Five New Nortropane Alkaloids and Six New Amino Acids from the Fruit of *Morus alba* Linne Growing in Turkey

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Investigation of the constituents of the fruits of *Morus alba* Linne (Moraceae) afforded five new nortropane alkaloids (1—5) along with nor-ψ-tropine (6) and six new amino acids, morusimic acids A—F (7—12). The structures of the new compounds were determined to be 2α,3β-dihydroxynortropane (1), 2β,3β-dihydroxynortropane (2), 2α,3β,6*exo*-trihydroxynortropane (3), 2α,3β,4α-trihydroxynortropane (4), 3β,6*exo*-dihydroxynortropane (5), (3*R*)-3-hydroxy-12-{(1*S*,4*S*)-4-[(1*S*)-1-hydroxyethyl]-pyrrolidin-1-yl}-dodecanoic acid-3-*O*-β-D-glucopyranoside (7), (3*R*)-3-hydroxy-12-{(1*S*,4*S*)-4-[(1*S*)-1-hydroxyethyl]-pyrrolidin-1-yl}-dodecanoic acid (8), (3*R*)-3-hydroxy-12-[(1*R*,4*R*,5*S*)-4-hydroxy-5-methyl-piperidin-1-yl]-dodecanoic acid-3-*O*-β-D-glucopyranoside (9), (3*R*)-3-hydroxy-12-[(1*R*,4*R*,5*S*)-4-hydroxy-5-methyl-piperidin-1-yl]-dodecanoic acid (10), (3*R*)-3-hydroxy-12-[(1*R*,4*R*,5*S*)-4-hydroxy-5-hydroxymethyl-piperidin-1-yl]-dodecanoic acid-3-*O*-β-D-glucopyranoside (11), and (3*R*)-3-hydroxy-12-[(1*R*,4*S*,5*S*)-4-hydroxy-5-methyl-piperidin-1-yl]-dodecanoic acid (12) on the basis of spectral and chemical data.

Key words *Morus alba*; nortropane; pyrrolidinyl dodecanoic acid; piperidinyl dodecanoic acid; structural elucidation; α-glucosidase inhibition

White mulberry, *Morus alba* L. (Moracae), is native to China and Korea and has been introduced to other countries in Asia, and Europe. White mulberry (in Turkish, *Akdut*), a species with white ripened fruit, is common in Turkey and in Europe, although a species with dark purple ripened fruit is common in Asia. Fresh fruit of the former is sold in fruit stores, and dried fruit in cake shops in Turkey.[1)]

Numerous compounds as the constituents of mulberry tree have been reported.[2—5)] Among them polyhydroxy alkaloids,[6)] such as 1-deoxynojirimycin (DNJ), fagomine (FAG), 1,4-dideoxy-1,4-imino-D-arabinitol (D-AB1), and calystegine B_2, from the roots, leaves, and fruit appear interesting as glycosidase inhibitors, because the fruit is used as food.

In the course of studies on the biologically active constituents of Moraceae,[7)] we examined the constituents of the white ripened fruit of *M. alba* grown in Turkey. In this paper we deal with the isolation of five new nortropane alkaloids, along with nor-ψ-tropine and six new amino acids from them, the structural elucidation, and their inhibitory activities on α-glucosidase.

The fruit of *M. alba* grown in Turkey was extracted with MeOH–H_2O (1 : 1) and the alkaloidal constituents were concentrated as follows. The extract was subjected to chromatography on an Amberlite CG-50 column. The adsorbed fraction was eluted with ammonia solution (28% NH_3 : H_2O=1 : 9). The eluates were subjected to silica-gel column chromatography using $CHCl_3$, MeOH, and H_2O to provide 16 fractions, which were respectively subjected to Sep-Pak C_{18} cartridge and Dowex 50W-X4 column chromatographies, followed by preparative HPLC to provide purified alkaloids and amino acids.

Compound **1** was obtained as a colorless powder, $[\alpha]_D$ −33.9° (c=0.32, H_2O) and showed a purplish-red spot on TLC when sprayed with ninhydrin reagent followed by heating on a hot plate (ninhydrin reaction). The molecular formula was determined to be $C_7H_{13}NO_2$ by positive high-resolution secondary ion mass spectroscopy (pos. HR-SI-MS) (m/z: 144.1028 $[M+H]^+$, error, +0.4 mmu). The IR spectrum showed a strong OH and NH band and a CH band as described in the experimental section.

The ^{1}H-NMR spectrum of **1** suggested the presence of 3 methylene groups [δ 1.44 (1H, m), δ 1.95 (1H, ddd, J=13.0, 6.6, 3.0 Hz), δ 1.58 (1H, m), δ 1.81 (2H, m), δ 1.67 (1H, m)], 2 oxymethine groups [δ 3.49 (1H, m), δ 3.64 (1H, ddd, J=11.0, 6.6, 8.5 Hz)], 2 methine groups attached to a nitrogen atom [δ 3.51 (1H, m), 3.41 (1H, dd, J=3.7, 6.9 Hz)].

The ^{1}H- and ^{13}C-NMR signals were reasonably assigned on the basis of ^{1}H–^{1}H correlated spectroscopy (^{1}H–^{1}H COSY), total correlation spectroscopy (TOCSY), and heteronuclear single quantum coherence (HSQC), as summarized in Table 1.

Thus, **1** was assumed to be 2α,3β-dihydroxynortorpane as follows. Nuclear Overhauser effects (NOEs) were found between H-2β and H-4β, H-3α and H-6*endo*, and H-3α and H-7*endo* in the nuclear Overhauser enhancement and exchange spectroscopy (NOESY) spectrum. The absolute configuration of the 2- and 3-carbons was determined to be 2*R* and 3*R* using a benzoate chirality method[8)] as follows. The acetamide (**1a**) was prepared from **1** with acetic anhydride in pyridine at −4 °C, and then the dibenzoate (**1b**) was obtained by benzoylation of **1a** and purification of the product in preparative HPLC.

The circular dichroism (CD) curve of **1b** showed a negative Cotton effect ($\Delta\varepsilon$238 −15.9) and a positive effect ($\Delta\varepsilon$223 +16.4) to establish the chiral arrangement in a counterclockwise manner. Therefore, the above supposition that **1** should be 2α,3β-dihydroxynortropane proved to be correct when including the absolute stereostructure (1*S*,2*R*,3*R*,5*R*). It is notable that **1** showed $[\alpha]_D$ −33.9°, while the enantiomer, 3β,4α-dihydroxynortropane (no data supporting the absolute stereostructure) showed $[\alpha]_D$ +48.4°.[9)]

Compound **2** was obtained as a colorless powder, $[\alpha]_D$ −34.0° (c=0.61, H_2O), and showed a purplish-red spot on TLC by ninhydrin reaction, and the molecular formula was

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Table 1. ^{1}H- and ^{13}C-NMR Spectral Data of **1**—**6**

