Three Novel Constituents from *Curculigo capitulata* and Revision of C-2 Stereochemistry in Nyasicoside

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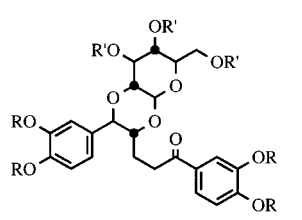
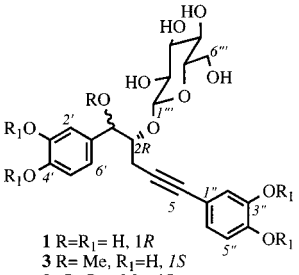
Continuing study of the constituents of the rhizomes of *Curculigo capitulata* provided three novel compounds, including two norlignan glucosides, curcapicycloside (**2**) and (1*S*,2*R*)-*O*-methylnyasicoside (**3**), and a phenanthrofuran, curcapital (**9**). The former two compounds were characterized as their tetra-*O*-methyl derivatives. Compound **2** possesses a glucosyl-fused skeleton with 1*R*,2*R* configuration. Biogenetic consideration led to a revision of the previously assigned 2*S* configuration of nyasicoside (**1**) to 2*R*, which was confirmed by NOE studies of the acetonide of its tetra-*O*-methyl derivative. The 2*R* configuration in tetra-*O*-methyl-1-*O*-methyl curculigine (**7a**) and isocurculigine (**8a**) was also established by chemical correlation of the former with (1*R*,2*R*)-tetra-*O*-methyl-1-*O*-methylnyasicoside (**10a**). Curcapital (**9**) represents the first natural product having a phenanthro[9,10,*b*]furan skeleton.

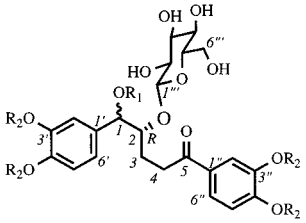
We have reported the isolation and structure characterization of a novel glucosyl-fused phenanthrene, curcapitoside,[1] and five acetylenic norlignan glucosides[2] from the rhizomes of *Curculigo capitulata* (Lour.) O. Kuntze (Amaryllidaceae), alias *C. recurvata*. These acetylenic norlignan glucosides, especially nyasicoside (**1**) and (+)-1-*O*-butylnyasicoside, displayed potent activity against ouabain-induced arrhythmia.[2] To further explore potential antiarrhythmic agents, the minor constituents of this plant were exhaustively investigated. A combination of chromatographic techniques and chemical derivatization provided eight additional compounds (**2a**, **3a**, **4**−**9**) from the H_2O-soluble fraction of EtOH extract of the rhizomes. Among these, curculigine (**4**), isocurculigine (**5**), 1-*O*-methyl curculigine (**7**), and 1-*O*-methyl isocurculigine (**8**) were isolated and characterized as their respective tetra-*O*-methyl ethers (**4a**, **5a**, **7a**, **8a**). Compound **6** was characterized as 1-*O*-methylcurculigine peracetate.[3] In the following, we report the structure characterization of three novel compounds, curcapicycloside (**2**), (1*S*,2*R*)-1-*O*-methylnyasicoside (**3**), and curcapital (**9**). In addition, the revision of C-2 stereochemistry in nyasicoside (**1**) and related compounds and the chemical confirmation of C-2 stereochemistry of **4a** and **7a** and their C-1 epimers are also reported.



2 R= R'= H
2a R= Me, R'= H
2b R= Me, R'= Ac



1 R=R_1= H, 1*R*
3 R= Me, R_1=H, 1*S*
3a R=R_1= Me, 1*S*
10 R= Me, R_1=H, 1*R*
10a R=R_1= Me, 1*R*



4 R_1=R_2= H, 1*R*
4a R_1= H, R_2= Me, 1*R*
5 R_1=R_2= H, 1*S*
5a R_1= H, R_2= Me, 1*S*
7 R_1= Me, R_2= H, 1*R*
7a R_1=R_2= Me, 1*R*
8 R_1= Me, R_2= H, 1*S*
8a R_1=R_2= Me, 1*S*

