

Meehanines L–W, Spermidine Alkaloidal Glycosides from *Meehania urticifolia*

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Twelve new spermidine alkaloidal glycosides, meehanines L–W (**1**–**12**), were isolated from the whole plant *Meehania urticifolia*. The structures of these new compounds were elucidated on the basis of spectroscopic data analyses.

Meehania urticifolia (Miq.) Makino belongs to the family Lamiaceae. It is a popular wild plant due to its large violet flowers that appear from April to May and is named “Rashomon-kazura” in Japan. In our previous paper, 11 spermidine alkaloidal glycosides, meehanines A–K, were reported from this plant.¹ Various cyclic spermidine alkaloids^{2,3} and their glucosides⁴ have been reported from plants classified in the Celastraceae, Flacourtiaceae, Equisetaceae, Apocynaceae, Cannabaceae, Cruciferae, and Gyrostemonaceae. Recently, four alkaloidal glycosides similar to meehanines were also reported from another Lamiaceae plant, *Dracocephalum tanguticum* Maxim.⁵ The differences between meehanines and other cyclic spermidine alkaloids are that meehanines are diglycosides, have a C-8 hydroxy group or *O*-acetyl group, and possess a rich diversity of acylated moieties. In this study, the alkaloids of *M. urticifolia* were investigated, and 12 new cyclic spermidine glycosides were isolated.

Results and Discussion

The methanol and acetone extracts of whole plants of *M. urticifolia* were dissolved in H₂O and partitioned with Et₂O. Each H₂O layer was fractionated by multistep column chromatography, and 12 cyclic spermidine alkaloidal glycosides, meehanines L–W (**1**–**12**), were isolated as amorphous powders. Their molecular formulas were determined on the basis of HRFABMS. The ¹H and ¹³C NMR spectra of compounds **9**, **11**, and **12**, measured in pyridine-*d*₅ at 30 °C, and of compounds **5**–**8**, **10**, and **12**, which were acquired in methanol-*d*₄ at 30 °C, showed the presence of two sets of closely spaced resonances (Tables 1 and 2) similar to those of meehanines A–K, found in our previous study.¹ However, compounds **1**–**4**, lacking a 10-*N* amide moiety, showed only one set of resonances (Table 1). The observation of duplicated signals for **5**–**12** may be attributed to cis–trans isomerism due to the partial C=N double-bond character of the 10-*N* amide functional group.^{5,6}

Meehanine L (**1**) showed an [M + H]⁺ at *m/z* 762.3449 in the HRFABMS, which indicated the molecular formula C₃₇H₅₁N₃O₁₄. In the ¹H and ¹³C NMR spectra acquired in pyridine-*d*₅ at 30 °C (Table 1), 15 sp² carbon signals and 22 sp³ carbon signals were observed. Two methine, seven methylene, six aromatic, and two carbonyl carbons and their corresponding proton signals were considered to be components of an aglycone moiety. A set of AA′BB′-type aromatic protons at δ_H 7.38 (2H, br d, *J* = 8.5 Hz) and 7.19 (2H, overlapped) and carbons at δ_C 134.7 (C-1′), 128.5 (C-2′ and C-6′), 117.2 (C-3′ and C-5′), and 156.4 (C-4′) suggested the presence of a 1,4-disubstituted benzene ring. A methine proton at δ_H 4.41 (1H, dd, *J* = 11.5 and 3.5 Hz) and methylene protons at δ_H 2.67 (1H, br dd, *J* = 13.0 and 3.5 Hz) and 3.13 (1H, br dd, *J* = 13.0 and 11.5 Hz) were ascribed to the C-4 and C-3 protons,

respectively. In the ¹H–¹H COSY spectrum, the oxymethine proton at δ_H 5.19 (1H, overlapped, H-8) was correlated with the C-7 methylene protons (2H, δ_H 1.93, overlapped) and H₂-9 (2H, δ_H 3.32, br d, *J* = 4.0 Hz). The C-7 methylene protons correlated with the C-6 protons at δ_H 2.23 (1H, br dd, *J* = 11.5 and 10.0 Hz) and 2.75 (1H, m). The chemical shift of H-8 (δ_H 5.19) and a carbonyl carbon at δ_C 169.7 suggested the presence of an C-8 acyl group. However, the methyl proton and carbon signals of an acetyl group were not clearly discernible in pyridine-*d*₅. ¹H and ¹³C NMR spectra acquired in methanol-*d*₄ (Table 2) showed acetyl protons at δ_H 2.08 (3H, s) and a carbon at δ_C 20.8. These data suggested the presence of an N–CH₂–CH₂–CH(–O–Ac)–CH₂–N moiety. An amide proton at δ_H 9.69 (1H, br t, *J* = 6.0 Hz, H-1), methylene protons at δ_H 3.36 (2H, overlapped, H₂-11), 1.97 (1H, overlapped, H-12), 2.08 (1H, overlapped, H-12), 3.05 (1H, m, H-13), and 3.90 (1H, m, H-13), and their ¹H–¹H COSY correlations showed the presence of an N–(CH₂)₃–N spin system. The presence of a 13-membered spermidine ring was established using the correlations observed in the HMBC spectra. The CD spectrum of **1** showed negative Cotton effects in the 210–230 nm region, suggesting the absolute configuration of C-4 to be *S*.⁷ The optical rotation of **1** in MeOH was negative, similar to those of meehanines A–K.¹ Accordingly, the absolute configuration of C-8 of compound **1** was assumed to be *R*.

Two anomeric carbons at δ_C 98.6 and 107.1 (Table 1) suggested the presence of two monosaccharide moieties. Their corresponding anomeric protons resonated at δ_H 6.20 (1H, br s) and 5.38 (1H, d, *J* = 7.5 Hz), respectively, which were also observed in the ¹H–¹H COSY and HMQC spectra, showing the presence of a rhamnopyranose and a glucopyranose unit. Sugar analyses showed the presence of L-rhamnose and D-glucose units.⁸ The anomeric α-configuration of the L-rhamnosyl residue was determined from the ¹³C NMR chemical shifts of C-3 and C-5.⁹ Furthermore, the D-glucosyl residue was determined to be β from the coupling constant of the anomeric proton. The ¹H NMR signals of Glc-6 at δ_H 4.95 (1H, dd, *J* = 11.5 and 4.5 Hz) and 5.19 (1H, br d, *J* = 11.5 Hz) were shifted downfield relative to that of the glucosyl moiety of meechanine C. In the HMBC spectrum, they were long-range coupled with a carbonyl carbon at δ_C 166.6 (C-1′′), revealing that the C-6 hydroxy group of the glucosyl unit was acylated. The aromatic protons at δ_H 8.07 (2H, br d, *J* = 7.5 Hz, H-3′′ and H-7′′), 7.24 (2H, br t, *J* = 7.5 Hz, H-4′′ and H-6′′), and 7.46 (1H, br t, *J* = 7.5 Hz, H-5′′) showed a benzoate moiety, and the H-3′′ and H-7′′ signals were long-range coupled with the C-1′′ signal. In the HMBC spectrum, the anomeric proton of the 6-benzoyl-β-D-glucosyl moiety was long-range coupled with the carbon signal at δ_C 81.4 (Rha-2), and the anomeric proton of α-L-rhamnose was long-range coupled with the 1,4-disubstituted benzene ring carbon at δ_C 156.4 (C-4′). Hence, the structure of **1** was formulated as shown in Figure 1.