	1		**2**			**3**			**4**			**5**			**6**	
	Proton	Carbon	Proton		Carbon	Proton		Carbon	Proton		Carbon	Proton		Carbon	Proton	Carbon
1	3.41 dd (3.7, 6.9)	60.71	3.41[a]		60.56	3.58 dd (3.4, 7.1)		61.24	3.45[a] m		60.43	3.82[a]		56.82	3.63[a] m	56.25
2	3.49[a]	78.40	3.70 t (3.4)		73.04	3.46 dd (3.4, 9.0)		76.76	3.57 dd (3.9, 8.7)		76.60	1.95 m	α	40.38	1.97[a] m	42.23
											β	1.49[a]			1.46[a] m	
3	3.64 ddd (11.0, 6.6, 8.5)	71.73	3.87 ddd (12.0, 6.0, 3.4)		66.59	3.40 ddd (11.0, 6.6, 9.0)		71.58	3.32[a] t (8.7)		77.26	3.80[a]		65.51	4.01[a] m (12.0, 6.0)	65.80
4	α 1.95 ddd (13.0, 6.6, 3.0)	41.63	1.74 ddd (12.0, 6.0, 2.5)	α	38.51	2.01 ddd (6.6, 3.4, 13.0)	α	37.60	3.57[a] dd (3.9, 8.7)		76.60	2.08 m	α	38.93	1.97[a] m	42.23
	β 1.44 m		1.57[a]	β		1.44 ddd (11.0, 3.4, 13.0)	β					1.49[a]	β		1.46[a] m	
5	3.51[a]	55.92	3.41[a]		54.58	3.33		64.64	3.45[a] m		60.43	3.48		64.92	3.63[a] m	56.25
6	*endo* 1.58 m	30.39	*endo* 1.59[a]		28.23	4.23 dd (7.1, 2.5)		76.50	*endo* 1.84[a] m		25.50	4.34 dd (7.3, 2.7)		76.10	*endo* 1.70[a] m	30.13
	exo 1.81[a] m		*exo* 1.80[a]						*exo* 1.75[a] m						*exo* 1.82[a] m	
7	*endo* 1.81[a] m	25.98	*endo* 1.55[a]		26.62	*endo* 2.35 dd (7.1, 14.6)		37.84	*endo* 1.84[a] m		25.50	*endo* 2.28 dd (7.3, 14.4)		41.83	*endo* 1.70[a] m	30.13
	exo 1.67 m		*exo* 1.80[a]			*exo* 1.55 m			*exo* 1.75[a] m			*exo* 1.72 m			*exo* 1.82[a] m	

ppm (Hz)

a) Overlapped signals. δ in D_2O. ^{1}H-NMR at 500 MHz. ^{13}C-NMR at 125 MHz.

determined to be $C_7H_{13}NO_2$ by pos. HR-SI-MS (*m/z*: 144.1022, $[M+H]^+$, error, -0.2 mmu). The IR spectrum showed a strong OH and NH band and a CH band.

The ^{1}H- and ^{13}C-NMR signals were similar to those of **1**, except for the ^{1}H-splitting pattern (H-2α) and ^{13}C-chemical shifts of the hydroxy methines (C-2,3), and assigned as shown in Table 1 by analyzing the ^{1}H–^{1}H COSY, TOCSY, and HSQC spectra. Thus, **2** was assumed to be 2β,3β-dihydroxynortorpane, which is the 2-epimer of **1**, by the vicinal coupling constants ($J_{2,3}$=3.4 Hz) and NOEs between H-2α and H-7*endo* in the NOESY spectrum.

The absolute configuration of 2- and 3-carbons was determined to be 2*S* and 3*R* by using a benzoate chirality method as follows. The CD curve of the dibenzoate (**2b**), prepared from the acetamide (**2a**), showed a positive Cotton effect ($\Delta\varepsilon$238 +13.7) and a negative effect ($\Delta\varepsilon$221 −8.0) to establish the chiral arrangement in a clockwise manner. Therefore, the supposition that **2** should be 2β,3β-dihydroxynortropane proved correct when including the absolute stereostructure (1*S*,2*S*,3*R*,5*R*).

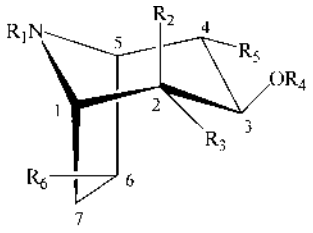
Compound **3** was obtained as a colorless powder, $[\alpha]_D$ −27.3° (*c*=0.55, H_2O), showed a purplish-red spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_7H_{13}NO_3$ by pos. HR-SI-MS (*m/z*: 160.0971 $[M+H]^+$, error, −0.2 mmu). The IR spectrum showed a strong OH and NH band and a CH band.

The ^{1}H-NMR spectrum of **3** was similar to that of **1**, except for the presence of an additional hydroxymethine (C-6), as summarized in Table 1. **3** was assumed to be 2α,3β,6*exo*-trihydroxynortropane by NOEs between H-2β and H-4β, H-3α and H-6*endo*, and H-3α and H-7*endo* in the NOESY spectrum.

After the confirmation of the relative stereostructure as above, the selection of one enatiomer was tried by the benzoate chirality method. The tribenzoate of 3-acetamide **3b** was prepared similarly as in **1** and **2**, and it showed a weak Cotton effect probably owing to overlapping clockwise (2,6-*O*-dibenzoyl) and counter clockwise (2,3-*O*-dibenzoyl) contribution by molecular model consideration. The difference CD curve between **1b** and **3b** showed a positive Cotton effect ($\Delta\varepsilon$237 +14.8) and a negative Cotton effect ($\Delta\varepsilon$224 −13.2) to establish the chiral arrangement of 2,6-*O*-dibenzoyl in a clockwise manner. The $[\alpha]_D$ and $[M]_D$ values (−27.7°, −43.4°) similar to the difference (−32.6°, −46.6°) between those of **1** and **5**, and the small contribution of the 6*exo*-hydroxy group in $[\alpha]_D$ and $[M]_D$ of nortropane alkaloids, judging from those of **5** and **6**, and from the reference,[10] also supported that the absolute stereostructure of **3** was proposed as shown in Fig. 1. Therefore, the above assumption proved correct when including the absolute stereostructure (1*S*,2*R*,3*R*,5*S*,6*R*).

Compound **4** was obtained as a colorless powder, $[\alpha]_D$ ±0° (*c*=0.40, H_2O), showed a purplish-red spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_7H_{13}NO_3$ by pos. HR-SI-MS (*m/z*: 160.0983 $[M+H]^+$, error, +1.0 mmu). The IR spectrum showed a strong OH and NH band and a CH band.

The ^{13}C-NMR spectrum showed only 4 signals, suggesting that the structure of **4** has a plane of intramolecular symmetry. Thus, **4** was assumed to be 2α,3β,4α-trihydroxynortropane by the vicinal coupling constants ($J_{2,3}$=$J_{3,4}$=8.7



1 : R_1 – H, R_2 – H, R_3 –OH R_4 – R_5 – R_6 H
1a : R_1 – Ac, R_2 = H, R_3 = OH, R_4 = R_5 = R_6 = H
1b : R_1 – Ac, R_2 – H, R_3 – OCOPh, R_4 – COPh, R_5 = R_6 = H
2 : R_1 – H, R_2 – OH, R_3 – R_4 – R_5 = R_6 – H
2a : R_1 = Ac, R_2 = OH, R_3 = R_4 – R_5 = R_6 – H
2b : R_1 – Ac, R_2 = OCOPh, R_3 = H, R_4 = COPh, R_5 = R_6 – H
3 : R_1 – R_2 – H, R_3 – OH, R_4 = R_5 = H, R_6 = OH
3a : R_1 – Ac, R_2 – H, R_3 = OH, R_4 = R_5 – H, R_6 – OH
3b : R_1 = Ac, R_2 – H, R_3 – OCOPh, R_4 – COPh, R_5 – H, R_6 – OCOPh
4 : R_1 = R_2 = H, R_3 = OH, R_4 – H, R_5 – OH, R_6 H
5 : R_1 = R_2 = R_3 = R_4 = R_5 = H, R_6 = OH
5a : R_1 – Me, R_2 = R_3 = R_4 = R_5 = H, R_6 = OH
5b : R_1 – Me, R_2 – R_3 – H, R_4 = MTPA, R_5 = H, R_6 = OMTPA
6 : R_1 – R_2 – R_3 – R_4 – R_5 = R_6 – H

Fig. 1. Structures of **1**—**6** and Their Derivative

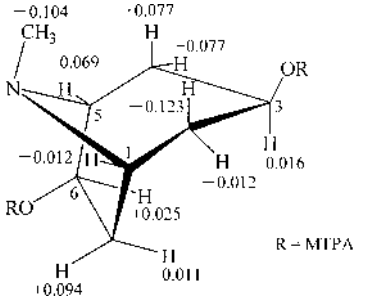


Fig. 2. $\Delta\delta$ Values (=**5b***S*—**5b***R*) Obtained for the MTPA Esters

Hz) and NOEs between H-3α and H-6*endo*, and H-3α and H-7*endo* in the NOESY spectrum.

