a Horiba FT-210 Fourier transform infrared spectrometer. ^1H and ^{13}C NMR spectra were measured with a JEOL JNM-A500 and/or Bruker AVANCE 500 spectrometer, using TMS as an internal reference. Mass spectra were recorded using a JEOL JMS-SX102 (HR-FAB) and/or JEOL JMS-T100LC (HR-ESI) spectrometer. X-Ray crystallographic measurements were made on Rigaku AFC7R diffractometer with graphite monochromated Cu-Kα radiation and a rotation anode generator. All calculations of the measurements were performed using the teXsan crystallographic software package of Molecular Structure Corporation. TLC was performed on Kieselgel 60 F_{254} (Merck), and column chromatography was carried out on Kieselgel 60 (Merck).

Caprazamycin B1 (8) and 2,3,4-tri-*O*-methyl-L-rhamnose (9)

A solution of **2** (301 mg, 0.263 mmol) in 4.5 ml of trifluoroacetic acid - MeOH (4 : 1) was kept for 1 hour at room temparature. Concentration gave a syrup, which was added to diethyl ether. The precipitate obtained was filtered and thoroughly washed with diethyl ether to give a colorless solid of **8** (278.4 mg, 99% as the mono CF_3COOH salt). The filtrate and washings were combined and concentrated to give **9** (52.5 mg, 97%) as a syrup.

8: $[\alpha]_D^{20}$ +12° (*c* 0.5, DMSO); HR-MS (ESI, positive): *m/z* 958.4918 $(M+H)^+$ (calcd for $C_{44}H_{72}N_5O_{18}$, 958.4872); ^1H NMR (500 MHz, DMSO-d_6) δ 0.84 (6H, d, *J*=7 Hz, 14a-Me_2), 0.91 (3H, d, *J*=6 Hz, 3b-Me), 1.44 (1H, m, 14a-H), 1.57 (2H, br s, 4a-H_2), 2.26 (3H, s, 5‴-*N*Me), 2.94 (3H, s, 8‴-*N*Me), 5.03 (1H, s, 1″-H), 5.13 (1H, m, 3a-H), 5.37 (1H, br s, 3‴-H), 5.56 (1H, d, *J*=~1.5 Hz, 1′-H), 5.64 (1H, d, *J*=8 Hz, 5-H), 7.80 (1H, d, *J*=8 Hz, 6-H), 11.30 (1H, br, 3-NH).

9: ^1H NMR (500 MHz, $CDCl_3$) α-isomer: δ 1.30 (3H, d, *J*=6 Hz, 5-Me), 3.15 (1H, t, *J*=9.5 and 9.5 Hz, 4-H), 3.51 (6H, s, OMe×2), ~3.55 (1H, 3-H), 3.56 (3H, s, OMe), 3.62 (1H, dd, *J*=2 and 3 Hz, 2-H), 3.81 (1H, dq, *J*=6, 6, 6 and 9.5 Hz, 5-H), 5.27 (1H, d, *J*=1.8 Hz, 1-H); β-isomer: δ 1.33 (3H, d, *J*=6 Hz, 5-Me), 3.08 (1H, t, *J*=9.5 and 9.5 Hz, 4-H), 3.20 (1H, dd, *J*=3 and 9.5 Hz, 3-H), 3.24 (1H, dq, *J*=6, 6, 6 and 9.5 Hz, 5-H), 3.53 (OMe), 3.64 (1H, slightly br d, *J*=3 Hz, 2-H), 3.67 (3H, s, OMe), 4.65 (1H, d, *J*=~1 Hz, 1-H).

Methyl 2,3,4-tri-*O*-methyl-α- and β-L-rhamnopyranoside (10a and 10b)

To a solution of **9** (96.5 mg, 0.468 mmol) in MeOH (1.5 ml) was added sulfuric acid (30 μl, 0.563 mmol) and the solution was heated for 5 hours at 50°C. TLC (1 : 1 hexane - diethyl ether) of the solution showed two spots at Rf 0.25 (**10a**, major) and 0.15 (**10b**) (cf. **9**: Rf 0.05). The solution was concentrated to a low volume, diluted with $CHCl_3$, and washed with aq $NaHCO_3$ and water. The organic layer was dried (Na_2SO_4) and concentrated to give a syrupy mixture (89.7 mg, 87%) of **10a** and **10b** (the ratio was 5 : 1; determined from the ^1H NMR spectrum). Column chromatography (1 : 1 hexane - diethyl ether) of the syrup

permitted separation of the anomers.