For meechanine M (**2**), confirmation of the molecular formula of C₃₅H₄₉N₃O₁₃ was achieved by HRFABMS, which was C₂H₂O less than that of **1**, indicating the absence of an acetyl group. The ¹H

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Table 1. NMR Data (400 MHz, pyridine-*d*₅) for Compounds **1–4**, **9**, **11**, **12**, and Meehanines C, G, and H

	1		2		3		4		9	
position	δ_{H} (<i>J</i> in Hz)	δ_{C}	δ_{H} (<i>J</i> in Hz)	δ_{C}	δ_{H} (<i>J</i> in Hz)	δ_{C}	δ_{H} (<i>J</i> in Hz)	δ_{C}	δ_{H} (<i>J</i> in Hz)	δ_{C}
1	9.69, brt (6.0)		9.76, brt (6.0)		9.68, brt (5.5)		9.78, brt (6.5)		8.43, brt (6.0) 8.56, m	
2		172.2		172.5		172.2		172.5	172.0 ^b	
3	2.67, brdd (13.0, 3.5) 3.13, brdd (13.0, 11.5)	45.6	2.70, dd (13.0, 3.5) 3.10, dd (13.0, 12.0)	45.9	2.67, dd (12.5, 3.5) 3.12, dd (12.5, 12.0)	45.6	2.72, dd (12.5, 3.5) 3.12, dd (12.5, 11.5)	45.9	2.76, m	46.7
4	4.41, dd (11.5, 3.5)	60.8	4.41, dd (12.0, 3.5)	60.6	4.42, dd (12.0, 3.5)	60.8	4.44, dd (11.5, 3.5)	60.6	4.42 ^a	60.2 ^b , 61.2
6	2.23, brdd (11.5, 10.0) 2.75, m	41.7	2.24, dd (13.0, 10.0) 2.83, dd (13.0, 8.0)	41.3	2.25, m 2.77, ddd (12.5, 6.5, 2.0)	41.7	2.26, dd (13.0, 10.0) 2.86, dd (13.0, 7.5)	41.4	2.42, m 2.54, m 2.72 ^a	45.5 ^b , 45.9 ^b
7	1.93 ^a	31.2	1.89, m 2.02, m	34.5	1.97 ^a	31.2	1.86–2.10 ^a	34.5	1.55–1.63 ^a	32.6, 32.8
8	5.19 ^a	70.4 ^c	4.25 ^a	67.3	5.19, m	70.4	4.26 ^a	67.3	5.39 ^a 5.52, m	74.9, 81.3
9	3.32, brd (4.0)	51.8	3.33 ^a 3.42 ^a	49.3	3.31, brd (4.0)	51.8	3.25, dd (12.5, 6.0) 3.41 ^a	48.7	3.82, m 4.15 ^a 4.68 ^a	49.7
11	3.36 ^a	49.6	3.39, m	49.5	3.36, m	49.6	3.40 ^a	49.5	3.50–3.60 ^a	43.8, 44.7
12	1.97 ^a 2.08 ^a	26.6	1.99, m 2.24, m	26.5	1.86–2.13 ^a	26.6	2.00 ^a 2.15 ^a	26.5	1.76 ^a 2.00–2.25 ^a	32.0
13	3.05, m 3.90, m	39.0	3.24, dd (12.5, 6.0) 3.85, m	39.0	3.03, m 3.89, m	39.4	3.19 ^a 3.85, m	39.0	3.30, m 3.43, m 3.73, m	36.6, 36.7
Ac C=O		169.7				169.7				169.1 ^b , 171.1 ^b
Ac CH ₃	1.80–1.84 ^b	20.3, br			1.78–1.83 ^b	20.8, br			2.02, s	21.5
1'		134.7		134.9		134.9		135.5 ^a		137.6 ^b
2'	7.38, brd (8.5)	128.5	7.41, brd (8.5)	128.5	7.43, brd (8.5)	128.5	7.47, brd (8.5)	128.5	7.30 ^a	128.3
3'	7.19 ^a	117.2	7.20 ^a	117.1	7.24, brd (8.5)	117.2	7.26, brd (8.5)	117.2	7.30 ^a	117.4
4'		156.4		156.3		156.5		156.4		155.9
5'	7.19 ^a	117.2	7.20 ^a	117.1	7.24, brd (8.5)	117.2	7.26, brd (8.5)	117.2	7.30 ^a	117.4
6'	7.38, brd (8.5)	128.5	7.41, brd (8.5)	128.5	7.43, brd (8.5)	128.5	7.47, brd (8.5)	128.5	7.30 ^a	128.3
Rha-1	6.20, brs	98.6	6.20, brs	98.6	6.15, d (1.5)	98.7	6.16, brs	98.7	6.06, brs	100.4
-2	4.71, dd (4.0, 1.5)	81.4	4.69, dd (4.0, 2.0)	81.5	4.67, dd (3.5, 1.5)	81.3	4.68, dd (3.0, 1.5)	81.4	4.71, m	72.3
-3	4.60, dd (8.5, 4.0)	72.5	4.59, dd (9.0, 3.0)	72.4	4.59, dd (8.5, 3.5)	72.5	4.61, dd (8.5, 3.0)	72.5	4.64, m	72.8
-4	4.21, dd (9.5, 8.5)	74.1	4.20, dd (9.5, 9.0)	74.1	4.17 ^a	74.1	4.20 ^a	74.1	4.35, m	74.0
-5	4.16 ^a	70.5 ^c	4.17 ^a	70.5	4.17 ^a	70.5	4.18 ^a	70.5	4.15–4.35 ^a	71.0
-6	1.44, d (5.5)	18.3	1.42, d (6.0)	18.3	1.45, d (5.5)	18.4	1.45, d (5.5)	18.3	1.55, d (6.0) 1.56, d (6.0)	18.8
Glc-1	5.38, d (7.5)	107.1	5.36 ^a	107.1	5.32, d (7.5)	106.9	5.33, d (7.5)	106.9		
-2	4.15 ^a	75.7	4.17 ^a	75.7	4.10, dd (7.5, 9.0)	75.7	4.11, dd (7.5, 9.0)	75.6		
-3	4.25, m	78.3	4.25 ^a	78.3	4.19, dd (9.0, 9.0)	78.3	4.15–4.25 ^a	78.2		
-4	4.16 ^a	71.5	4.16 ^a	71.5	4.03 ^a	71.5	4.15–4.25 ^a	74.1		
-5	4.15a	75.6	4.16 ^a	75.6	4.02 ^a	75.6	4.04 ^a	75.6		
-6	4.95, dd (11.5, 4.5) 5.19, brd (11.5)	65.1	4.94, dd (11.5, 4.0) 5.19, brd (11.5)	65.1	4.74, dd (12.5, 5.0) 4.95, dd (12.5, 2.0)	64.3	4.75, dd (11.5, 5.5) 4.96, dd (11.5, 1.5)	64.3		4.49, dd (11.0, 2.0)
1''		166.6		166.6		176.3		176.3		175.9 ^b , 176.8 ^b
2''		130.8		130.8	2.32, m	41.2	2.33, m	41.2	2.58, m 2.82, m	37.2, 37.3
3''	8.07, brd (7.5)	129.8	8.06, brd (7.5)	129.8	1.31, m 1.58, m	27.1	1.32, m 1.58, m	27.0	1.20–1.60 ^a 1.90–2.05 ^a	27.4, 27.8
4''	7.24, brdd (7.5, 7.5)	128.7	7.23, brdd (7.5, 7.5)	128.7	0.76, t (7.5)	11.7	0.76, t (7.5)	11.7	0.89, t (7.0) 0.95, t (7.0)	12.7, 12.8
5''	7.46, dd (7.5, 7.5)	133.1	7.45, dd (7.5, 7.5)	133.1	1.01, d (7.0)	16.6	1.02, d (7.0)	16.6	1.12, d (6.5) 1.18, d (6.5)	18.3, 18.6
6''	7.24, brdd (7.5, 7.5)	128.7	7.23, brdd (7.5, 7.5)	128.7						
7''	8.07, brd (7.5)	129.8	8.06, brd (7.5)	129.8						
1'''										
2'''										
3'''										
4'''										
5'''										
6'''										
7'''										