Compound **5** was obtained as a colorless powder, $[\alpha]_D$ −1.3° (c=0.60, H_2O), showed a purplish-red spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_7H_{13}NO_2$ by pos. HR-SI-MS (*m/z*: 144.1028 $[M+H]^+$, error, +0.5 mmu). The IR spectrum showed a strong OH and NH band and a CH band.

The ^{1}H-NMR spectrum suggested the presence of 2 hydroxymethines and 2 methines attached to a nitrogen atom. Then, **5** was assumed to be 3β,6*exo*-dihydroxytropane by NOEs between H-3α and H-6*endo*, H-3α and H-7*endo*, and H-4α and H-6*endo* in the NOESY. The absolute configuration of the 3- and 6-carbons was deduced from $\Delta\delta$ values between a pair of the di-2-methoxy-2-phenyl-2-(trifluoromethyl)acetic acid (MTPA) due to **5** (Fig. 2).[11] Therefore, the above assumption that **5** should be 3β,6*exo*-dihydoxynortropane proved correct when including the absolute stereostructure (1*R*,3*S*,5*S*,6*R*).

Compound **6** was obtained as a colorless powder, $[\alpha]_D$ ±0° (c=0.60, H_2O), showed a purplish-red spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_7H_{13}NO$ by pos. HR-SI-MS (*m/z*: 128.1069 $[M+H]^+$, error, −0.6 mmu). The IR spectrum showed a strong OH and NH band and a CH band.

The ^{13}C-NMR spectrum showed only 4 signals, suggesting that the structure of **6** has a plane of intramolecular symmetry. Then, **6** was assumed to be 3β-hydroxynortropane (=nor-ψ-tropine)[12] by NOEs between H-3α and H-6*endo*, and H-3α and H-7*endo* in the NOESY spectrum. ψ-Tropine is common, and nor-ψ-tropine has been reported as a synthesized compound. This was the first isolation of **6** from natural sources to our knowledge.

Compound **7**, morusimic acid A, was obtained as a colorless powder, $[\alpha]_D$ +15.3° (c=0.18, MeOH), showing a reddish-brown spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{24}H_{45}NO_9$ by pos. HR-SI-MS (*m/z*: 492.3163 $[M+H]^+$, error, −0.7 mmu). The IR spectrum showed a strong OH and NH band and a COOH band as described in the experimental section.

The ^{1}H-NMR spectrum showed an anomeric proton [δ 4.40 (1H, d, J=7.7 Hz)]. Hydrolysis of **7** with 3.5% HCl provided a genuine aglycone (**8**) and D-glucose ($[\alpha]_D$ +38.8°). Partial structures **A1**, **B1**, and **C1** of **7** were obtained by ^{1}H–^{1}H COSY cross peaks, and they were connected by heteronuclear maltiple bond connectivity (HMBC) spectrum to establish the planar structure (Fig. 4). The ^{1}H- and ^{13}C-NMR signals were reasonably assigned to the structure by TOCSY, HSQC, and distortionless enhancement by polarization transfer (DEPT), as shown in Table 2.

The relative stereostructure of the pyrrolidine moiety in **7** was disclosed by the vicinal coupling constants ($J_{1'',4'}$= 4.0 Hz) and NOEs between H-3′α and H-2″, H-3′α and H-1″, and H-4′ and H-2″ in the NOESY spectrum (Fig. 5). The same stereostructure was confirmed by the NOESY spectrum of *N*-methyl-**8** (**8a**) (Fig. 5). The absolute stereostructure of **7** was determined to be 3*R*,1′*S*,4′*S*,1″*S* by a modification of Mosher's method[11] of **8a**, as shown in Fig. 6.

Compound **8**, morusimic acid B, was obtained as a colorless powder, $[\alpha]_D$ +8.8° (c=0.42, MeOH), showing a reddish-brown spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{18}H_{35}NO_4$ by pos. HR-SI-MS (*m/z*: 330.2638 $[M+H]^+$, error, −0.5 mmu). The IR spectrum showed a strong OH and NH band and a COOH band.

The spectroscopic data and the specific rotation value of **8** were identical to those of the aglycone of **7**. Thus, **8** was formulated as (3*R*)-3-hydroxy-12-{(1*S*,4*S*)-4-[(1*S*)-1-hydroxyethyl]-pyrrolidin-1-yl}-dodecanoic acid, and **7** as (3*R*)-3-hydroxy-12-{(1*S*,4*S*)-4-[(1*S*)-1-hydroxyethyl]-pyrrolidin-1-yl}-dodecanoic acid-3-*O*-β-D-glucopyranoside, as shown in Fig. 3.

Compound **9**, morusimic acid C, was obtained as a colorless powder, $[\alpha]_D$ −20.3° (c=0.24, MeOH), showing a brownish spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{24}H_{45}NO_9$ by pos. HR-SI-MS (*m/z*: 492.3173 $[M+H]^+$, error, −0.3 mmu). The IR spectrum showed a strong OH and NH band and a COOH band.

The ^{1}H-NMR spectrum showed an anomeric proton [δ 4.40 (1H, d, J=7.7 Hz)]. Hydrolysis of **9** with 3.5% HCl provided a genuine aglycone (**10**) and D-glucose ($[\alpha]_D$ +52.3°). The ^{1}H- and ^{13}C-NMR spectra of **9** were similar to those of **7**, except for the presence of a methyl group instead of the 1-hydroxyethyl group. Partial structures **A2**, **B2**, and **C2** of **9** were obtained by ^{1}H–^{1}H COSY cross peaks and they were connected by HMBC spectrum to establish the planar structure (Fig. 4). These signals were assigned reasonably as sum-

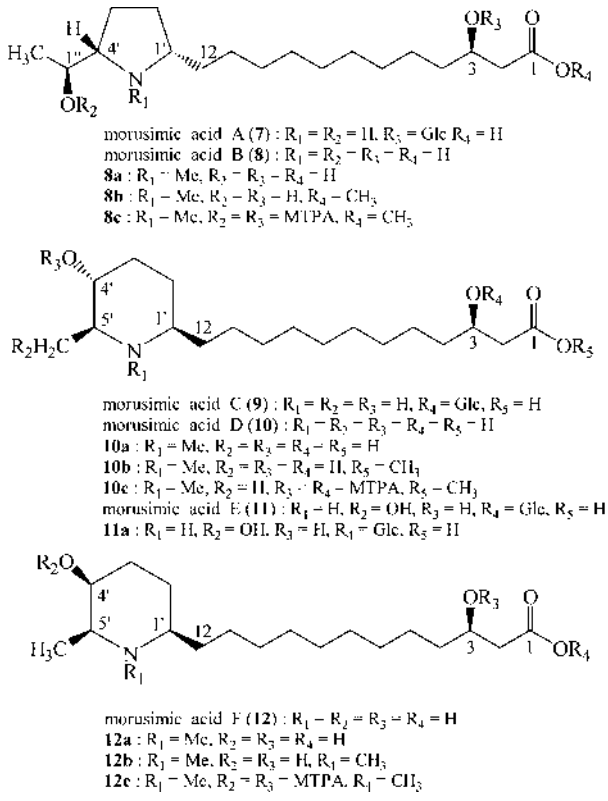


Fig. 3. Structures of **7**—**12**

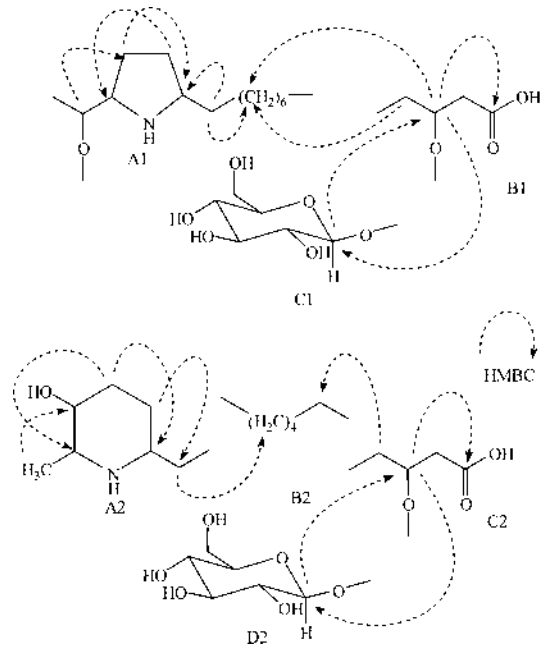


Fig. 4. Partial Structures and HMBC Spectra of **7** and **9**

marized in Table 2.