Results and Discussion

Curcapicycloside (**2**), being unstable during the final step of purification, was isolated and characterized as its tetra-*O*-methylated derivative, **2a**. Compound **2a**, a white amorphous solid, had a molecular formula of $C_{27}H_{35}O_{11}$ (HR-FABMS). The IR absorptions at 3400, 1665, 1590, and 1520 cm^{-1} indicated the presence of hydroxyl functions and an aryl ketone moiety. The ^1H NMR spectrum showed signals for six aromatic protons in two ABX systems, and seven sugar protons, both being corroborated by a COSY-45 spectrum, in addition to signals for six aliphatic protons and four aryl methoxys (δ 3.95, 3.93, 3.90, and 3.88). Both sets of ABX systems, one at δ 7.03 (d, J = 1.6 Hz, H-2′), 6.87 (d, J = 8.6 Hz, H-5′), and 7.03 (dd, J = 8.6, 1.6, H-6′) and the other at δ 7.50 (d, J = 1.3 Hz, H-2″), 6.92 (d, J = 8.4 Hz, H-5″), and 7.62 (dd, J = 1.3, 8.4 Hz, H-6″), were consistent with two catechol-like moieties, with the latter being conjugated with a carbonyl function (δ_C 198.47, s). That both C-3 and C-4 in each aryl group were methoxylated was revealed by NOE difference studies (Figure 1). Analysis of the signals of seven sugar protons suggested a β-D-glucosyl unit with the anomeric proton at δ 4.84 (d, J = 8.1 Hz). The COSY-45 spectrum also revealed the coupling pattern of two oxygenated methine protons at δ 4.57 (1H, m) and 4.70 (1H, d, J = 5.6 Hz), as well as two methylene protons at δ 1.89 (1H, m) and 2.18 (1H, m), the latter pair being further coupled to two methylene protons at δ 3.09 (1H, m) and 3.19 (1H, m). Taking all these chemical shifts and their coupling relationships into consideration, one would arrive at the structure sequence of Ar−$C_{(1)}$H(OR)−$C_{(2)}$H(OR′)−CH_2−CH_2−CO−Ar for **2a**, thus allowing the attachment of β-D-glucose moiety at the C-1 or C-2 position, similar to that in nyasicoside (**1**). However, the ^1H NMR spectrum of the peracetylated product, **2b**, revealed only three acetyl methyl singlets, in contrast with five signals of tetra-*O*-methyl nyasicoside peracetate. This would require a C-1/C-2 glucosyl-fused skeleton for **2a**. Comparison of the chemical shift of the corresponding sugar proton between **2a** and **2b** revealed large shift differences for H-3‴ (δ 3.44 vs δ 5.20), H-4‴ (δ 3.44 vs δ 4.96), and H-6‴ (δ 3.77 and 3.89 vs δ 4.10 and 4.20), in

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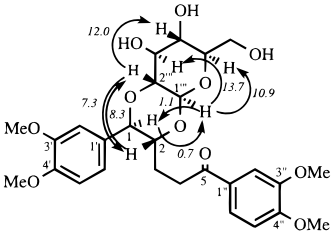


Figure 1. NOE's of **2a**.

Table 1. ^{1}H and ^{13}C NMR Data (δ/ppm), and 2D NMR Data for **2a** ($CDCl_3$ + CD_3OD = 4:1) and ^{1}H NMR Data of **2b** ($CDCl_3$)

	2a			2b
position	δ_C mult.[a]	δ_H mult. (J /Hz)[b]	HMBC (*J* = 8 Hz) correlated C (#)	δ_H mult. (J /Hz)[c]
1	78.17 d	4.70 d (5.6)	3, 2, 1′, 2′, 6′, 2‴	4.64 d (4.4)
2	74.10 d	4.57 m	1′	4.57 m
3	25.87 t	1.89 m, 2.18 m		2.00 d (6.0), 2.33 m
4	33.33 t	3.09 m, 3.19 m	3, 5	3.10 m
5	198.47 s			
1′	130.76 s			
2′	110.74 d	7.03 d (1.6)	1, 4′, 6′	7.91 d (1.5)
3′	148.70 s			
4′	148.83 s			
5′	110.86 d	6.87 d (8.6)	1′, 3′	6.83 d (8.6)
6′	120.00 d	7.03 dd (8.6, 1.6)	1, 2′	6.98 dd (8.4, 1.5)
1″	129.64 s			
2″	109.91 d	7.50 d (1.3)	5, 3″, 4″, 6″	7.48 d (1.6)
3″	148.78 s			
4″	153.19 s			
5″	109.91 d	6.92 d (8.4)	1″, 3″	6.86 d (8.5)
6″	122.69 d	7.62 dd (8.4, 1.3)	5, 2″, 4″	7.58 dd (8.5, 1.6)
Glc 1‴	95.58 d	4.84 d (8.1)	2‴, 5‴	4.85 d (8.5)
2‴	72.22 d	3.64 dd (9.2, 8.1)	2, 1‴	3.71 dd (9.6, 8.5)
3‴	77.32 d	3.44[b]		5.20 dd (9.6, 9.3)
4‴	70.42 d	3.44[b]		4.96 dd (9.3, 9.3)
5‴	74.29 d	3.60 m	4‴	3.79 m
6‴	61.28 t	3.77 dd (11.8, 4.9)	4‴	4.10 dd (12.7, 1.7)
		3.89[b]		4.20 dd (12.7, 4.8)
OMe	55.60 q, 55.70 q	3.88 s, 3.90 s		3.86 s, 3.87 s
	55.50 q (x2)	3.92 s, 3.95 s		3.90 s, 3.92 s