and ¹³C NMR spectra of **2** were similar to those of **1** except for the N–CH₂–CH₂–CH(–OAc)–CH₂–N moiety. The oxymethine proton at δ_{H} 4.25 (1H, overlapped, H-8) and carbon at δ_{C} 67.3 were shifted upfield relative to those of **1**. These data suggested that **2** is the 8-de-*O*-acetyl analogue of **1**, as shown.

Meehanine N (**3**) had the molecular formula C₃₅H₅₅N₃O₁₄. The ¹H and ¹³C NMR spectra of **3** were similar to those of **1**. However, an acyl group at 6-Glc of **3** was different from the benzoyl group of **1**. The ¹H NMR data at δ_{H} 0.76 (3H, t, *J* = 7.5 Hz, H₃-4''), 1.01 (3H, d, *J* = 7.0 Hz, H₃-5''), 1.31 (1H, m, H-3''), 1.58 (1H, m, H-3''), and 2.32 (1H, m, H-2'') and the ¹³C NMR peaks at δ_{C} 11.7, 16.6, 27.1, 41.2, and 176.3 were assigned to a 2-(*S*)-methylbutyrate moiety (see Experimental Section). Hence, the structure of **3** was formulated as shown.

Table 1. Continued

	11		12		meehanine C		meehanine G		meehanine H	
position	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}
1	8.45, m		8.44, m		8.43, m		8.43, brt (6.0)		8.43, brt (6.0)	
	8.54, m		8.54, m		8.56, m		8.52, m		8.55, brdd (7.0, 4.0)	
2		171.9, 172.0		171.6		171.6, 171.8		171.6, 171.7		171.6, 171.8
3	2.74, m	47.1	2.76, m	46.5, 46.8	2.75, m	46.5, 46.8	2.74, brt (5.5)	46.5, 46.8	2.76, m	46.5, 46.8
4	4.27 ^a	61.4	4.42, m	61.6	4.39 ^a	60.9, 61.1	4.38, m	61.1	4.42, m	61.0, 61.2
6	2.43 ^a	45.7	2.54 ^a	45.4	2.41, m	45.3, 45.7	2.33–2.56 ^a	45.5	2.44, m	45.2, 45.7
			2.79 ^a		2.57 ^a		2.67–2.78 ^a		2.58, m	
									2.75 ^a	
7	1.46–1.65 ^a	32.7	1.45–1.80 ^a	32.4	1.45–1.63 ^a	32.4, 32.5	1.49 ^a	32.5	1.50–1.70 ^a	32.4, 32.5
							1.60 ^a			
8	5.37 ^a	74.5, 75.2	5.37, m	73.6, 74.8	5.38, m	73.6, 74.7	5.36, m	73.7, 74.8	5.38, m	73.5, 74.7
	5.49, brt (8.0)		5.49, m		5.52, brt (8.5)		5.49, m		5.53, brt (8.5)	
9	3.83, m	52.6	3.78, m	49.7, 52.4	3.83, m	49.7, 51.8	3.76, m	49.4, 52.4	3.43 ^a	49.5, 51.8
	4.64, m		4.61 ^a		4.67, m		4.64 ^a		3.83, brt (5.0)	
									4.67 ^a	
11	3.42–3.90 ^a	43.6, 45.0	3.40–3.80 ^a	43.4, 44.5	3.38–3.60 ^a	43.5, 44.4	3.50 ^a	43.4, 44.6	3.56 ^a	43.5, 44.4
					4.14 ^a		3.70 ^a		4.08 ^a	
							4.17 ^a			
12	1.95–2.32 ^a	30.1	2.00 ^a	29.8	1.76 ^a	29.7, 30.0	2.00 ^a	29.9, 30.9	2.00 ^a	29.7
			2.20, m				2.20 ^a		2.19 ^a	
13	3.27, m	36.6, 36.8	3.40–3.80 ^a	36.6	2.04–2.25 ^a	36.3, 36.5	3.44 ^a	36.3, 36.6	3.31, m	36.3, 36.5
	3.44 ^a						3.70 ^a		3.45 ^a	
	3.66 ^a								3.73 ^a	
Ac C=O		170.8		170.4		170.6, 170.7		170.5, 170.8		170.6, 170.7
Ac CH ₃	1.98, s	21.2, 21.6	1.94, s	20.9, 21.3	2.03, s	21.1, 21.3	1.96, s	20.9, 21.3	2.03, s	21.1, 21.3
	2.04, s		2.02, s				2.02, s			
1'		137.6		137.4		137.3, 173.4		137.4		137.4
2'	7.22, brd (8.0)	128.2	7.29, brd (7.0)	128.0	7.24, brd (8.5)	128.0	7.22 ^a	128.0	7.28, brd (8.0)	128.0
3'	7.16, brd (8.0)	117.2	7.27, brd (7.0)	117.0	7.17, brd (8.5)	116.9	7.22 ^a	117.0	7.30, brd (8.0)	117.0
4'		156.3		156.1		156.0		156.0		156.1
5'	7.16, brd (8.0)	117.2	7.27, brd (7.0)	117.0	7.17, brd (8.5)	116.9	7.22 ^a	117.0	7.30, brd (8.0)	117.0
6'	7.22, brd (8.0)	128.2	7.29, brd (7.0)	128.0	7.24, brd (8.5)	128.0	7.22 ^a	128.0	7.28, brd (8.0)	128.0
Rha-1	6.16, brs	98.8	6.17, brs	98.7	6.16, d (1.0)	98.6	6.24, brs	98.6	6.18, brs	98.7
-2	4.74, dd (3.5, 2.0)	81.8	4.69, dd (3.5, 1.5)	81.4	4.73, m	81.5	4.72, dd (3.5, 1.5)	81.5	4.68, dd (4.0, 2.0)	81.4
-3	4.61, dd (6.0, 3.5)	72.9	4.62, m	72.5	4.61, m	72.6	4.62, dd (8.0, 3.5)	72.5	4.63, m	72.5
-4	4.21–4.30 ^a	74.5	4.19 ^a	74.2	4.26 ^a	74.2	4.18 ^a	74.2	4.21 ^a	74.1
-5	4.20 ^a	70.8	4.19 ^a	70.5	4.21 ^a	70.6	4.22 ^a	70.5	4.21 ^a	70.5
-6	1.49, d (5.5)	18.7, 18.8	1.46, d (5.5)	18.4	1.48, d (6.0)	18.4	1.44, d (5.5)	18.3	1.46, d (6.5)	18.4
	1.50 d (5.5)				1.49, d (6.0)		1.45, d (5.5)		1.47, d (6.5)	
Glc-1	5.40, d (8.0)	107.5	5.32, d (7.5)	106.9	5.39, d (8.0)	107.2	5.38, d (7.5)	107.1	5.32, brd (7.5)	106.9
-2	4.14, dd (8.0, 8.5)	76.2	4.11, dd (7.5, 9.0)	75.7	4.14, m	75.9	4.16 ^a	75.7	4.11, dd (8.5, 7.5)	75.6
-3	4.21–4.30 ^a	78.7	4.21, dd (9.5, 9.0)	78.3	4.22–4.29 ^a	78.5	4.26, m	78.3	4.20 ^a	78.2
-4	4.21 ^a	71.6	4.21, dd (9.5, 9.5)	71.5	4.22–4.29 ^a	71.4	4.18 ^a	71.4	4.03 ^a	71.5
-5	3.98, m	79.1	4.04, m	75.6	3.98, m	78.8	4.18 ^a	75.7	4.04 ^a	75.6
-6	4.39, dd (11.0, 5.0)	62.7	4.76, dd (11.5, 5.0)	64.3	4.38, dd (11.5, 4.0)	62.5	4.97 ^a	65.1	4.75, m	64.3
	4.49, dd (11.0, 2.0)		4.96, dd (11.5, 2.0)		4.48 dd (11.5, 2.0)		5.19, dd (11.5, 2.0)		4.96, brd (11.5)	
1''		172.6, 172.9		173.2				173.2, 173.4		176.1
2''	2.53, m	35.0	2.41, dd (15.5, 7.5)	26.1, 26.2			2.41, dd (15.5, 7.5)	26.1, 26.2	2.58, m	37.0, 37.7
			2.59, dd (15.5, 7.5)				2.59, dd (15.5, 7.5)		2.83, m	
3''	1.81, m	19.4, 19.5	1.21, t (7.5)	9.9, 10.1			1.21, t (7.5)	9.9, 10.1	1.44 ^a	27.1, 27.6
			1.24, t (7.5)				1.24, t (7.5)		1.47 ^a	
4''	0.96, t (7.5)	14.4, 14.5							0.89, t (7.5)	12.4, 12.5
	0.98, t (7.5)								0.95, t (7.5)	
5''									1.12, d (7.0)	18.0, 18.6
									1.18, d (7.0)	
6''										
7''										
1'''				176.3				166.6		176.3
2'''			2.33, m	41.2				130.8	2.33, m	41.2
3'''			1.31, m	27.1			8.07, dd (8.0, 1.0)	129.8	1.32, m	27.1
			1.58, m						1.57 ^a	
4'''			0.76, t (7.0)	11.7			7.22 ^a	128.7	0.76, t (7.5)	11.7
									0.77, t (7.5)	
5'''			1.02, d (7.0)	16.6			7.41, m	133.1	1.01, d (7.0)	16.6
									1.02, d (7.0)	
6'''							7.22 ^a	128.7		
7'''							8.07, dd (8.0, 1.0)	129.8		