The relative stereostructure of the piperidine moiety in **9** was disclosed by the vicinal coupling constants ($J_{4',5'}$=12.8 Hz) and NOEs between H-1′ and H-5′, H-3′α and H-5′, and H-4′ and CH_3 in the NOESY spectrum. The absolute stereostructure of **9** was determined to be 3*R*,1′*R*,4′*R*,5′*S* by the $\Delta\delta$ value between both MTPA esters from **10** by a modification of Mosher's method,[11] as shown in Fig. 6.

Compound **10**, morusimic acid D, was obtained as a colorless powder, $[\alpha]_D$ −14.6° (*c*=0.25, MeOH), showing a brownish spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{18}H_{35}NO_4$ by pos. HR-SI-MS (*m/z*: 330.2653 $[M+H]^+$, error, +1.1 mmu). The IR spectrum showed a strong OH and NH and a COOH band as above.

The spectroscopic data and $[\alpha]_D$ value of **10** were identical to those of the aglycone of **9**. Thus, **10** was formulated as (3*R*)-3-hydroxy-12-[(1*R*,4*R*,5*S*)-4-hydroxy-5-methyl-piperidin-1-yl]-dodecanoic acid, and **9** as **10**-3-*O*-β-D-glucopyranoside.

Compound **11**, morusimic acid E, was obtained as a colorless powder, $[\alpha]_D$ −17.2° (*c*=0.61, MeOH), showing a yellowish-brown spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{24}H_{45}NO_{10}$ by pos. HR-SI-MS (*m/z*: 508.3124 $[M+H]^+$, error, +0.5 mmu). The IR spectrum showed a strong OH and NH and a COOH band as above.

The ^{1}H- and ^{13}C-NMR spectra of **11** were strikingly similar to those of **9**, except for the presence of a hydroxymethyl group [δ 3.80 (1H, dd, *J*=5.5, 12.0 Hz), δ 3.93 (1H, dd, *J*=3.0, 12.0 Hz), δ_c 60.09] instead of a methyl group. These signals were assigned as summarized in Table 2. Hydolysis of **11** with 3.5% HCl provided a genuine aglycone (**11a**) ($[\alpha]_D$ −12.7°) and D-glucose. After the relative stereostructure was deduced as in **9**, the absolute stereostructure of **11** was established by comparison of the values such as $[\alpha]_D$ −12.7° ($[M]_D$ −43.8°) for **11a** and −14.6° ($[M]_D$ −48.0°) for **10**. Because of the low yield of **11a**, any application of a modification of Mosher's Method and a dibenzoate chirality method ended in a failure. Thus, **11** was formulated as (3*R*)-3-hydroxy-12-[(1*R*,4*R*,5*S*)-4-hydroxy-5-hydroxymethyl-piperidin-1-yl]-dodecanoic acid-3-*O*-β-D-glucopyranoside.

Compound **12**, morusimic acid F, was obtained as a colorless powder, $[\alpha]_D$ +6.4° (*c*=0.28, MeOH), showing a brownish spot on TLC by ninhydrin reaction, and the molecular formula was determined to be $C_{18}H_{35}NO_4$ on the basis of pos. HR-SI-MS (*m/z*: 330.2635 $[M+H]^+$, error, −0.7 mmu). The IR spectrum showed a strong OH and NH band and a COOH band as above.

The ^{1}H- and ^{13}C-NMR spectra of **12** were strikingly similar to those of **10**, except for the ^{1}H-splitting pattern and ^{13}C-chemical shift of the hydroxymethine (4′). These signals were assigned as summarized in Table 2. Then, **12** was established to be the 4′-epimer of **10** by the vicinal coupling constants ($J_{4',5'}$=1.5 Hz) and NOEs between H-1′ and H-5′, and H-3′α and H-5′ in the NOESY spectrum.

The absolute stereostructure of **12** was determined by a modification of Mosher's method[11] between the *N*-methyl MTPA esters from **12**, as shown in Fig 6.

The inhibitory activities of **1**—**12**, DNJ and FAG were assessed with respect to α-glucosidase by methods described in the experimental section, and the results are summarized in Table 3.

Compounds **3**, **4**, and **5** inhibited α-glucosidase weakly, suggesting that more than 3 hydroxy groups or the 6*exo*-hydroxy group on nortropane skeleton may enhance the inhibitory activity.

Table 2. ^{1}H- and ^{13}C-NMR Spectral Data for **7**—**12**

	7			**8**			**9**	
	Proton	Carbon		Proton	Carbon		Proton	Carbon
1′	3.48 m	62.23	1′	3.43[a)]	62.29	CH_3	1.37 d (6.5)	16.18
2′	1.65[a)], 2.16 m	30.91	2′	1.64[a)], 2.15 m	31.73	1′	3.01 m	58.09
3′	2.02 m	23.77	3′	2.01 m	24.71	2′	1.45[a)], 2.04[a)]	28.65
4′	3.52 ddd (4.0, 8.5, 8.5)	65.89	4′	3.45[a)]	66.22	3′	1.48[a)], 2.08[a)]	33.05
1″	4.03 dddd (4.0, 6.5, 6.5, 6.5)	66.12	1″	3.98 dddd (3.9, 6.4, 6.4, 6.4)	67.07	4′	3.34[a)] m	71.19
2″	1.22 d (6.5)	20.69	2″	1.22 d (6.4)	21.30	5′	2.89 dddd (12.8, 6.5, 6.5, 6.5)	59.06
1		180.26	1		180.94	1		179.98
2	2.37 (6.0, 14.2)	43.93	2	2.26 dd (7.6, 14.9)	45.62	2	2.36 dd (6.2, 14.2)	43.95
	2.44 dd (6.0, 14.2)			2.32 dd (5.5, 14.9)			2.45 dd (6.2, 14.2)	
3	4.07 m	79.04	3	3.88 m	70.61	3	4.08 q (6.2)	78.93
4	1.59[a)], 1.62[a)]	36.08	4	1.46[a)]	38.18	4	1.66 m	35.99
5	1.42[a)]	27.70	5—11	1.30[a)]—1.49[a)]	26.75, 28.25, 30.51	5	1.41[a)]	25.86
6	1.40[a)]	26.03			30.59, 30.65	6	1.41[a)]	26.15
7—11	1.31[a)]—1.38[a)]	30.06, 30.16, 30.19			30.71, 30.78	7—11	1.31[a)]—1.35[a)]	29.78, 29.93, 29.98
		30.21, 30.33						30.12, 30.15
12	1.65[a)], 1.78 m	33.21	12	1.64[a)], 1.75 m	36.08	12	1.48[a)], 1.58[a)]	34.42
1‴	4.40 d (7.7)	103.41				1‴	4.40 d (7.7)	103.30
2‴	3.16 dd (7.7, 8.9)	75.53				2‴	3.16 dd (7.7, 8.9)	75.49
3‴	3.38 t (8.9)	78.12				3‴	3.38 t (8.9)	78.11
4‴	3.29[a)]	71.66				4‴	3.30[a)]	71.67
5‴	3.27[a)]	77.97				5‴	3.28[a)]	77.92
6‴	3.68 dd (11.9, 5.1)	62.93				6‴	3.68 dd (11.9, 5.0)	62.95
	3.84 dd (11.9, 2.2)						3.84 dd (11.9, 2.3)	