10a: syrup, $[\alpha]_D^{23}$ −59° (*c* 1, $CHCl_3$); lit. [6] $[\alpha]_D^{24}$ −62.5° (*c* 1.0, $CHCl_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 18.2 (Me-5), 55.1 (MeO-1), 58.1 (MeO-3), 59.4 (MeO-2), 61.3 (MeO-4), 68.1 (C-5), 77.8 (C-2), 81.5 (C-3), 82.5 (C-4), 98.3 (C-1); $J_{C\text{-}1,H\text{-}1}$=167 Hz.

10b: syrup, ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 18.1 (Me-5), 57.4 (MeO-1), 57.8 (MeO-3), 61.4 (MeO-4), 62.1 (MeO-2), 72.2 (C-5), 77.5 (C-2), 82.3 (C-4), 84.4 (C-3), 102.8 (C-1); $J_{C\text{-}1,H\text{-}1}$=153 Hz.

Caprazene (11)

A solution of **2** (200 mg, 0.174 mmol) in 80% aq AcOH (6 ml) was heated for 2 hours at 70°C. Concentration gave a syrup, which was added to acetone. The precipitate obtained was thoroughly washed with acetone to give **11** (96.3 mg, 99%) as a colorless solid. An analytical sample was prepared by crystallization from H_2O - acetone, mp 210～211°C (dec.); $[\alpha]_D^{19}$ +85° (*c* 0.5, H_2O); HR-MS (ESI, positive): *m/z* 580.1849 $(M+Na)^+$ (calcd for $C_{22}H_{31}N_5O_{12}Na$, 580.1867); ^1H NMR (500 MHz, D_2O) δ 2.42 (3H, s, 5‴-*N*Me), 2.94 (1H, dd, *J*=7 and 12.5 Hz, 4‴a-H), 2.99 (3H, s, 8‴-*N*Me), 3.18 (1H, dd, *J*=5 and 14 Hz, 5″a-H), 3.34 (1H, dd, *J*=7 and 12.5 Hz, 4‴b-H), 3.35 (1H, dd, *J*=4 and 14 Hz, 5″b-H), 3.92 (1H, d, *J*=9.5 Hz, 6‴-H), 4.12 (1H, dd, *J*=5 and ～8 Hz, 3′-H), 4.13 (1H, slightly br d, *J*=～5 Hz, 2″-H), 4.20 (1H, m, 4″-H), 4.24 (1H, slightly br d, *J*=～8 Hz, 4′-H), 4.26 (1H, dd, *J*=～5 and ～8 Hz, 3″-H), 4.28 (1H, dd, *J*=2.5 and 5 Hz, 2′-H), 4.34 (1H, dd, *J*=2 and 9.5 Hz, 5′-H), 5.22 (1H, slightly br s, 1″-H), 5.62 (1H, d, *J*=2.5 Hz, 1′-H), 5.82 (1H, d, *J*=8 Hz, 5-H), 6.49 (1H, t, *J*=7 and 7 Hz, 3‴-H), 7.69 (1H, d, *J*=8 Hz, 6-H); ^{13}C NMR (125.8 MHz, D_2O) δ 33.2 (*N*Me-8‴), 40.5 (*N*Me-5‴ and C-5″), 51.5 (C-4‴), 63.6 (broad, C-6‴), 69.4 (C-3′), 70.7 (C-3″), 73.9(C-2′), 75.3 (C-2″), 77.0 (C-5′), 79.0 (C-4″), 82.7 (C-4′), 91.4(C-1′), 102.0 (C-5), 110.0 (C-1″), 123.5 (C-3‴), 142.4 (C-6), 144.7 (C-2‴), 151.7 (C-2), 166.8 (C-4), 169.2 (C-1‴), 171.3 (C-7‴).