[a] Multiplicities were obtained from DEPT experiments. [b] Signals without multiplicity were assigned from COSY-45 or HMQC spectra. [c] Three −OCO*Me* signals at 1.99 (2 Me, s) and 2.04 (1 Me, s).

contrast with small differences for H-1‴ (δ 4.84 vs δ 4.85) and H-2‴ (δ 3.64 vs δ 3.71). This suggested ether linkage between C-1 and C-2 of the sugar moiety with C-1 and C-2 of the aglycon to form a 1,4-dioxan skeleton for **2a**, which is consistent with a total ring and double-bond equivalent of 11, including two catechols, one ketone, and one glucose unit. Without consideration of stereochemistry, these data would narrow the structure for **2a** to two possibilities, depending on alternative ways of fusion with glucose unit: that is, $C_1-O-C_{1'''}/C_2-O-C_{2'''}$ or $C_1-O-C_{2'''}/C_2-O-C_{1'''}$.

An HMBC spectrum (Table 1) revealed a key coupling of H-1 to C-2‴, establishing C-2‴ of the glucose fused to C-1 of the aglycon. NOE studies of **2a** (Figure 1) revealed the enhancement of the H-1 signal (δ 4.70) upon irradiation of H-1‴ and that of the H-2 signal (δ 4.57) upon irradiation of H-2‴, thus confirming the $C_1-O-C_{2'''}/C_2-O-C_{1'''}$ linkage. Incorporating the β-D-glucosyl unit, the common glycone of nyasicoside, and related compounds from the same plant established the trans relationship of H-1 and

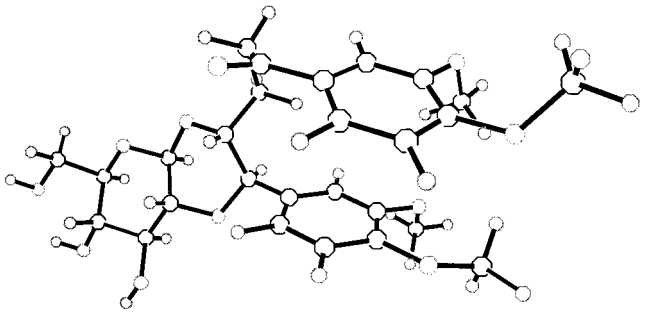
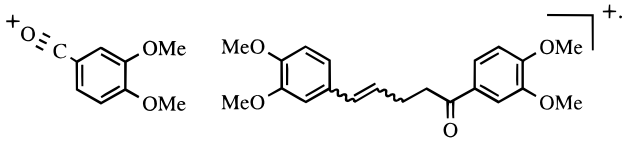


Figure 2. Energy-minimized conformation of **2a**.

H-2. This would require 1*R* and 2*R* stereochemistry in **2a**, elucidated on the basis of the known stereochemistry of the β-D-glucosyl unit. The larger NOE of H-2‴ to H-2 (7.3%) than that of H-1‴ to H-1 (1.1%) also suggests a twisted boat conformation for the dioxan moiety. This was supported by a computer-assisted modeling study[4] of **2a** that afforded an energy-minimized conformation (Figure 2) consistent with the NOE data. Analysis of HMBC (Table 1) and HMQC data by incorporating the NOE and COSY-45 correlations, furnished the complete ^{1}H and ^{13}C NMR assignments (Table 1) for **2a**. The MS revealed the base fragment ions at *m*/*z* 165 (**A**), obtained via α-cleavage of the aliphatic chain, and a characteristic fragment ion at *m*/*z* 356 (**B**), obtained via a retro Diels−Alder-type fragmentation of the dioxan ring, both supporting the assigned structure. To our knowledge, **2a** represents the first natural occurrence of a 1,5-diphenylpentanone-type norlignan glycoside. The trivial name for the parent compound of **2a**, curcapicycloside (**2**), was made after its plant origin.