	10			**11**			**12**	
	Proton	Carbon		Proton	Carbon		Proton	Carbon
CH_3	1.38 d (6.4)	16.75	CH_2OH	3.80 dd (5.5, 12.0)	60.09	CH_3	1.29 d (6.5)	16.28
1′	3.01 m	58.38		3.93 dd (3.0, 12.0)		1′	2.98 m	58.47
2′	1.50[a)], 2.05[a)]	29.24	1′	2.96 m	58.25	2′	1.64[a)], 1.75 m	24.01
3′	1.48[a)], 2.08[a)]	33.50	2′	2.01[a)], 2.03[a)]	28.58	3′	1.68[a)], 1.95 m	31.30
4′	3.35 m	70.55	3′	2.09[a)], 2.12[a)]	33.25	4′	3.80 m	66.24
5′	2.88 dddd (12.8, 6.4, 6.4, 6.4)	59.38	4′	3.16 ddd (5.5, 10.5, 10.5)	66.62	5′	3.16 dddd (6.5, 6.5, 6.5, 1.5)	57.23
1		180.63	5′	2.84 ddd (5.5, 3.0, 10.5)	64.48	1		180.67
2	2.27 dd (7.6, 14.9)	45.66	1		179.93	2	2.24 dd (7.7, 15.0)	45.42
	2.33 dd (5.3, 14.9)		2	2.37 dd (6.0, 14.2)	43.75		2.31 dd (5.0, 15.0)	
3	3.89 m	71.65		2.47 dd (6.0, 14.2)		3	3.78 m	70.31
4	1.46[a)]	38.14	3	4.08 q (6.0)	79.00	4	1.45[a)]	37.82
5—11	1.28[a)]—1.54[a)]	26.66, 27.79, 30.22,	4	1.61 m	35.99	5	1.45[a)]	26.37
		30.37, 30.45, 30.58,	5	1.42[a)]	25.84	6	1.35[a)]	26.22
		30.71	6	1.39[a)]	26.36	7—11	1.30[a)]—1.34[a)]	30.04, 30.13, 30.16
			7—11	1.30[a)]—1.38[a)]	29.75, 29.86, 29.88			30.29, 30.43
					30.08, 30.12			
12	1.46[a)], 1.66[a)]	34.97	12	1.50[a)], 1.71[a)]	34.35	12	1.51 m, 1.62[a)]	
			1‴	4.40 d (7.8)	103.33			35.11
			2‴	3.16 dd (7.8 9.2)	75.48			
			3‴	3.38 t (9.2)	78.10			
			4‴	3.30[a)]	71.66			
			5‴	3.28[a)]	77.91			
			6‴	3.68 dd (11.9, 5.0)	62.94			
				3.84 dd (11.9, 2.3)				

a) Overlapped signals. δ in CD_3OD. ^{1}H-NMR at 500 MHz. ^{13}C-NMR at 125 MHz. ppm (Hz)

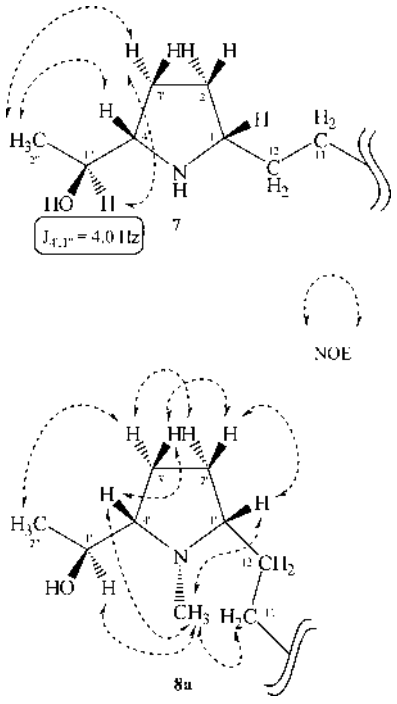


Fig. 5. NOEs Detected for **7** and **8a**

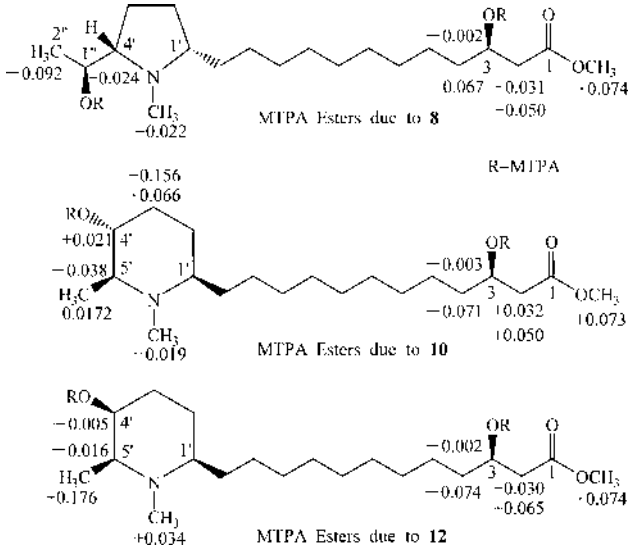


Fig. 6. $\Delta\delta$ Values (=**8c***S*—**8c***R*, **10c***S*—**10c***R*, **12c***S*—**12c***R*) Obtained for the MTPA Esters

Experimental

General The instruments used in the work were a JASCO digital polarimeter (for specific rotation, measured at 25 °C); a Perkin-Elmer 1720X-FTIR spectrometer (for IR spectra); a Hitachi M-80 spectrometer (for MS spectra); a Varian Mercury 300, Unity Inova-500 (for NMR spectra, measured in pyridine-d_5 on the δ scale using tetramethylsilane as an internal standard); and a Shimadzu spectrophotometer UV 1200 (for enzyme assay).

Column chromatography was carried out on ion-exchange resin (Amberlite CG-50, Amberlite IRA-67, Organo Company, and Dowex 50W-X4, Dow Chemical Company), and silica gel (Chromatorex DM1020, Fuji Silysia Chemical Ltd.). HPLC was conducted on a Gilson 305 pump or a JASCO-PU 980 equipped with a JASCO 830-RI or UV-970 as a detector. Silica gel $60F_{254}$ (Merck)-precoated TLC plates were used, developed with a $CHCl_3$–MeOH–AcOH–H_2O (20 : 10 : 7 : 5) solvent system, and detection was carried out with ninhydrin reagent followed by heating.

Table 3. α-Glucosidase Inhibition

Compounds	IC_{50} (M)
DNJ	9.8×10^{-4}
FAG	1.5×10^{-2}
1	NI
2	NI
3	2.5×10^{-2}
4	1.5×10^{-2}
5	3.3×10^{-2}
6	NI
7	NI
8	NI
9	NI
10	NI
11	NI
12	NI

NI: no inhibition.