^a Unclear signal pattern due to overlapping. ^b Data were obtained from HMQC and HMBC spectra. ^c Assignments are interchangeable.

For meehanine O (**4**), confirmation of the molecular formula of C₃₃H₅₃N₃O₁₃ was obtained from HRFABMS, which was C₂H₂O less than that of **3**, indicating the absence of an acetyl group. The ¹H and ¹³C NMR spectra of the aglycone moiety of **4** were similar

to those of **2**. These data suggested that **4** is the 8-de-*O*-acetyl analogue of **3**, as shown.

Meehanines P (**5**), Q (**6**), R (**7**), S (**8**), and T (**9**) had an (*S*)-(4-hydroxyphenyl)-8-(*R*)-*O*-acetyl-10-*N*-[(*S*)-2-methylbutyl]amidated-

Table 2. NMR Data (400 MHz, Methanol-*d*₄) for Compounds **1**, **3**, **5**–**8**, **10**, and **12**

	1		3		5		6		7		8		10		12	
position	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C	δ H (δ in Hz)	δ C
2	1.70–2.60 ^a	174.7	missing	174.8	174.7	174.8	174.8	174.7	2.40, m	174.7	2.39, m	174.7	2.34–2.43 ^a	174.7	2.40 ^a	174.7, 174.8
3	4.01 ^a	60.2	missing	60.4	46.4 ^b , 46.8 ^b	46.5, 46.7	46.5, 46.7	46.6, 46.8	4.04, m	61.6, 61.8	4.03, m	61.9 ^a , 62.3 ^b	4.03, m	46.8 ^b	46.5, 46.7	46.5, 46.7
4	2.50–2.80 ^a	41.6	2.50–2.90 ^a	41.7	46.0 ^b , 46.9 ^a	46.0, 46.9	46.0, 46.9	46.1, 47.0	2.37 ^a	46.1, 47.0	2.20–2.7 0 ^a	46.1 ^b , 46.8	2.30–2.43 ^a	46.3, 47.0	4.03, m	61.8, 61.8
6			2.65 ^a		2.52, m	2.52, m	2.52, m	2.52, m	2.68 ^a				2.56 ^a		2.67, m	46.2, 47.0
7	1.75–1.95 ^a	27.1	1.70–2.20 ^a	27.3	1.54, m	33.1	33.1, 33.2	33.1, 33.3	1.54 ^a	33.1, 33.3	1.50–1.70 ^a	32.9	1.56–1.67 ^a	33.1	1.42–1.65 ^a	33.1, 33.2
8	5.09, m	69.6	5.10, brs	69.9	4.96, m	75.4	74.8, 74.9	74.8, 75.7	4.99, brt (9.0)	74.8, 75.7	4.98, m	74.9	4.98, m	75.1, 75.8	4.99, brt (9.0)	75.0, 75.8
9	3.21, m	39.4	3.21, m	39.5	3.78 ^a	50.7, 52.8	50.7, 53.0	50.8, 53.0	5.10, brt (9.0)	51.0, m	5.10, m	50.5 ^{a,b} , 53.0	3.74, m	50.6 ^b , 53.6	5.06, brt (9.0)	50.7, 53.5
	3.62, m		3.64, m		4.20 ^a	4.19, m			3.60 ^a	3.60 ^a	3.60 ^a		4.20, m	4.20, brdd (15.5, 9.5)		
11	3.20–3.70 ^a	missing	3.15–3.70 ^a	missing	3.37–3.51 ^a	44.5, 45.5	44.4, 45.4	44.5, 45.4	3.58 ^a	44.5, 45.4	3.53–3.64 ^a	44.3, 45.3	3.55–3.80 ^a	44.2 ^b , 45.7	3.55–3.80 ^a	44.2, 45.6
12	1.97–2.10 ^a	30.4 ^b	1.70–2.20 ^a	missing	1.55 ^a	29.8, 32.0	30.3, 32.0	29.8, 32.0	1.55 ^a	29.8, 32.0	1.50–1.70 ^a	30.7, 30.8	1.50–1.65 ^a	30.2, 30.3	1.45–1.60 ^a	29.9, 31.0
13	3.20–3.70 ^a	missing	3.15–3.70 ^a	missing	3.37–3.51 ^a	37.0, 37.2	37.2	37.0, 37.2	3.04, m	37.0, 37.2	3.05–3.50 ^a	36.9, 37.2	3.05–3.20 ^a	36.8, 37.2 ^b	3.00–3.12 ^a	37.0, 37.2
						3.33 ^a			3.33 ^a		3.44–3.72 ^a		3.40–3.51 ^a		3.30–3.50 ^a	
Ac C=O	171.3	171.3		172.3, 172.6		172.3, 172.6		172.3, 172.7		172.3, 172.7	Ac C=O			172.2, 172.8 ^b		172.2, 172.7
Ac CH ₃	20.8	20.8	2.08, s	20.4	1.91, s	21.3	21.3	21.2	1.91, s	21.2, 21.3	2.00, s	191, s	1.93, s	21.0, 21.2	1.93, s	21.0, 21.2
1'	134.1	134.5		137.8		137.9		138.0		137.5		137.9		137.9		137.9
2'	7.21, brd (8.5)	129.3	7.31, brd (8.0)	129.4	7.20, brd (8.5)	128.7	128.6	128.6	7.23, brd (8.5)	128.7	7.23, brd (8.5)	128.6	7.23, brd (8.5)	128.6	7.22, brd (8.5)	128.6
3'	7.02, brd (8.5)	117.9	7.12, brd (8.0)	118.1	7.03, brd (8.5)	117.9	117.7	117.7	7.05, brd (8.5)	117.7	7.05, brd (8.5)	117.6	7.05, brd (8.5)	117.6	7.05, brd (8.5)	117.6
4'	157.5	157.7		157.1		156.6		156.9		156.9		156.9		156.9		156.8