A *m*/*z* 165 **B** *m*/*z* 356

On the basis of biogenetic point of view, the C-2 configuration of nyasicoside (**1**) might be the same (i.e., 2*R*) as that in curcapicycloside (**2**). Previous elucidation of 1*R*,2*S* configuration for **1** by Chifundera et al.[5] was based on the following points: (a) comparison of the CD curves between **1** and (1*R*)-phenylethanediol or ephedrine·HCl to derive the C-1 configuration, (b) the exciton coupling in the CD spectrum of the 1,2-dibromobenzoate derivative to derive C-2 configuration; and (c) the coupling constant of H-1 and H-2 (*J* = 8.5 Hz) of the acetonide derivative to establish the cis relationship between H-1 and H-2. We further confirmed the 1*R* configuration in **1** by observation of the similar CD curve between the prepared tetra-*O*-methyltetrahydronyasicoside (**11**) and the model compound adrenaline, both showing a negative Cotton effect around 230 nm. To examine the C-2 stereochemistry of **1**, we prepared the same acetonide derivative, tetra-*O*-methylnyasicol 1,2-acetonide (**12**), which has identical physical data to those reported,[5] including the coupling constant of H-1 and H-2. The NOE studies of **12** (Figure 3) revealed that the signals of H-1 (δ 4.84) and H-2 (δ 3.96) were enhanced, respectively, upon irradiation of each methyl frequency (δ 1.54, and δ 1.57) of acetonide. Both signals of H-2′ and H-6′ were enhanced upon irradiation of H-1 or H-2 frequency. From a chemical model study, these results could be rationalized only if H-1 and H-2 were trans oriented. These data provided solid evidence for a trans relationship between H-1 and H-2, instead of the reported cis. Based on this

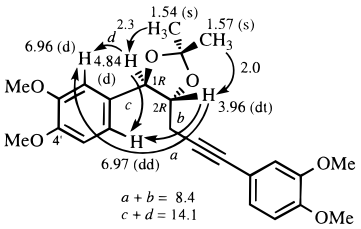


Figure 3. NOE's of compound **12**.

study, nyasicoside (**1**) was revised to have the same 1*R*,2*R* stereochemistry as curcapicycloside (**2**), instead of the previously reported 1*R*,2*S* configuration.

This revision for C-2 stereochemistry in **1** should be applicable to other nyasicoside-related compounds, including 1-*O*-methyl-, 1-*O*-butyl-, and 3″-dehydroxy-nyasicosides.[2] That is, they should all possess 2*R* configuration.

Compound **3a**, $[\alpha]^{23}_D$ −74.3° (*c* 0.7, MeOH), has a molecular formula of $C_{28}H_{36}O_{11}$ as deduced from negative HRFABMS, which is 56 amu more than that of (+)-(1*R*,2*R*)-1-*O*-methyl nyasicoside (**10**).[2] Except for the additional four aryl methoxyl signals at δ 3.83 (3 × OMe) and 3.85, the ^{1}H NMR spectrum of **3a** is very similar to that of **10**. Further ^{1}H NMR analysis of **3a** and **10a**, a tetra-*O*-methylated derivative of **10**, however, revealed differences in chemical shifts and coupling constants for H-1, H-2, and H-3, of which $J_{1,2}$ coupling in **3a** is 4.2 Hz as compared with 6.1 Hz in **10a**, the former coupling being similar to that in (−)-(1*S*,2*R*)-1-*O*-butylnyasicoside.[2] The ^{13}C NMR spectrum of **3a** is also very similar to that of **10** except for the differences in signals of two aryl groups. The CD spectrum of **3a** is almost a mirror image of that of **10** with 1*R* configuration, suggesting 1*S* stereochemistry for **3a**. These data pooled together would establish the structure of **3a** to be a novel (−)-(1*S*,2*R*)-tetramethyl-1-*O*-methylnyasicoside, and the parent compound to be (−)-(1*S*,2*R*)-1-*O*-methylnyasicoside (**3**).

This study characterized the structure of tetra-*O*-methylcurcapicycloside (**2a**), which induced the revision of C-2 stereochemistry of nyasicoside-type norlignan glycosides. Curculigine (**4**), a nyasicoside-derived 1,5-diphenylpentanone-type norlignan glycoside, has been demonstrated by the CD exciton coupling method[3] to have the same 2*R* stereochemistry as that in **1** and **2a**. In view of their biogenetic relationship, this consistency in C-2 stereochemistry among these lignan glycosides lends firm support for this revision.

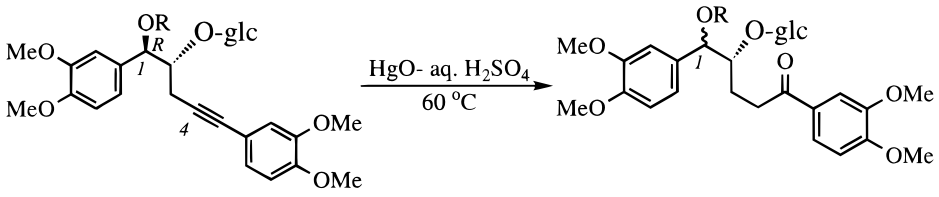
Compounds **4** and **5** were found to be a 1:1 mixture of curculigine and isocurculigine.[3] Both compounds were reported to be inseparable and were characterized as mixture. We found that their tetra-*O*-methylated derivatives (**4a**, **5a**) could be separated by reversed-phase preparative HPLC. After Lobar RP_{18} column separation, compounds **7** and **8** were found to be a 1:1 mixture of 1-*O*-methylcurculigine and 1-*O*-methylisocurculigine as reported,[3] based on ^{1}H NMR spectral analysis. Although we observed that they could be separated by HPLC (ODS), decomposition occurred upon concentration of the eluents. To overcome this problem, the phenolic groups were protected by treating them with diazomethane to give tetra-*O*-methylated derivatives (**7a** and **8a**), which were found to be separable by reversed-phase preparative HPLC.