Isolation of Compounds 1—12 Dried fruit of *M. alba* (4.5 kg collected in Turkey in 1999) was refluxed with methanol–water (1 : 1) (30 l) in a water bath for 1 h. The extracted solution was chromatographed on an Amberlite CG-50 (H^+ form) column (i.d. 5.0×20 cm, repeated 6 times). After washing the column with water and then MeOH, the adsorbed material was eluted with 50% MeOH–28% ammonia solution (9 : 1). The eluted fraction was concentrated *in vacuo* to give a fraction (4.5 g). This fraction was chromatographed on a silica gel (Chromatorex DM1020) and eluted with $CHCl_3$–MeOH (10 : 0), (10 : 1), (9 : 1), (7 : 1), (5 : 1), (3 : 1), (1 : 1), and (0 : 1) and MeOH–H_2O (10 : 1), (9 : 1), (7 : 1), (5 : 1), (3 : 1), (1 : 1), and (0 : 1). The fractions eluted with CH_3Cl–MeOH were respectively chromatographed on a Sep-pak C_{18} cartridge (Waters) and eluted with H_2O. The H_2O fractions were chromatographed on Dowex 50W-X4 column (200—400 mesh) pretreated with formic acid–ammonium formate buffer (0.2 M ammonia formate, adjusted to pH 5.7 with 1 N formic acid), with gradient elution (H_2O (200 ml)→H_2O–28% ammonia solution (9 : 1, 200 ml)). The fractions containing **1**—**6** were rechromatographed on preparative HPLC [(a) Develosil ODS-UG-5 (i.d. 10×250 mm); solvent: CH_3CN–H_2O (3 : 97), adjusted to pH 12.0 with ammonia solution; flow rate: 1.2 ml/min; detection: refractive index (RI); column temperature: ambient or (b) COSMOSIL PAKED COLUMN $5NH_2$-MS (i.d. 6.0×250 mm); solvent: CH_3CN–H_2O (80 : 20); flow rate: 0.8 ml/min; detection: RI; column temperature: 30 °C]. Compounds **1** (11.2 mg), **2** (30.2 mg), **3** (8 mg), **4** (2.8 mg), **5** (0.6 mg), and **6** (28.6 mg) were finally obtained.

The fractions eluted with MeOH–H_2O were chromatographed on a Sep-pak C_{18} cartridge (Waters) and eluted with MeOH, respectively. The fractions containing **7**—**12** were rechromatographed on preparative HPLC [(a) Develosil ODS-UG-5 (i.d. 10×250 mm); solvent: CH_3CN–H_2O (13 : 87), adjusted to pH 12.0 with ammonia solution; flow rate: 1.2 ml/min; detection: RI; column temperature: ambient or (b) Develosil ODS-UG-5 (i.d. 10×250 mm); solvent: CH_3CN–H_2O (14 : 86), adjusted to pH 12.0 with ammonia solution; flow rate: 1.2 ml/min; detection: RI; column temperature: ambient]. Compounds **7** (35.7 mg), **8** (25.0 mg), **9** (16.8 mg), **10** (8.7 mg), **11** (4.6 mg), and **12** (9.3 mg) were finally obtained.

1: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ −33.9° (c=0.32, H_2O), $C_7H_{13}NO_2$, pos. HR-SI-MS m/z; 144.1028 ($[M+H]^+$), error, +0.4 mmu, IR ν (KBr) cm^{-1}: 3414 (OH, NH), 2925 (CH), ^1H- and ^{13}C-NMR (D_2O): Table 1.

2: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ −34.0° (c=0.61, H_2O), $C_7H_{13}NO_2$, pos. HR-SI-MS m/z; 144.1022 ($[M+H]^+$), error, −0.2 mmu, IR ν (KBr) cm^{-1}: 3303 (OH, NH), 2927 (CH), ^1H- and ^{13}C-NMR (D_2O): Table 1.

3: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ −27.3° (c=0.55, H_2O), $C_7H_{13}NO_3$, pos. HR-SI-MS m/z; 160.0971 ($[M+H]^+$), error, −0.2 mmu, IR ν (KBr) cm^{-1}: 3400 (OH, NH), 2925 (CH), ^1H- and ^{13}C-NMR (D_2O): Table 1.

4: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ ±0° (c=0.40, H_2O), $C_7H_{13}NO_3$, pos. HR-SI-MS m/z; 160.0983 ($[M+H]^+$), error, +1.0 mmu, IR ν (KBr) cm^{-1}: 3469 (OH, NH), 2928 (CH), ^1H- and ^{13}C-NMR (D_2O): Table 1.

5: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ −1.3° (c=0.60, H_2O), $C_7H_{13}NO_2$, pos. HR-SI-MS m/z;

144.1028 ([M+H]$^+$), error, +0.5 mmu, IR ν (KBr) cm^{-1}: 3430 (OH, NH), 2933 (CH), ^{1}H- and ^{13}C-NMR (D_2O): Table 1.

6: Colorless powder, ninhydrin reaction: positive (a purplish-red spot on TLC), $[\alpha]_D$ ±0° (c=0.60, H_2O), $C_7H_{13}NO$, pos. HR-SI-MS m/z; 128.1069 ([M+H]$^+$), error, −0.6 mmu, IR ν (KBr) cm^{-1}: 3404 (OH, NH), 2971 (CH), ^{1}H- and ^{13}C-NMR (D_2O): Table 1.

7: Colorless powder, ninhydrin reaction: positive (a redish-brown spot on TLC), $[\alpha]_D$ +15.3° (c=0.18, MeOH), $C_{24}H_{45}NO_9$, pos. HR-SI-MS m/z; 492.3163 ([M+H]$^+$), error, −0.7 mmu, IR ν (KBr) cm^{-1}: 3385 (OH, NH), 1562 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

8: Colorless powder, ninhydrin reaction: positive (a redish-brown spot on TLC), $[\alpha]_D$ +8.8° (c=0.42, MeOH), $C_{18}H_{35}NO_4$, pos. HR-SI-MS m/z; 330.2638 ([M+H]$^+$), error, −0.5 mmu, IR ν (KBr) cm^{-1}: 3389 (OH, NH), 1553 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

9: Colorless powder, ninhydrin reaction: positive (a brown spot on TLC), $[\alpha]_D$ −20.3° (c=0.24, MeOH), $C_{24}H_{45}NO_9$, pos. HR-SI-MS m/z; 492.3173 ([M+H]$^+$), error, −0.3 mmu, IR ν (KBr) cm^{-1}: 3403 (OH, NH), 1567 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

10: Colorless powder, ninhydrin reaction: positive (a brown spot on TLC), $[\alpha]_D$ −14.6° (c=0.25, MeOH), $C_{18}H_{35}NO_4$, pos. HR-SI-MS m/z; 330.2653 ([M+H]$^+$), error, +1.1 mmu, IR ν (KBr) cm^{-1}: 3371 (OH, NH), 1548 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

11: Colorless powder, ninhydrin reaction: positive (a yellow spot on TLC), $[\alpha]_D$ −17.2° (c=0.61, MeOH), $C_{24}H_{45}NO_{10}$, pos. HR-SI-MS m/z; 508.3124 ([M+H]$^+$), error, +0.5 mmu, IR ν (KBr) cm^{-1}: 3414 (OH, NH), 1560 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

12: Colorless powder, ninhydrin reaction: positive (a brown spot on TLC), $[\alpha]_D$ +6.4° (c=0.28, MeOH), $C_{18}H_{35}NO_4$, pos. HR-SI-MS m/z; 330.2635 ([M+H]$^+$), error, −0.7 mmu, IR ν (KBr) cm^{-1}: 3399 (OH, NH), 1560 (COOH), ^{1}H- and ^{13}C-NMR (CD_3OD): Table 2.