(3S,3′*R*)-3-(4′-Carboxy-3′-methylbutanoyloxy)-14-methylpentadecanoic Acid (12) and (11)

A solution of **8** (240 mg, 0.224 mmol as the mono CF_3COOH salt) in 80% aq AcOH (6 ml) was heated for 2 hours at 70°C. TLC (2 : 1 : 1 EtOAc - 1-PrOH - 20% aq AcOH) of the solution showed two spots at Rf 0.95 (**12**) and 0.05 (**11**) (cf. **8**: Rf 0.35). Concentration gave a residue, which was washed with acetone to give **11** (123.5 mg, 99%). The washings were concentrated and the resulting syrup was extracted with $CHCl_3$. The extract was washed with water and concentrated to give **12** (82.5 mg, 92%) as a colorless syrup.

12: $[\alpha]_D^{20}$ +6° (*c* 1, $CHCl_3$); MS (ESI) *m/z* 423 $(M+Na)^+$; ^1H NMR (500 MHz, $CDCl_3$) δ 0.86 (6H, d, *J*=6.5 Hz, 14-Me_2), 1.03 (3H, d, *J*=6.5 Hz, 3′-Me), 1.15 (2H, m, 13-H_2), 1.23～1.32 (16H, 5, 6, 7, 8, 9, 10, 11 and 12-H_2), 1.51 (1H, m, 14-H), 1.56 (1H, m, 4a-H), 1.65 (1H, m, 4b-H), 2.20 (1H, dd, *J*=6.5 and 14.5 Hz, 2′a-H), 2.27 (1H, dd, *J*=7 and 15 Hz, 4′a-H), ～2.38 (1H, m, 4′b-H), ～2.40 (1H, m, 2′b-H), 2.45 (1H, m, 3′-H), 2.57 (1H, dd, *J*=9 and 15.5 Hz, 2a-H), 2.61 (1H, dd, *J*=4 and 15.5 Hz, 2b-H), 5.28 (1H, m, 3-H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 20.3 (Me-3′), 23.1 (Me_2-14), 25.5 (C-5), 27.8 (C-12 and C-3′), 28.4 (C-14), 29.7, 29.8, 29.9, 30.0, 30.1, 30.3, 34.6 (C-4), 39.5 (C-2 and C-13), 40.8 (C-4′), 41.2 (C-2′), 70.9 (C-3), 172.1 (C-1′), 177.7 (C-1), 179.4 (C-5′).

(3*R*,1′*S*)-1′-{[*N*-(4-Bromophenyl)carbamoyl]methyl}-12′-methyltridecyl-4-[*N*-(4-bromophenyl)carbamoyl]-3-methylbutanoate (13)

To a solution of **12** (28.5 mg, 0.0712 mmol) in THF (1 ml) were added triethylamine (70 μl, 0.502 mmol), bis(2-oxo-3-oxazolidinyl)phosphinic chloride (40.0 mg, 0.157 mmol), and 4-bromoaniline (30.7 mg, 0.178 mmol) and the mixture was stirred for 1 hour at room temperature. TLC (3 : 1 $CHCl_3$ - EtOAc) of the organic layer showed a major spot at Rf 0.55. Concentration of the resulting suspension gave a residue, which was extracted with $CHCl_3$. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography with $CHCl_3$ to give **13** (35.1 mg, 70%) as a solid. An analytical sample (prism) was prepared by crystallization from acetone, mp 160～161°C; $[\alpha]_D^{23}$ −12° (*c* 0.5, $CHCl_3$); HR-MS (ESI, positive): *m/z* 729.1876 $(M+Na)^+$ (calcd for $C_{34}H_{48}Br_2N_2O_4Na$, 729.1879), ^1H NMR (500 MHz, $CDCl_3$) δ 0.86 (6H, d, *J*=6.5 Hz, 12′-Me_2), 1.08 (3H, d, *J*=6.5 Hz, 3-Me), 1.15 (2H, m, 11′-H_2), 1.20～1.36 (16H, 3′, 4′, 5′, 6′, 7′, 8′, 9′ and 10′-H_2), 1.51 (1H, m, 12′-H), 1.60～1.75 (2H, m, 2′-H_2), 2.28 (1H, dd, *J*=6.5 and 13.5 Hz, 4a-H), 2.33～2.42 (3H, m, 2-H_2 and 4b-H), 2.49 (1H, m, 3-H), 2.55 (1H, dd, *J*=7 and 14.5 Hz, 1′-C(*Ha*Hb)CO), 2.63 (1H, dd, *J*=4 and 14.5 Hz, 1′-C(Ha*Hb*)CO), 5.25 (1H, m, 1′-H), 7.3～7.45 (8H, m, aromatic), 7.80 (1H, s, 4-CON*H*), 7.92 (1H, s, 1′-CH_2CON*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 21.1 (Me-3), 23.1 (Me_2-12′), 25.8 (C-3′), 27.8 (C-10′), 28.4 (C-12′), 29.0 (C-3), 29.7, 29.88, 29.94, 30.0, 30.1, 30.3, 34.3 (C-2′), 39.5 (C-11′), 41.1 (C-2), 43.1 (NHCO*C*H_2-1′), 44.2 (C-4), 72.0 (C-1′), 117.3, 117.5, 122.0, 122.1, 132.3, 132.4, 137.2, 137.3, 168.7 (NH*C*OCH_2-1′), 170.8 (*C*ONH-4), 172.9 (C-1).