On the basis of biogenetic point of view, the C-1 and C-2 configuration of curculigine (**4**) might be the same (i.e., 1*R*,2*R*) as that in nyasicoside (**1**). However, the CD curves of both compounds are quite different, owing to the distinct chromophores (i.e., phenylacetylene in **1** vs benzophenone in **4a**). To confirm the assigned 1*R*,2*R* stereochemistry made by the exciton coupling of the benzoate derivatives,[3] the stereochemistry at C-1 and C-2 of curculigine-type norlignans was further elucidated by chemical correlation. Hydration of tetra-*O*-methylnyasicoside (**1a**)[6] catalyzed with mercuric oxide in H_2SO_4−H_2O[7] yielded tetra-*O*-methylisocurculigine (**5a**) in addition to the expected tetra-*O*-methylcurculigine (**4a**) (Figure 4), a result indicating the susceptible epimerization at the C-1 benzylic position under acidic conditions. The same reaction performed on (1*R*,2*R*)-tetra-*O*-methyl-1-*O*-methylnyasicoside (**10a**) yielded the desired product, **7a** (CD and NMR data), in addition to a mixture of **4a** and **5a** (Figure 4), confirming this suggestion. This result provided solid support for the 1*R*,2*R* stereochemistry of 1-*O*-methylcurculigine tetra-*O*-methyl ether (**7a**). As the CD curve of **8a** was almost a counterpart of **7a**, the 1*S*,2*R* stereochemistry of **8a** was established inasmuch as the chirality at the benzylic position generally dominated the Cotton effect as that of C-2 in flavanones.[8] Complementary support for the stereochemistry assignment of **4a** (1*R*,2*R*) and **5a** (1*S*,2*R*) also comes from the comparable coupling constant between H-1 and H-2 in **4a** (8.3 Hz) as compared with **7a** (5.6 Hz), and in **5a** (2.4 Hz) as compared with **8a** (2.9 Hz) (Table 2), a similar situation being observed for C-1 epimers of 1-*O*-butylnyasicoside[2] and 1-*O*-methylnyasicoside.

Having these pure C-1 epimers at hand, the ^{1}H and ^{13}C NMR spectral data of **4a**, **5a**, **7a**, and **8a**, which were assigned previously in a mixture stage,[3] were examined directly. The resulting assignments are listed in Tables 2 and 3.

Curcapital (**9**) was isolated from a MeOH-soluble fraction as an orange amorphous solid. The molecular formula of **9** was deduced as $C_{17}H_{10}O_6$ from HRFABMS. The UV absorptions at 221, 250, 276, 309, and 376 nm were similar to those in curcapitoside peracetate,[1] suggesting the presence of phenanthrene chromophore. It contained an aryl formyl group as revealed by the presence of an IR absorption at 1630 cm^{-1}, a ^{1}H NMR signal at δ 9.64 (s), and a ^{13}C NMR signal at δ 179.70 (d). The ^{1}H NMR (CD_3OD) spectra showed five singlets for aromatic protons at δ 7.40, 7.54, 7.73, 7.74, and 7.96, suggesting the presence of two pairs of *para* aryl protons. This was partially corroborated by a COSY-45 spectrum, which showed a long-range coupling between the singlets at δ 7.74 (H-5) and 7.54 (H-8). NOE studies (Figure 5) showed mutual enhancements between both singlets at δ 7.73 (H-4) and 7.74 (H-5). Mutual enhancements were also observed between the singlet at δ 7.96 (H-11) and the singlet at δ 7.40 (H-1) as well as the signal of aldehydic proton (δ 9.64). Pooling all these data together one would derive the structure 2,3,6,7-tetrahydroxy-phenanthro[10,9-d]furan-2-carboxaldehyde for compound **9**.

The HMBC spectrum revealed couplings of H-11 (δ 7.96) to carbons in the furan moiety, including C-9 (J^3), C-10, and C-12 (J^2), and the aldehydic carbon (C-13, J^3), of which C-9 (δ 153.51) and C-10 (δ 120.10) are further three-bond coupled to H-8 and H-1, respectively, in the phenanthrene moiety. These data confirmed the assigned structure for **9**. Analysis of the 2D NMR spectra, HMQC, and HMBC also allowed complete ^{13}C NMR assignment for **9** as listed in Table 4. To our knowledge, **9** represents the first natural occurrence of phenanthro[10,9d]furan skeleton. The trivial name curcapital is made for **9** after its plant origin and structural character.