Dibenzoate (1b) Compound **1** (7.5 mg) was treated with acetic anhydride (50 μl) in pyridine at −4 °C for 1 h to provide an acetamide (**1a**). **1a** was dissolved in pyridine (3.0 ml), benzoylchloride (500 μl) was added, and the solution was stirred at room temperature for 48 h. The reaction products were subjected to HPLC [column, Develosil UG-5 (i.d. 10×250 mm); solvent, CH_3CN–H_2O (30 : 70→100 : 0, 60 min); flow rate, 2.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. **1b** was obtained as a colorless oil. **1b**: pos. SI-MS m/z: 394 ([M+H]$^+$, 28.0%). ^{1}H-NMR ($CDCl_3$) δ: 1.89 (1H, m, H-4*exo*), 1.95 (1H, m, H-6*endo*), 2.02 (1H, m, H-7*exo*), 2.20 (2H, m, H-6*exo*, H-7*endo*), 2.27 (1H, ddd, J=13.0, 6.6, 2.5 Hz, H-4*exo*), 2.28 (3H, s, $COCH_3$), 4.47 (1H, m, H-1), 4.80 (1H, m, H-5), 5.14 (1H, dd, J=9.0, 3.7 Hz, H-2*exo*), 5.68 (1H, ddd, J=11.0, 9.0, 6.6 Hz, H-3*endo*), 7.37—7.58 (6H, m, ArH), 7.94 (4H, m, ArH). CD (MeOH): $\Delta\varepsilon$: −15.9 (238), +16.4 (223).

Dibenzoate (2b) Compound **2** (11.4 mg) was treated as above to provide an acetamide (**2a**). **2a** was treated as above to provide **2b** as a colorless oil, pos. SI-MS m/z: 394 ([M+H]$^+$, 28.0%). ^{1}H-NMR ($CDCl_3$) δ: 1.95 (1H, m, H-6*endo*), 1.97 (1H, m, H-4*exo*), 2.00 (1H, m, H-7*endo*), 2.02 (2H, m, H-6*exo*, H-7*exo*), 2.09 (1H, m, H-4*endo*), 2.21 (3H, s, $COCH_3$), 4.61 (1H, m, H-1), 5.01 (1H, m, H-5), 5.51 (1H, t, J=3.7 Hz, H-2*endo*), 5.60 (1H, m, H-3*endo*), 7.75—7.86 (6H, m, ArH), 7.97 (4H, m, ArH). CD (MeOH): $\Delta\varepsilon$: +13.7 (238), −8.0 (221).

***N*-Methyl Derivative (5a)** Compound **5** (2.0 mg) was treated with formaldehyde solution (1.0 ml) in MeOH (2.0 ml) and palladium carbon (10%, 5.0 mg) was added, and then the reaction solution was stirred under a hydrogen atmosphere at room temperature overnight. **5a** (2.0 mg) was provided by filtration in Millex®-LH (0.45 μm) and the removal of the solvent from the reaction solution *in vacuo.*

(*S*)-(−)-MTPA Ester ((*S*)-5b) Compound **5a** (1.0 mg) was treated with (*R*)-(−)-MTPA-Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propanediamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*S*)-**5b** was obtained as a colorless oil (1.0 mg), $C_{28}H_{29}NO_6F_6$, pos. SI-MS m/z: 590 (M+H)$^+$, ^{1}H-NMR ($CDCl_3$) δ: 1.714 (1H, m, H-2*exo*), 1.845 (1H, dd, J= 3.4, 11.4, 11.4 Hz, H-4*exo*), 1.906 (1H, m, H-2*exo*), 2.156 (1H, m, H-4*endo*), 2.242* (3H, s, N-C$\underline{H}_3$), 2.262 (2H, m, H-7), 3.236 (1H, m, H-5), 3.383 (1H, m, H-1), 3.552 (3H, s, OC$\underline{H}_3$), 3.544 (3H, s, OC$\underline{H}_3$), 5.055 (1H, m, H-3), 5.360 (1H, dd, J=4.6, 6.4 Hz, H-6), 7.340*—7.530* (10H, m, MTPA–ArH) (*overlapped signals).

(*R*)-(+)-MTPA Ester ((*R*)-5b) Compound **5a** (1.0 mg) was treated with (*S*)-(+)-MTPA–Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propanediamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*R*)-**5b** was obtained as a colorless oil (1.0 mg), $C_{28}H_{29}NO_6F_6$, pos. SI-MS m/z: 590 (M+H)$^+$, ^{1}H-NMR ($CDCl_3$) δ: 1.768 (1H, ddd, J=3.4, 11.4, 11.4 Hz, H-4*exo*), 1.837 (1H, m, H-2*exo*), 1.918 (1H, m, H-2*endo*), 2.079 (1H, m, H-4*endo*), 2.168 (1H, m, H-7*exo*), 2.273 (1H, dd, J=7.7, 14.4 Hz, H-7*endo*), 2.346 (3H, s, N-C$\underline{H}_3$), 3.305 (1H, m, H-5), 3.395 (1H, m, H-1), 3.530* (3H, s, OC$\underline{H}_3$), 3.535* (3H, s, OC$\underline{H}_3$), 5.071 (1H, m, H-3), 5.335 (1H, dd. J=3.3, 7.7 Hz, H-6), 7.360*—7.540* (10H, m, MTPA–ArH) (*overlapped signals).

Hydrolysis of 7 Compound **7** (6 mg) was dissolved in 3.5% HCl (10 ml) and the solution was refluxed in a water bath for 2 h. After cooling, the reaction mixture was passed through an Amberlite IRA-67 (OH^- form) column (i.d. 20×50 mm) to neutralize. The resulting solution was chromatogaphed on a Sep-pak C_{18} column (Waters), eluted with water, and afforded D-glucose (1.2 mg), $[\alpha]_D$ +38.9° (c=0.09, H_2O), which was identified by TLC (Rf=0.34, AcOEt : AcOH : MeOH : H_2O=6 : 1.5 : 1.5 : 1), and ^{1}H-NMR. Elution with MeOH afforded the aglycone (**8**) (4 mg) as a colorless powder (identified by comparison of ^{1}H-, ^{13}C-NMR, and HPLC data).

***N*-Methyl Derivative (8a)** Compound **8** (7.1 mg), which was prepared as in **5a**, was treated as above to provide **8a** (3.5 mg).

Methyl Ester (8b) Compound **8a** (3.5 mg) in MeOH (2.0 ml) was treated with a diazomethane–ether solution (5.0 ml) prepared from *p*-toluenesulfonyl-*N*-methyl-*N*-nitrosoamide (1.0 g) in diethylether (20 ml) and 50% KOH solution (10 ml) at room temperature overnight, and then **8b** (2.0 mg) was provided by the removal of ether from the solution *in vacuo.*

(*S*)-(−)-MTPA Ester ((*S*)-8c) Compound **8b** (1.0 mg) was treated with (*R*)-(−)-MTPA–Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propane diamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*S*)-**8c** was obtained as a colorless oil (1.0 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS m/z: 790 (M+H)$^+$; ^{1}H-NMR ($CDCl_3$) δ: 1.239* (3H, d, J=6.6 Hz, H-2″), 1.267* (1H, H-2′), 1.642* (2H, H-4), 1.713* (2H, H-3′), 1.808 (1H, quintet, J=6.4 Hz, H-2), 2.192 (1H, m, H-1′), 2.284 (3H, s, N-C$\underline{H}_3$), 2.359 (1H, ddd, J=2.3, 7.9, 7.9 Hz, H-4′), 2.605 (1H, dd, J=4.7, 15.8 Hz, H-2), 2.697 (1H, dd, J=8.2, 15.8 Hz, H-2), 3.542 (3H, s, OC$\underline{H}_3$), 3.574 (3H, s, OC$\underline{H}_3$), 3.661 (3H, s, COOC$\underline{H}_3$), 5.373 (1H, dddd, J=2.3, 6.5, 6.5, 6.5 Hz, H-1″), 5.475 (1H, m, H-3), 7.330*—7.700* (10H, m, MTPA–ArH) (*overlapped signals).