Caprazol (14)

To a solution of **2** (150 mg, 0.131 mmol) in DMF (1.5 ml)

was added 28% aq NH_3 (1.5 ml), and the mixture was stirred for 4 days at room temperature. Filtration followed by concentration *in vacuo* gave a residue, which was thoroughly washed with acetone to give **14** (74.7 mg, 99%) as a colorless solid. An analytical sample (prism) was prepared by crystallization from MeOH - H_2O, mp 205～206°C (dec.); $[\alpha]_D^{19}$ +28° (*c* 0.5, DMSO); HR-MS (ESI, positive): *m/z* 576.2155 $(M+H)^+$ (calcd for $C_{22}H_{34}N_5O_{13}$, 576.2153); ^{1}H NMR (500 MHz, D_2O) δ 2.43 (3H, s, 5‴-*N*Me), 3.01 (1H, slightly br d, *J*=15 Hz, 4‴a-H), 3.07 (3H, s, 8‴-*N*Me), 3.13 (1H, slightly br d, *J*=15 Hz, 4‴b-H), 3.20 (1H, dd, *J*=4 and 13.5 Hz, 5″a-H), 3.32 (1H, dd, *J*=3.5 and 13.5 Hz, 5″b-H), 3.85 (1H, d, *J*=9 Hz, 6‴-H), 4.08 (1H, dd, *J*=5 and 8 Hz, 3′-H), 4.13 (1H, d, *J*=～8 Hz, 4′-H), 4.14 (1H, d, *J*=～3 Hz, 2″-H), 4.20 (1H, d, *J*=～5 Hz, 2‴-H), ～4.21 (1H, m, 4″-H), 4.25 (1H, m, 3″-H), 4.31 (1H, br d, *J*=5 Hz, 2′-H), 4.39 (1H, d, *J*=9 Hz, 5′-H), 4.44 (1H, br s, 3‴-H), 5.17 (1H, slightly br s, 1″-H), 5.60 (1H, slightly br s, 1′-H), 5.82 (1H, d, *J*=8 Hz, 5-H), 7.77 (1H, d, *J*=8 Hz, 6-H); ^{13}C NMR (125.8 MHz, D_2O) δ 37.0 (*N*Me-5‴), 39.2 (*N*Me-8‴), 40.2 (C-5″), 59.1 (C-4‴), 63.5 (C-6‴), 69.3 (C-3′ and C-3‴), 70.0 (C-2‴), 70.6 (C-3″), 74.0 (C-2′), 75.4 (C-2″), 77.6 (C-5′), 79.0 (C-4″), 82.4 (C-4′), 91.8 (C-1′), 101.7 (C-5), 111.2 (C-1″), 142.9 (C-6), 151.8 (C-2), 167.1 (C-4), 172.7 (C-7‴), 174.1 (C-1‴).

Methyl 5-Azido-5-deoxy-α- and β-D-Ribofuranoside (16a and 16b) and Methyl 5-Azido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (17)

To a solution of **15** (860 mg, 4.00 mmol) in MeOH (40 ml) was added Amberlite CG 120 (H^+ form, 2.7 g) and the mixture was refluxed for 30 minutes. TLC (1 : 2 hexane - EtOAc) of the organic layer showed spots at Rf 0.8 (**17**), 0.35 (**16b**), and 0.25 (**16a**) (cf. **15**: Rf 0.55). Filtration followed by concentration gave a syrup, which was subjected to column chromatography (10 : 1 $CHCl_3$ - MeOH) to give a syrupy mixture (472.8 mg, 63%) of **16a** and **16b** (the ratio was 1 : 2.9; determined by ^{1}H NMR spectrum), along with **17** (204.8 mg, 22%) as a syrup. An analytical sample of **16b** was prepared by further column chromatography (3 : 5 hexane - EtOAc) of the anomeric mixture.