1a R= H
10a R= Me

4a R= H, 1*R* (from **1a** and **10a**)
5a R= H, 1*S* (from **1a** and **10a**)
7a R= Me, 1*R* (from **10a**)

Figure 4. Hydration of tetra-*O*-methylnyasicoside and its 1-*O*-methyl derivative catalyzed by mercuric ion.

Table 2. ^{1}H NMR Data for Compounds **4a**, **5a**, **7a**, and **8a** (δ/ppm, *J* in Hz)[a]

position	**4a**[b]	**5a**[b]	**7a**[c]	**8a**[c]
1	4.40 d (8.3)	4.78 d (2.4)	4.48 d (5.6)	4.64 d (2.9)
2	3.80 m	3.80 m	4.02 m	3.80 m
3	1.61 q (7.2)	1.72 m	1.53 dd (5.4, 17.1) 1.93 dd (4.2, 17.1)	1.89 m
4	2.92 m	2.91 m	3.04 m	2.98 m
	3.07 m	3.03 m	3.30 m	3.26 m
2′	6.86 d (1.6)	6.92 d (1.4)	7.01 d (1.5)	6.98 d (1.5)
5′	6.76 d (8.2)	6.74 d (8.2)	6.90 d (8.2)	6.89 d (8.2)
6′	6.83 dd (1.6, 8.2)	6.81 dd (1.4, 8.2)	6.93 dd (1.5, 8.2)	6.89 dd (1.5, 8.2)
2″	7.36 d (1.9)	7.38 d (1.8)	6.81 d (1.9)	6.82 d (1.9)
5″	6.80 d (8.6)	6.81 d (8.4)	6.96 d (8.4)	6.96 d (8.4)
6″	7.47 dd (8.6, 1.9)	7.48 dd (8.4, 1.8)	7.59 dd (1.9, 8.4)	7.61 dd (8.4, 1.9)
Glc				
1‴	4.41 d (7.8)	4.38 d (7.6)	4.47 d (8.0)	4.42 d (7.7)
2‴−5‴	3.30−3.39	3.28−3.39	3.30−3.39	3.30−3.39
6‴	3.67 dd (4.6, 12.1) 3.80	3.68 dd (4.6, 12.1) 3.80	3.69 dd (4.9, 11.8) 3.86 dd (1.4, 11.8)	3.69 dd (4.9, 11.8) 3.86 dd (1.4, 11.8)
Ar−OMe	3.78, 3.82, 3.84, 3.94 s	3.77, 3.81, 3.82, 3.86 s	3.80 (x 2), 3.84, 3.87 s	3.80, 3.81, 3.84, 3.88 s
1-OMe			3.26 s	3.32 s

[a] Signals without multiplicity were assigned from COSY-45 or HMQC spectra. [b] In $CDCl_3$−CD_3OD (4:1). [c] In CD_3OD.

Table 3. ^{13}C NMR Assignments for Compounds **4a**, **5a**, **7a**, and **8a** (δ/ppm)[a]

position	**4a**[a]	**5a**[a]	**7a**[c]	**8a**[c]
1	77.02 d	75.02 d	86.15 d	87.00 d
2	85.78 d	84.79 d	81.83 d	84.65 d
3	26.94 t	25.11 t	26.32 t	24.86 t
4	33.68 t	34.31 t	34.80 t	35.36 t
5	200.14 s	200.45 s	201.60 s	201.94 s
1′	132.67 s	132.98 s	132.16 s	132.90 s
2′	110.39 d	110.42 d	112.46 d	112.18 d
3′	149.09 s	148.81 s	150.20 s	150.32 s
4′	149.23 s	149.09 s	150.34 s	150.40 s
5′	111.39 d	111.00 d	113.12 d	112.66 d
6′	120.34 d	119.43 d	121.84 d	120.91 d
1″	129.94 s	129.92 s	131.20 s	131.18 s
2″	110.34 d	110.34 d	111.73 d	111.69 d
3″	149.08 s	148.36 s	150.11 s	149.85 s
4″	153.60 s	153.62 s	155.00 s	154.98 s
5″	110.53 d	110.58 d	111.73 d	111.75 d
6″	123.34 d	123.41 d	124.37 d	124.40 d
Glc				
1‴	103.37 d	103.86 d	104.34 d	105.40 d
2‴	73.86 d	73.92 d	75.33 d	75.34 d
3‴	76.78 d	76.48 d	78.00 d	77.88 d
4‴	70.07 d	70.11 d	71.76 d	71.82 d
5‴	76.78 d	76.61 d	78.06 d	78.16 d
6‴	61.58 t	61.59 t	62.91 t	63.00 t
Ar−OMe	55.96, 56.00, 56.02, 56.12 q	55.94, 55.97, 56.02, 56.12 q	56.40 (× 2), 56.60 (× 2) q	56.40, 56.50 (× 3) q
1-OMe			57.31 q	57.79 q

[a] Multiplicities were obtained from DEPT experiments. [b] In $CDCl_3$−CD_3OD (4:1) [c] In CD_3OD.