5'	7.02, brd (8.5)	117.9	7.12, brd (8.0)	118.1	7.03, brd (8.5)	117.9	117.7	117.7	7.05, brd (8.5)	117.7	7.05, brd (8.5)	117.6	7.05, brd (8.5)	117.6	7.05, brd (8.5)	117.6
6'	7.21, brd (8.5)	129.3	7.31, brd (8.0)	129.4	7.20, brd (8.5)	128.7	128.6	128.6	7.23, brd (8.5)	128.7	7.23, brd (8.5)	128.6	7.23, brd (8.5)	128.6	7.22, brd (8.5)	128.6
Rhu-1	5.78, d (1.5)	98.8	5.72, brs	98.9	5.75, brs	98.6	98.6	98.9	5.73, brs	98.9	5.73, brs	98.9	5.73, brs	98.9	5.70, d (1.5)	98.9
-2	4.04, dd (3.5, 1.5)	81.6	3.99, dd (3.5, 1.5)	82.4	4.04, dd (3.5, 1.5)	81.9	81.9	82.1	3.99, dd (3.5, 1.5)	82.1	4.00, dd (3.5, 1.5)	82.2	3.99, dd (3.5, 1.5)	82.1	3.98, dd (3.5, 1.5)	82.0
-3	3.89, dd (9.5, 3.5)	72.0	3.89, dd (9.5, 3.5)	72.1	3.91, dd (9.5, 3.5)	72.0	72.0	72.1	3.90, dd (9.5, 3.5)	72.1	3.90, dd (9.5, 3.5)	72.1	3.90, dd (9.5, 3.5)	72.0	3.90, dd (9.5, 3.5)	72.1
-4	3.43 ^a	74.1	3.45 ^a	74.1	3.44, dd (9.5, 9.5)	74.3	74.2	74.2	3.44, dd (9.5, 9.5)	74.2	3.44, dd (9.5, 9.5)	74.2	3.44, dd (9.5, 9.5)	74.2	3.44, dd (9.5, 9.5)	74.2
-5	3.53 ^a	70.5	3.57 ^a	70.6	3.59 ^a	70.6	70.5	70.5	3.62 ^a	70.5	3.60 ^a	70.5	3.60 ^a	70.4	3.60, m	70.4
-6	1.16, d (6.0)	18.0	1.19, d (6.5)	18.1	1.21, d (6.5)	18.1	18.1	18.1	1.22, d (6.0)	18.1	1.22, d (6.0)	18.1	1.21, d (6.0)	18.0	1.21, d (6.0)	18.0
Glc-1	4.57, d (7.5)	106.7	4.49, d (8.0)	106.8	4.42, d (7.5)	107.0	106.8	106.8	4.48, d (7.5)	106.9	4.49, d (7.5)	106.9	4.48, d (7.5)	106.8	4.48, d (7.5)	106.8
-2	3.40–3.45 ^a	75.7	3.30 ^a	75.7	3.30 ^a	75.4	75.7	75.6	3.32 ^a	75.6	3.32 ^a	75.5	3.35, dd (9.0, 7.5)	75.5	3.30 ^a	75.6
-3	3.40–3.50 ^a	77.8	3.38 ^a	77.8	3.30–3.40 ^a	77.4	77.9	77.8	3.30 ^a	77.8	3.30–3.50 ^a	77.8	3.30 ^a	77.8	3.36, m	77.8
-4	3.40 ^a	71.6	3.30 ^a	71.5	3.30–3.40 ^a	71.7	71.8	71.7	3.28 ^a	71.7	3.28 ^a	71.8	3.28 ^a	71.7	3.30 ^a	71.6
-5	3.53 ^a	75.5	3.49 ^a	75.5	3.57 ^a	75.5	75.5	75.4	3.48 ^a	75.4	3.46 ^a	75.4	3.48, m	75.4	3.47 ^a	75.4
-6	4.36, dd (11.5, 6.5)	65.1	4.12, dd (11.5, 6.5)	64.1	4.12, dd (12.0, 6.5)	64.7	65.0	64.5	4.12, dd (11.5, 6.5)	64.5	4.12, dd (12.0, 7.0)	64.2 ^b	4.12, dd (11.5, 7.0)	64.5	4.11, dd (11.5, 6.5)	64.3
	4.71, dd (11.5, 2.0)		4.50, dd (11.5, 2.0)		4.53 ^a		4.47, dd (11.5, 2.0)		4.47, dd (11.5, 2.0)		4.43, dd (12.0, 2.0)		4.45, dd (11.5, 2.0)		4.50, dd (11.5, 2.0)	
1''	167.8	167.8		177.9		179.2		179.1, 179.2		179.1, 179.2		179.7, 180.7		175.5		176.4
2''	131.2	131.2	2.22, m	42.4	2.65 ^a	38.2, 38.8	38.2, 38.8	38.2, 38.8	2.65 ^a	38.2, 38.8	2.65, m	38.2, 38.8	2.20–2.36 ^a	35.5, 35.6	2.39, q (7.5)	26.9, 26.9
3''	7.86, dd (7.5, 1.0)	130.5	1.31, m	27.9	2.81 ^a	2.80, m	2.81, m	2.81, m	2.80, m	2.80, m	2.80, m	2.80, m	2.47, q (7.5)	2.47, q (7.5)	2.47, q (7.5)	2.47, q (7.5)
4''	7.30, dd (7.5, 1.0)	129.5	0.79, t (7.0)	12.1	0.85, t (7.0)	12.5	12.4, 12.5	12.4, 12.5	0.85, t (7.5)	12.4, 12.5	0.85, t (7.5)	12.5 ^b , 12.6 ^b	0.95, t (7.5)	0.95, t (7.5)	1.09, t (7.0, 5)	9.9, 10.1
5''	7.50, dd (7.5, 1.0)	134.1	0.98, d (7.0)	17.0	1.06, d (7.0)	17.8, 18.5	17.8, 18.5	17.5, 18.5	1.04, d (7.0)	17.5, 18.5	1.05, d (7.0)	17.6	0.96, t (7.5)	14.2, 14.4	1.10, t (7.5)	
6''	7.30, dd (7.5, 7.5)	129.5														
7''	7.86, dd (7.5, 1.0)	130.5														
1'''																
2'''																
3'''																
4'''																
5'''																
6'''																
7'''																
8'''																
9'''																

^a Unclear signal pattern due to overlapping. ^b Data were obtained from HMQC and HMBC spectra.