16a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64 (1H, d, *J*=8 Hz, 3-OH), 2.91 (1H, d, *J*=8 Hz, 2-OH), 3.38 (1H, dd, *J*=5 and 13 Hz, 5a-H), 3.51 (3H, s, 1-OMe), 3.58 (1H, dd, *J*=3.5 and 13 Hz, 5b-H), 3.89 (1H, ddd, *J*=4, 6.5 and 8 Hz, 3-H), 4.10 (1H, apparently q, *J*=～4, ～4 and ～4 Hz, 4-H), 4.15 (1H, ddd, *J*=4.5, 6.5 and 8 Hz, 2-H), 5.00 (1H, d, *J*=4.5 Hz, 1-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 52.3 (C-5), 55.7 (MeO-1), 71.2 (C-2), 71.4 (C-3), 82.8 (C-4), 102.6 (C-1).

16b: syrup, $[\alpha]_D^{23}$ −6° (*c* 1, $CHCl_3$); MS (ESI) *m/z* 212 $(M+Na)^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.54 (1H, d, *J*=7 Hz, 3-OH), 2.70 (1H, d, *J*=4 Hz, 2-OH), 3.40 (1H, dd, *J*=6 and 13 Hz, 5a-H), 3.41 (3H, s, 1-OMe), 3.50 (1H, dd, *J*=4 and 13 Hz, 5b-H), 4.04～4.09 (2H, m, 2-H and 4-H), 4.25 (1H, dt, *J*=5, 7 and 7 Hz, 3-H), 4.87 (1H, s, 1-H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 53.7 (C-5), 55.6 (MeO-1), 72.6 (C-3), 75.1 (C-2), 81.8 (C-4), 108.5 (C-1).

Methyl 5-Amino-5-deoxy-α- and β-D-Ribofuranoside (18a and 18b)

(a) From **16a** and **16b**: To a solution of the mixture (220 mg, 1.16 mmol) of **16a** and **16b** in THF - H_2O (4 : 1, 3 ml) was added triphenylphospine (336 mg, 1.28 mmol) and the solution was kept overnight at room temperature. TLC (4 : 4 : 1 $CHCl_3$ - MeOH - 5% aq NH_3) of the solution showed two spots at Rf 0.35 (**18b**) and 0.25 (**18a**). The solution was concentrated to a low volume, diluted with water, and washed with diethyl ether. Concentration of the aqueous solution afforded a mixture (186 mg, 99%) of **18a** and **18b**, as a syrup. Column chromatography (4 : 4 : 1 $CHCl_3$ - MeOH - 5% aq NH_3) of the syrup permitted separation of the anomeric mixture.

(b) From caprazene (**11**): A mixture of **11** (1.23 g, 2.21 mmol) and Amberlite CG 120 (H^+ form, 3.7 g) in MeOH (40 ml) was refluxed for 14 hours. After filtration, the resin was washed with MeOH and eluted with MeOH containing 1% aq NH_3. Ninhydrin-positive fractions were collected and concentrated to afford a syrup. TLC (4 : 7 : 2 : 7 1-PrOH - EtOAc - $CHCl_3$ - 28% aq NH_3) of the syrup showed spots at Rf 0.55 (**18b**) and 0.45 (**18a**) (cf. **2**: Rf 0.3). Chromatography (4 : 4 : 1 $CHCl_3$ - MeOH - 5% aq NH_3) over a short column gave a mixture (184 mg, 51%) of **18a** and **18b** (the ratio was 1 : 2.2; determined from the ^{1}H NMR spectrum).