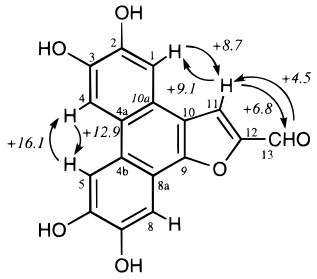


Figure 5. NOE's (italics, %) of **9** (CD_3OD)

Table 4. ^{1}H and ^{13}C NMR Data (δ/ppm) and HMBC Data for **9** in CD_3OD

position	δ_H (mult.)	COSY-45 corr. H (#)	δ_C (mult.)[a]	HMBC (*J* = 8.0 Hz) corr. C (#)
1	7.40 s	11	109.34 d	2, 3, 4a, 10
2			147.13 s	
3			147.31 s	
4	7.73 s	8	109.24 d	2, 3, 4a, 4b, 10a
4a			123.57 s	
4b			127.90 s	
5	7.74 s	8, 11	109.19 d	4a, 6, 7, 8a, 9
6			149.17 s	
7			146.71 s	
8	7.54 s	5	106.52 d	4b, 6, 7, 9
8a			115.54 s	
9			153.51 s	
10			120.10 s	
10a			121.05 s	
11	7.96 s	1, 5, 13	120.30 d	9, 10, 12, 13
12			152.85 s	
13	9.64 s	11	179.70 d	12

[a] Multiplicities were obtained from DEPT experiments.

Experimental Section

General Experimental Procedures. Perkin−Elmer 1760-X infrared FT spectrometer (KBr); Hitachi 2000 UV (MeOH); JASCO J-710 spectropolarimeter (MeOH); JEOL JMX-HX110 mass spectrometer; Bruker AMX-400 NMR spectrometer in MeOH-d_4 (δ_H 3.30, δ_C 49.0) or $CDCl_3$ (δ_H 7.24, δ_C 77.0) using Bruker's standard pulse programs; in the HMQC and HMBC experiments, Δ = 1 s and *J* = 140, 8 Hz, respectively, the correlation maps consisted of 512 × 1 K data points per spectrum, each composed of 16 to 64 transients.

Plant Material. The rhizomes of *Curculigo capitulata*

(Lour.) O. Kuntze for this study were re-collected in January 1995, from the suburban mountain of Wen-Xi, Taipei, Taiwan. A voucher specimen has been deposited in the School of Pharmacy, National Taiwan University.

Extraction and Isolation. The ground, dry powders of the rhizomes (1.1 kg) were percolated with 95% EtOH (7 L × 5). The EtOH extract (110 g) was partitioned between H_2O (1 L) and $CHCl_3$ (1 L × 3) to give a $CHCl_3$-soluble fraction (8.10 g). The aqueous layer, after removal of the residual $CHCl_3$ in vacuo, was passed through an Amberlite XAD-2 column (2 kg), washed with H_2O, and eluted with 30% to 100% MeOH in H_2O, to give fractions of 30% MeOH (35.01 g), 50% MeOH (3.60 g), and MeOH (0.98 g).

Part of the 30% MeOH fraction (4.96 g) was further separated on a Lobar RP8 column (B type, Merck), eluted with MeOH−H_2O (3:7) to give six fractions. Fraction 4 (1.31 g) was pure nyasicoside (**1**).[2,5,6] Fraction 2 (360 mg out of 952 mg), containing the mixture of curculigine (**4**) and isocurculigine (**5**),[3] was dissolved in MeOH and was *O*-methylated by reacting with freshly prepared ethereal CH_2N_2 at 4 °C for 3 days. The residue (394 mg) obtained after evaporating the organic solvents was separated on a Lobar RP_8 column (B type, 50% MeOH in H_2O) and subsequently on a preparative C_{18} HPLC column (32% MeOH in H_2O) to give curculigine tetra-*O*-methyl ether (**4a**, 30 mg) and isocurculigine tetra-*O*-methyl ether (**5a**, 20 mg).