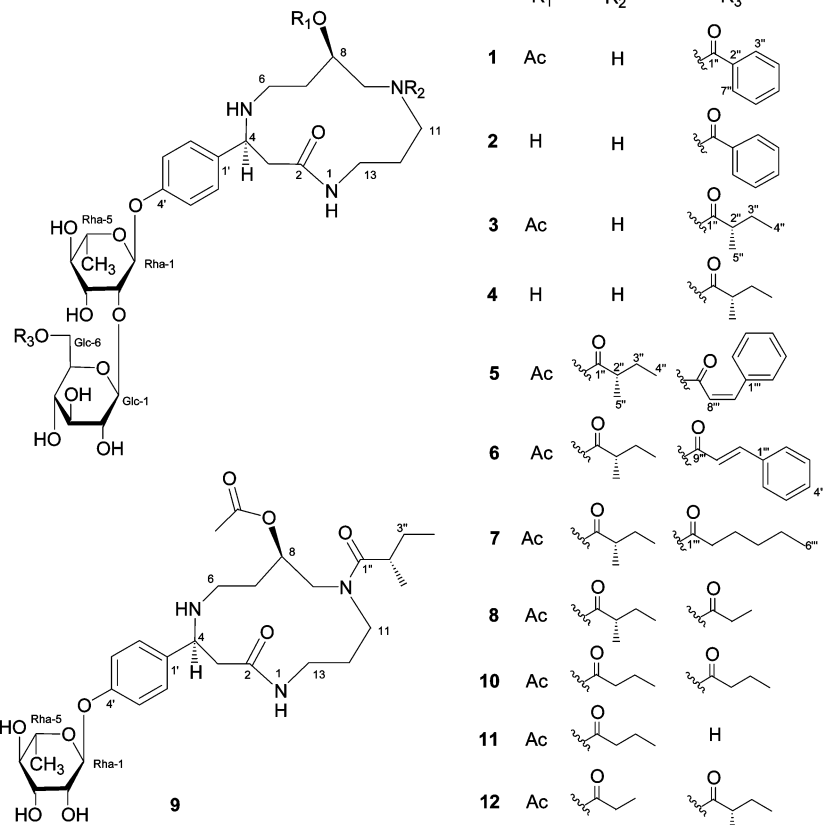


Figure 1. Structures of **1–12**.

1,5,10-triazacyclotridecan-2-one cyclic spermidine alkaloidal skeleton as their common aglycone, which was the same as that of meehanines A, C, H, J, and K in our previous report.¹ The aglycone was yielded by acid hydrolysis of these compounds. The ¹H and ¹³C NMR spectra of **5–8** measured in methanol-*d*₄ were similar to those of meehanine C¹ except for the presence of a 6-acylated β-D-glucosyl moiety. Compounds **5** and **6** had the molecular formula C₄₄H₆₁N₃O₁₅ (see Experimental Section). Aromatic proton and carbon signals suggested the presence of a cinnamoyl group; the olefinic protons at δ_H 5.66 (1H, d, *J* = 12.5 Hz, H-8''') and 6.78 (1H, d, *J* = 12.5 Hz, H-7''') of **5** indicated a *cis*-cinnamoyl group. The duplicated C-8''' and C-7''' olefinic protons [δ_H 6.25 (d, *J* = 16.0 Hz) and 6.26 (d, *J* = 16.0 Hz), 7.54 (d, *J* = 16.0 Hz), and 7.55 (d, *J* = 16.0 Hz), respectively] of **6** showed a *trans*-cinnamoyl group. For compound **7**, confirmation of the molecular formula of C₄₁H₆₅N₃O₁₅ was achieved by HRFABMS, which was C₆H₁₀O more than that of meehanine C. A methyl carbon at δ_C 14.3 (C-6'''), four methylene carbons at δ_C 23.4 (C-5'''), 32.4 (C-4'''), 25.7 (C-3'''), and 34.9 (C-2'''), and a carbonyl carbon at δ_C 175.2 (C-1''') suggested the presence of a hexanoyl moiety. Methyl protons at δ_H 0.86 (3H, t, *J* = 7.0 Hz, H-6'''), methylene protons at δ_H 1.22 (2H, m, H-5'''), 1.15 (2H, m, H-4'''), 1.44 (2H, m, H-3'''), and 2.06 (2H, t, *J* = 7.5 Hz, H-2'''), and their ¹H–¹H COSY correlations supported the presence of a CH₃(CH₂)₄ spin system. The H-2''' and H-Glc-6 (δ_H 4.12, dd, *J* = 11.5, 6.5 Hz, and 4.47, dd, *J* = 11.5, 2.0 Hz) signals were long-range coupled with the carbonyl carbon at δ_C 175.2 (C-1'''). Thus, compound **7** had a hexanoyl moiety at Glc-6. For compound **8**, confirmation of the molecular formula of C₃₈H₅₉N₃O₁₅ was established by HRFABMS, which was C₃H₄O more than that of meehanine C. A methyl carbon at δ_C 13.7 (C-3'''), a methylene carbon at δ_C 28.1 (C-2'''), and a carbonyl carbon at δ_C 175.8 (C-1''') suggested the presence of a propanoyl moiety on Glc-6. For compound **9**, the molecular formula C₂₉H₄₅N₃O₉ was established by HRFABMS, which was C₆H₁₀O₅ less than that of

meehanine C, indicating the absence of a glucosyl moiety. Hence, the structures of **5–9** were formulated as shown in Figure 1.

Meehanines U (**10**) and V (**11**) had a 10-*N*-butylamidated cyclic spermidine alkaloidal skeleton, which was suggested by ¹H, ¹³C, and 2D (¹H–¹H COSY, HMQC, HMBC) NMR spectra acquired in methanol-*d*₄ at 30 °C (Table 2) and in pyridine-*d*₅ at 30 °C (Table 1), respectively. Compound **10** showed a protonated molecular peak at *m/z* 798.4031 [M + H]⁺ in the HRFABMS, which indicated the molecular formula C₃₈H₅₉N₃O₁₅. A methyl proton at δ_H 0.79 (3H, t, *J* = 7.5 Hz), two methylene signals [δ_H 1.42 (2H, m, H-3''') and 2.04 (2H, t, *J* = 7.0 Hz, H-2'')], and carbons at δ_C 14.0, 19.4, 36.8, and 175.0 suggested the presence of a butanoyl groups on the β-D-glucosyl moiety. Compound **11** had the molecular formula C₃₄H₅₃N₃O₁₄. The ¹H and ¹³C NMR spectra (Table 1) of **11** were similar to those of meehanine C except for the presence of a 10-*N*-butylamide moiety instead of a 10-*N*-(methyl)butylamide group for meehanine C. Hence, the structures of **10** and **11** were formulated as shown in Figure 1.