18a: syrup, $[\alpha]_D^{21}$ +164° (*c* 0.5, MeOH); MS (ESI) *m/z* 164 $(M+H)^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.40 (2H, br s, 5-NH_2), 2.58 (1H, dd, *J*=5 and 13 Hz, 5a-H), 2.65 (1H, dd, *J*=5 and 13 Hz, 5b-H), 3.28 (3H, s, 1-OMe), 3.70～3.76 (2H, m, 3-H and 4-H), 3.83 (1H, br s, 2-H), 4.18 (1H, br s, 2-OH), 4.53 (1H, br s, 3-OH), 4.72 (1H, d, *J*=4.5 Hz, 1-H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 44.8 (C-5), 55.3 (MeO-1), 70.8 (C-3), 72.3 (C-2), 86.4 (C-4), 103.6 (C-1).

18b: syrup, $[\alpha]_D^{21}$ −58° (*c* 1, MeOH); MS (ESI) *m/z* 164 $(M+H)^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.43 (2H, br s, 5-NH_2), 2.54 (1H, dd, *J*=6 and 13 Hz, 5a-H), 2.70 (1H, dd, *J*=4 and 13 Hz, 5b-H), 3.22 (3H, s, 1-OMe), 3.69～3.74 (2H, m, 2-H and 4-H), 3.86 (1H, dd, *J*=5 and 7 Hz, 3-H), 4.61 (1H, s, 1-H), 4.75 (1H, br s, OH), 4.97 (1H, br s, OH); (500 MHz, D_2O) δ 2.69 (1H, dd, *J*=7 and 14 Hz, 5a-H),

2.87 (1H, dd, J=4 and 14 Hz, 5b-H), 3.36 (3H, s, 1-OMe), 3.92 (1H, dt, J=4, 7 and 7 Hz, 4-H), 3.99 (1H, d, J=5 Hz, 2-H), 4.09 (1H, dd, J=5 and 7 Hz, 3-H), 4.85 (1H, s, 1-H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 45.7 (C-5), 55.1 (MeO-1), 72.4 (C-3), 75.4 (C-2), 84.9 (C-4), 108.9 (C-1); ^{13}C NMR (125.8 MHz, D_2O) δ 44.0 (C-5), 55.6 (MeO-1), 72.2 (C-3), 74.7 (C-2), 83.5 (C-4), 108.3 (C-1).

X-Ray Crystallographic Analysis of 13

A colorless prism crystal described for **13**, having approximate dimensions of 0.02×0.18×0.40 mm was chosen for X-ray crystallography. The crystal data are as follows: Empirical formula; $C_{34}H_{48}N_2O_4Br_2$. F.W.; 708.57. Crystal system; monoclinic. Space group, $P2_1$ (#4). Lattice parameters; a=4.883(2) Å, b=26.383(2) Å, c=13.875(1) Å, β=93.970(2)°, V=1783.4(7) Å^3. Z value; 2. Dcalc; 1.319 g/cm^3. μ(CuKα); 31.71 cm^{-1}. Of the 3523 reflections which were collected, 3118 were unique. The intensities of three representative reflections were measured after every 150 reflections. Over the course of data collection, the standards decreased by 6.4%. A linear correction factor was applied to the data to account for this phenomenon. The structure was solved by direct method (SIR92) [16] and expanded using a Fourier technique (DIRDIF94) [17]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 2803 observed reflections and 379 variable parameters and converged with unweighted and weighted agreement factors of R=0.089 and Rw=0.134. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.37 and −0.39e$^-$/Å^3, respectively. The absolute configuration of the molecule was determined based on Flack parameter, −0.076 (59).

X-Ray Crystallographic Analysis of 14

A colorless prism crystal described for **14**, having approximate dimensions of 0.06×0.06×0.30 mm was chosen for X-ray crystallography. The crystal data are as follows: Empirical formula $C_{22}H_{33}N_5O_{13}\cdot 4H_2O$; F.W. 647.59; Crystal system Monoclinic; Space group $P3_2$; Lattice parameters a=14.558(1) Å, c=11.406(2) Å, V=2093.4(4) Å^3; Z value 3. Dcalc 1.541 g/cm^3; μ(CuKα) 11.56 cm^{-1}. Of the 2835 reflections which were collected, 2525 were unique. No decay correction was applied. The structure was solved by the direct method (SIR92) and expanded using Fourier techniques (DIRDIF94). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 2525 observed reflections and 397 variable parameters and converged with unweighted and weighted agreement factors of R=0.063 and Rw=0.099. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.27 and −0.21e$^-$/Å^3, respectively.

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