(*R*)-(+)-MTPA Ester ((*R*)-8c) Compound **8b** (1.0 mg) was treated with (*S*)-(+)-MTPA–Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propanediamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*R*)-**8c** was obtained as a colorless oil (1.0 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS m/z: 790 (M+H)$^+$; ^{1}H-NMR ($CDCl_3$) δ: 1.331* (1H, m, H-2″), 1.709* (2H, 4-H), 2.262 (3H, s, N-C$\underline{H}_3$), 2.574 (1H, dd, J=5.0, 16.0 Hz, H-2), 2.647 (1H, dd, J=8.0, 16.0 Hz, H-2), 3.527 (3H, s, OC$\underline{H}_3$), 3.551 (3H, s, OC$\underline{H}_3$), 3.587 (3H, s, COOC$\underline{H}_3$), 5.349 (1H, m, H-1″), 5.477 (1H, m, H-3), 7.330*—7.590* (10H, m, MTPA–ArH) (*overlapped signals).

Hydrolysis of 9 Compound **9** (5.0 mg) was dissolved in 3.5% HCl (10 ml) and the solution was treated as above to afford D-glucose (1.0 mg), $[\alpha]_D$ +52.3° (c=0.08, H_2O), which was identified by TLC (Rf=0.34, AcOEt : AcOH : MeOH : H_2O=6 : 1.5 : 1.5 : 1), and ^{1}H-NMR. Elution of the adsorbed fraction with MeOH afforded the aglycone (**10**) (3.2 mg) as a colorless powder (identified by comparison of ^{1}H-, ^{13}C-NMR, and HPLC data).

***N*-Methyl Derivative (10a)** Compound **10** (5.8 mg) was treated as above to provide **10a** (3.0 mg) by filtration in Millex®-LH (0.45 μm) and the removal of solvent from the reaction solution *in vacuo.*

Methyl Ester (10b) Compound **10a** (3.0 mg) in MeOH (2.0 ml) was treated with the diazomethane–ether solution (5.0 ml) as above to provide **10b** (2.0 mg).

(*S*)-(−)-MTPA Ester ((*S*)-10c) Compound **10b** (1.0 mg) was treated with (*R*)-(−)-MTPA–Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propanediamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*S*)-**10c** was obtained as a colorless oil (1.0 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS m/z: 790 (M+H)$^+$; ^{1}H-NMR ($CDCl_3$) δ: 0.965 (3H, d, J=6.2 Hz, CH_3-H), 1.468* (1H, m, H-3′), 1.633* (2H, m, H-4), 2.205* (3H, s, N-C$\underline{H}_3$), 2.234* (1H, m, H-3′), 2.343 (1H, m, H-5′), 2.604 (1H, dd, J=4.6, 16.0 Hz, H-2), 2.695 (1H, dd, J=8.2,

16.0 Hz, H-2), 3.540 (3H, s, OC$\underline{H}_3$), 3.565 (3H, s, OC$\underline{H}_3$), 3.661 (3H, s, COOC$\underline{H}_3$), 4.788 (1H, m, H-4′), 5.471 (1H, m, H-3), 7.360*—7.560* (10H, m, MTPA–ArH) (*overlapped signals).

(*R*)-(+)-MTPA Ester ((*R*)-10c) Compound **10b** (1.0 mg) was treated with (*S*)-(+)-MTPA–Cl (20 μl) in pyridine (300 μl) at room temperature overnight, and *N*,*N*-dimethyl-1,3-propanediamine was added. The reaction products were subjected to HPLC [column, CrestPak C18S (i.d. 4.6×150 mm); solvent, CH_3CN–H_2O (20 : 80→100 : 0, 40 min); flow rate, 1.0 ml/min; detection, UV 230 nm; column temperature, 40 °C]. (*R*)-**10c** was obtained as a colorless oil (1.0 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS *m*/*z*: 790 $(M+H)^+$; ^{1}H-NMR ($CDCl_3$) δ: 1.137 (3H, d, J=6.2 Hz, CH_3-H), 1.312** (1H, m, H-3′), 1.704* (1H, H-4), 2.168 (1H, m, H-3′), 2.224 (3H, s, N-C$\underline{H}_3$), 2.381 (1H, m, H-5′), 2.572 (1H, dd, J=4.9, 16.0 Hz, H-2), 2.645 (1H, dd, J=8.0, 16.0 Hz, H-2), 3.527* (3H, s, OC$\underline{H}_3$), 3.536* (3H, s, OC$\underline{H}_3$), 3.588 (3H, s, COOC$\underline{H}_3$), 4.767 (1H, m, H-4′), 5.474 (1H, m, H-3), 7.370*—7.550* (10H, m, MTPA–ArH) (*overlapped signals).

Hydrolysis of 11 Compound **11** (3.0 mg) was dissolved in 3.5% HCl (4 ml) and the solution was treated as above to afford D-glucose, which was identified by TLC (Rf=0.34, AcOEt : AcOH : MeOH : H_2O=6 : 1.5 : 1.5 : 1). Elution of the adsorbed fraction with MeOH afforded the aglycone (**11a**) (2.0 mg) as a colorless powder.

***N*-Methyl Derivative (12a)** Compound **12** (7.0 mg) was treated as above to provide **12a** by filtration in Millex®-LH (0.45 μm) and the removal of solvent from the reaction solution *in vacuo.*

Methyl Ester (12b) Compound **12a** (3.0 mg) in MeOH (2.0 ml) was treated with the diazomethane–ether solution (5 ml) as above to provide **12b** (1.4 mg).

(*S*)-(−)-MTPA ((*S*)-12c) Compound **12b** (0.7 mg) was treated with (*R*)-(−)-MTPA–Cl (20 μl) in pyridine (300 μl) as above to provide (*S*)-**12c** as a colorless oil (1.0 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS *m*/*z*: 790 $(M+H)^+$; ^{1}H-NMR ($CDCl_3$) δ: 1.126* (3H, m, CH_3-H), 1.610* (2H, m, H-4), 2.085 (3H, s, N-C$\underline{H}_3$), 2.538 (1H, m, H-5′), 2.603 (1H, dd, J=4.6, 16.0 Hz, H-2), 2.709 (1H, dd, J=8.2, 16.0 Hz, H-2), 3.540 (3H, s, OC$\underline{H}_3$), 3.572 (3H, s, OC$\underline{H}_3$), 3.661 (3H, s, COOC$\underline{H}_3$), 5.015 (1H, m, H-4′), 5.470 (1H, m, H-3), 7.360*—7.550* (10H, m, MTPA–ArH) (*overlapped signals).

(*R*)-(+)-MTPA Ester((*R*)-12c) Compound **12b** (0.7 mg) was treated with (*S*)-(+)-MTPA–Cl (20 μl) in pyridine (300 μl) as above to provide (*R*)-**12c** as a colorless oil (0.7 mg), $C_{40}H_{53}NO_8F_6$, pos. SI-MS *m*/*z*: 790 $(M+H)^+$; ^{1}H-NMR ($CDCl_3$) δ: 0.950 (3H, m, CH_3-H), 1.684* (2H, H-4), 2.051* (3H, s, N-C$\underline{H}_3$), 2.554* (1H, m, H-5′), 2.573* (1H, dd, J=5.0, 16.0 Hz, H-2), 2.644 (1H, dd, J=8.0, 16.0 Hz, H-2), 3.527 (3H, s, OC$\underline{H}_3$), 3.587* (3H, s, OC$\underline{H}_3$), 3.587* (3H, s, COOC$\underline{H}_3$), 5.020 (1H, m, H-4′), 5.472 (1H, m, H-3), 7.370*—7.600* (10H, m, MTPA–ArH) (*overlapped signals).

Assay of α-Glucosidase Inhibition The α-glucosidase activity was measured by the modified method of Dahlvist.[13] The reaction mixture consisted of 50 mM phosphate buffer 200 μl (pH 7.0), 100 mM sucrose 175 μl in phosphate buffer, α-glucosidase (stock solution of 1.0 mg/ml in 10 mM phosphate buffer, pH 7.8, was diluted 40 times with the same buffer), with the substrates **1**—**12**, DNJ, or FAG (25 μl solution, concentration: 20—0.1 mg/ml).

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