Meehanine W (**12**) showed a protonated molecular peak at *m/z* 798.4031 [M + H]⁺ in the HRFABMS, which indicated the molecular formula C₃₈H₅₉N₃O₁₅. In the ¹H and ¹³C NMR spectra acquired in pyridine-*d*₅ at 30 °C (Table 1), an aglycone moiety and a sugar moiety of **12** were almost superimposable onto those of meehanines G and H, respectively. The full assignments of the ¹H and ¹³C NMR spectra of **12** in pyridine-*d*₅ and methanol-*d*₄ (Tables 1 and 2) were established using ¹H–¹H COSY, HMQC, and HMBC spectra, and its structure was formulated as shown in Figure 1.

These 12 alkaloids are new members of the cyclic 13-membered spermidine alkaloidal glycosides that were reported recently from Lamiaceae plants.^{1,5} Most have various acyl groups on Glc-6 and N-10. Compounds **1–4** are characterized by the absence of the amide moiety at N-10. Unlike ¹H and ¹³C NMR spectra of meehanines A–K and compounds **5–12**, those of these compounds

were free of duplicated signals due to absence of the *cis*–*trans* isomerization of the 10-*N* amide bonds. Compounds **9** and **11** lack an acyl group on Glc-6 or an acylated glucosyl moiety, which was observed in meehanine C¹ and dracotanosides C and D.⁵ Compounds **5**–**8**, **10**, and **12** are acyl analogues of the spermidine alkaloids from *M. urticifolia*.

Although *M. urticifolia* is not utilized for folk medicine and is not blended in Kampo formulas in Japan, new findings concerning the biological activities of these constituents are expected.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO P-2300 polarimeter. CD spectra were recorded on a JASCO J-700 spectropolarimeter. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were recorded on a JEOL JNM-AL400 spectrometer, and chemical shifts are given as δ values with TMS as internal standard at 30 °C. Inverse-detected heteronuclear correlations were measured using HMQC (optimized for ¹J_{C–H} = 145 Hz) and HMBC (optimized for ²J_{C–H} = 8 Hz) pulse sequences with a pulsed field gradient. HRFABMS data were obtained on a JEOL JMS700 mass spectrometer, using a *m*-nitrobenzyl alcohol or glycerol matrix. Preparative LPLC and HPLC were performed on a Jasco 2089 instrument and detected by UV at 210 nm.

Plant Material. *M. urticifolia* (760 g) was collected in July 2007 and in September 2008 (670 g) in Sendai, Japan. The plant was identified by Dr. Koji Yonekura, Tohoku University, Sendai, Japan. A voucher specimen was deposited at the herbarium of Tohoku Pharmaceutical University under No. 20070727.

Extraction and Isolation. The dried and powdered whole plants (760 g) of *M. urticifolia* were extracted with MeOH (12 L) at room temperature for a month. The MeOH extract was concentrated at reduced pressure, suspended in H₂O (1.5 L), and partitioned with Et₂O (3 × 1.0 L). The H₂O layer (98.52 g) was passed through a porous polymer gel column (Mitsubishi Diaion HP-20, 70–180 mm) and eluted with H₂O; 10%, 45%, and 90% MeOH; and MeOH. The 90% MeOH eluate (5.5 g) was chromatographed on a reversed-phase column using ODS (Cosmosil 140C₁₈-OPN, Nacalai Tesque, 150 g) and was eluted with 20%, 30%, 40%, 50%, 60%, and 80% MeOH (fractions 1A–1F). Fractions 1E and 1F (259.1 mg) were subjected to preparative HPLC [columns, Tosoh, ODS-100 V, 20–250 mm; solvent, MeCN–H₂O (40:60), and Kanto Chemical, Mightysil RP-18 GP, 10 × 250 mm; solvent, MeCN–H₂O (30:70) and MeOH–H₂O (55:45)] to yield compounds **5** (1.4 mg), **6** (2.0 mg), and **7** (5.2 mg).

The dried and powdered whole plants (670 g) of *M. urticifolia* were extracted with 80% acetone (2 × 12 L) at 56 °C. The extract was concentrated at reduced pressure, suspended in H₂O (1.0 L), and partitioned with Et₂O (3 × 1.0 L). The H₂O layer (53.1 g) was passed through a Diaion HP-20 column (eluted with H₂O, 10% and 90% MeOH, and MeOH). The 90% MeOH eluate (12.9 g) was chromatographed on an ODS column and eluted with 20%, 30%, 40%, 50%, and 80% MeOH (fractions 2A–2E). Fraction 2C (1.06 g) was subjected to preparative LPLC [column, Yamazen, Ultra Pack ODS-SM-50C-M, 37 × 100 mm; solvent, MeOH–0.2% TFA (35:65)] to give 10 fractions (3A–3J). Fractions 3B and 3C (44.2 mg) were subjected to preparative HPLC [columns, Shiseido, Capcell-Pak Ph, 20 × 250 mm; solvent, MeCN–0.2% TFA (15:85), and YMC, ODS-AM, 10 × 300 mm; solvent, MeCN–H₂O (25:75 or 20:80)] to yield compounds **1** (15.2 mg), **2** (5.5 mg), **3** (4.0 mg), **8** (0.6 mg), **9** (1.0 mg), **10** (0.9 mg), and **12** (2.9 mg). Fractions 2A and 2B (10.3 g) were dissolved in H₂O, which was passed through a Diaion HP-20 column (eluted with 5%, 20%, and 50% MeOH, and MeOH), and the 50% MeOH eluate was subjected to preparative LPLC [solvent, MeOH–0.2% TFA (35:65)] to give nine fractions (4A–4I). Fractions 4B and 4C (185.7 mg) were subjected to preparative HPLC [columns, Cosmosil, AR-II, 20 × 250 mm; solvent, MeCN–0.2% TFA (15:85), and ODS-AM, solvent, MeCN–H₂O (22:78)] to yield compounds **4** (1.8 mg), **11** (1.3 mg), and **12** (0.8 mg).

Meehanine L (1): colorless, amorphous powder; [α]_D²³ –26.4 (c 0.66, MeOH); CD (c 0.066, MeOH) $\lambda(\theta)$ 236 (4100), 223 (–14 900), 216 (–11 300), 201 (–36 400) nm; ¹H and ¹³C NMR, Tables 1 and 2; HRFABMS *m/z* 762.3449 [M + H]⁺ (calcd for C₃₇H₅₂N₃O₁₄, 762.3451).

Meehanine M (2): colorless, amorphous powder; [α]_D²² –25.8 (c 0.48, MeOH); CD (c 0.053, MeOH) $\lambda(\theta)$ 236 (3300), 223 (–13 700),

215 (–10 600), 201 (–41 600) nm; ¹H and ¹³C NMR, Table 1; HRFABMS *m/z* 720.3368 [M + H]⁺ (calcd for C₃₅H₅₀N₃O₁₃, 720.3345).

Meehanine N (3): colorless, amorphous powder; [α]_D²³ –23.9 (c 0.36, MeOH); CD (c 0.036, MeOH) $\lambda(\theta)$ 243 (3500), 225 (–17 400), 210 (–7300), 201 (–29 100) nm; ¹H and ¹³C NMR, Tables 1 and 2; HRFABMS *m/z* 742.3782 [M + H]⁺ (calcd for C₃₅H₅₆N₃O₁₄, 742.3764).

Meehanine O (4): colorless, amorphous powder; [α]_D²¹ –16.7 (c 0.18, MeOH); CD (c 0.018, MeOH) $\lambda(\theta)$ 242 (8200), 224 (–8000), 207 (–700), 201 (–15 600) nm; ¹H and ¹³C NMR, Tables 1; HRFABMS *m/z* 700.3657 [M + H]⁺ (calcd for C₃₃H₅₄N₃O₁₃, 700.3658).

Meehanine P (5): colorless, amorphous powder; [α]_D²⁰ 1.4 (c 0.14, MeOH); CD (c 0.028, MeOH) $\lambda(\theta)$ 263 (8600), 224 (–24 600), 204 (29 300) nm; ¹H and ¹³C NMR, Table 2; HRFABMS *m/z* 872.4181 [M + H]⁺ (calcd for C₄₄H₆₂N₃O₁₅, 872.4183).

Meehanine Q (6): colorless, amorphous powder; [α]_D²⁰ 1.9 (c 0.21, MeOH); CD (c 0.018, MeOH) $\lambda(\theta)$ 261 (7400), 225 (–24 300), 204 (32 900) nm; ¹H and ¹³C NMR, Table 2; HRFABMS *m/z* 872.4203 [M + H]⁺ (calcd for C₄₄H₆₂N₃O₁₅, 872.4183).

Meehanine R (7): colorless, amorphous powder; [α]_D²¹ –2.2 (c 0.46, MeOH); CD (c 0.048, MeOH) $\lambda(\theta)$ 245 (5600), 224 (–24 400), 202 (33 400) nm; ¹H and ¹³C NMR, Table 2; HRFABMS *m/z* 840.4490 [M + H]⁺ (calcd for C₄₁H₆₆N₃O₁₅, 840.4496).

Meehanine S (8): colorless, amorphous powder; [α]_D²³ –6.7 (c 0.06, MeOH); CD (c 0.012, MeOH) $\lambda(\theta)$ 252 (15 100), 224 (–8700), 205 (25 800) nm; ¹H and ¹³C NMR, Table 2; HRFABMS *m/z* 798.4011 [M + H]⁺ (calcd for C₃₈H₆₀N₃O₁₅, 798.4026).

Meehanine T (9): colorless, amorphous powder; [α]_D²³ –21.7 (c 0.12, MeOH); CD (c 0.012, MeOH) $\lambda(\theta)$ 241 (10 600), 224 (–6700), 205 (14 300) nm; ¹H and ¹³C NMR, Table 1; HRFABMS *m/z* 580.3229 [M + H]⁺ (calcd for C₂₉H₄₆N₃O₉, 580.3236).

Meehanine U (10): colorless, amorphous powder; [α]_D²³ –10.0 (c 0.04, MeOH); CD (c 0.008, MeOH) $\lambda(\theta)$ 250 (22 700), 225 (–13 000), 205 (38 700) nm; ¹H and ¹³C NMR, Table 2; HRFABMS *m/z* 798.4031 [M + H]⁺ (calcd for C₃₈H₆₀N₃O₁₅, 798.4026).

Meehanine V (11): colorless, amorphous powder; [α]_D²³ –12.0 (c 0.20, MeOH); CD (c 0.020, MeOH) $\lambda(\theta)$ 253 (8000), 223 (–35 400), 203 (27 200) nm; ¹H and ¹³C NMR, Table 1; HRFABMS *m/z* 728.3600 [M + H]⁺ (calcd for C₃₄H₅₄N₃O₁₄, 728.3607).

Meehanine W (12): colorless, amorphous powder; [α]_D²² –13.0 (c 0.23, MeOH); CD (c 0.021, MeOH) $\lambda(\theta)$ 249 (2800), 224 (–29 300), 204 (8300) nm; ¹H and ¹³C NMR, Tables 1 and 2; HRFABMS *m/z* 798.4031 [M + H]⁺ (calcd for C₃₈H₆₀N₃O₁₅, 798.4026).

Acid Hydrolysis of 3 and 4 and Determination of the Configuration of 2-Methylbutyric Acid. Compounds **3** (1 mg) and **4** (0.5 mg) were separately dissolved in 7% HCl (1 mL) and stirred for 1 h at 60 °C. After cooling, the solution was extracted with CH₂Cl₂ (2 × 3 mL). From the CH₂Cl₂ layer, 2-methylbutyric acid was obtained. The CH₂Cl₂ layers were washed with H₂O and dried over 3 Å molecular sieves. To the solutions, 1-hydroxybenzotriazole monohydrate, *N,N'*-dicyclohexylcarbodiimide, and (*S*)-1-(1-naphthyl)ethylamine were added (10 mg each). After the mixtures had been stirred for 3 h at room temperature, filtration and concentration gave residues that were analyzed by HPLC with detection at 280 nm. Analytical HPLC was performed on a Shiseido Capcell pak C18 column (4.6 × 250 mm) at 20 °C using MeCN–H₂O (40:60) as the solvent. Peaks were detected with a Tosoh UV8010 UV detector. (*S*)-2-Methyl-*N*-[(*S*)-1-(1-naphthyl)ethyl]butyramide (*t*_R 33.0 min) was identified as the product resulting from the 2-methylbutyryl moiety of **3** and **4** by comparing their retention times with those of the authentic samples, (*S*)-2-methyl-*N*-[(*S*)-1-(1-naphthyl)ethyl]butyramide (*t*_R 33.0 min) and (*R*)-2-methyl-*N*-[(*S*)-1-(1-naphthyl)ethyl]butyramide (*t*_R 34.4 min).^{1,10,11}

Acid Hydrolysis of Compounds 1–12. Compounds **1**–**12** (0.5 mg each) were separately stirred for 1 h at 60 °C in 7% HCl (2 mL). After cooling, the reaction mixtures of compounds **1**–**4** and **10**–**12** were passed through an Amberlite IRA400 column, and the eluates were subjected to preparative HPLC [column, YMC Pack, ODS-AM, 10 × 300 mm; solvent, MeOH–H₂O (10:90); detector, UV 210 nm] to yield a sugar fraction. The reaction mixtures of compounds **5**–**9** were subjected to preparative HPLC [column, Kanto Chemical, Mightysil RP-18 GP, 10 × 250 mm; solvent, MeOH–H₂O (20:80); detector, UV 210 nm] to yield the (*S*)-(4-hydroxyphenyl)-8-(*R*)-*O*-hydroxy-10-*N*-[(*S*)-2-methylbutyl]amidated-1,5,10-triazacyclotridecan-2-one and sugar fractions.

Sugar Identification. Sugar fractions from the hydrolysis of compounds **1**–**12** were dissolved in pyridine (0.5 mL each) and stirred

with L-cysteine methyl ester (5 mg) before *o*-tolylisothiocyanate (20 μ L) was added to the mixture using the same procedures as in our previous report.¹ The reaction mixtures were analyzed by HPLC and detected at 250 nm. Analytical HPLC was performed on a Tosoh ODS-100 V column (4.6 \times 250 mm) at 25 °C using CH₃CN–0.2% TFA in H₂O (30:70) as the solvent. Peaks were detected with a Tosoh UV8010 detector. D-Glucose (t_R 12.0 min) and L-rhamnose (t_R 19.8 min) were identified as the sugar moieties of **1–12** and L-rhamnose in **9** by comparing their retention times with those of authentic samples of D-glucose (t_R 12.0 min), L-glucose (t_R 11.0 min), and L-rhamnose (t_R 19.8 min).⁸

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Supporting Information Available: NMR spectra and tables of ¹H, ¹³C, and HMBC data for compounds **1–12** and meehanines C, G, and H. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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