Part of fraction 5 (380 mg out of 960 mg) was separated on a preparative HPLC column (C_{18}, 32% MeOH in H_2O) to give two subfractions. The compounds in the first eluted subfraction, however, were decomposed during concentration. Upon evaporation, the residue of the second subfraction was peracetylated with Ac_2O−py. After general workup, the acetylated products were separated on a Si gel column (230−400 mesh, 1% MeOH in $CHCl_3$) to give curcapitoside peracetate (16 mg)[1] and 1-*O*-methylcurculigine peracetate (**6**, 40 mg).[3] Another portion of fraction 5 (360 mg) was dissolved in MeOH and *O*-methylated by reacting with freshly prepared ethereal CH_2N_2 at 4 °C for 3 days. The residue (390 mg) obtained after evaporating the organic solvents was separated on a Lobar RP_8 column (55% MeOH in H_2O) to give four subfractions. Subfractions 1 (140 mg) and 4 (30 mg) gave compound **2a** (24 mg) and tetramethylnyasicoside (**1a**)[6] (60 mg) (subfraction 1), and **3a** (8 mg) (subfraction 4) after separation by Si gel column chromatography (230−400 mesh, 1% MeOH in $CHCl_3$). Subfraction 2 (48 mg), shown to be a mixture of tetramethyl-1-*O*-methyl derivatives of curculigine and isocurculigine (**7a**, **8a**)[3] by ^{1}H and ^{13}C NMR spectral analysis, was further separated by successive chromatography on a Lobar RP_8 column (55% MeOH in H_2O) and a preparative HPLC column (C_{18}, 40% MeOH in H_2O) to give **7a** (16 mg) and **8a** (9 mg). Fraction 6 (780 mg) was subjected to a Lobar RP_8 column (30% MeOH in H_2O) to give 3″-dehydroxynyasicoside[2] (280 mg) and 1-*O*-methylnyasicoside[2] (**10**, 130 mg).

The MeOH-eluted fraction (980 mg) of the initial Amberlite XAD-2 column was subjected to a Lobar RP_8 column (54% MeOH in H_2O) to give compound **9** (98 mg).

Tetra-*O*-methylcurcapicycloside (2a): amorphous powder; mp 135−137 °C; UV λ_{max} (log ϵ) 230 (4.35), 276 (4.05), 308 (3.80) nm; $[\alpha]^{20}_D$ +58.3° [*c* 0.6, $CHCl_3$−MeOH (1:1)]; IR ν_{max} 3400 (br, OH), 2950, 1665 (C=O), 1590, 1520, 1420, 1280, 1020, 870, 800 cm^{-1}; CD (*c* 1.87 × 10^{-5} M) ($\Delta\epsilon$) 311 (+1.30), 287 (0), 276 (−1.55), 250 (0), 235 (+2.93), 220 (+1.60), 212 (+2.43); ^{1}H and ^{13}C NMR, see Table 1; FABMS (pos.) *m*/*z* [M + H]$^+$ 535 (4), 417 (5), 385 (8), 373 (12), 327 (12), 311 (12), 287 (10), 237 (27), 197 (40), 181 (42), 179 (33), 165 (49), 163 (25), 147 (43), 131 (26), 105 (32), 91 (100), 57 (51); HRFABMS (pos.) *m*/*z* [M + H]$^+$ 535.2208 (calcd for $C_{27}H_{35}O_{11}$ 535.2179).

Peracetylation of 2a. Compound **2a** (10 mg) was peracetylated with Ac_2O−py at room temperature for overnight and after general workup gave the peracetyl product **2b**.

Tetra-*O*-methylcurcapicycloside Triacetate (2b): ^{1}H NMR data ($CDCl_3$), see Table 1; HREIMS *m*/*z* [M]$^+$ 660.2410 (calcd for $C_{33}H_{40}O_{14}$ 660.2418); EIMS *m*/*z* [M]$^+$ 660 (4), 509 (3), 371 (24), 356 (6), 235 (8), 180 (16), 165 (100), 151 (10), 97 (10), 43 (12).

(1*S*)-Tetramethyl-1-*O*-methylnyasicoside (3a): amorphous powder; R_f 0.33 [MeOH−$CHCl_3$ (1:9)]; $[\alpha]^{23}_D$ −74.3° (*c* 0.7, MeOH); UV λ_{max} (log ϵ) 223 (sh, 4.44), 257 (4.36), 285 (3.89), 298 (sh, 3.72) nm; IR ν_{max} 3400 (br s), 2940, 1510, 1460, 1410, 1260, 1240, 1140, 1080, 1020, 900, 860, 820, 760, 620 cm^{-1}; CD (1.82 × 10^{-5} M) ($\Delta\epsilon$) 315 (0), 283 (−2.06), 252 (−6.62), 234 (−1.10), 224 (−6.18), 211 (−15.96) nm; ^{1}H NMR ($CDCl_3$) δ 6.96 (1H, dd, *J* = 1.7, 8.4 Hz, H-6″), 6.90 (1H, d, *J* = 1.4 Hz, H-2′), 6.88 (1H, d, *J* = 1.7 Hz, H-2″), 6.87 (1H, dd, *J* = 1.4, 8.6 Hz, H-6′), 6.82 (1H, d, *J* = 8.6 Hz, H-5′), 6.74 (1H, d, *J* = 8.4 Hz, H-5″), 4.52 (1H, d, *J* = 7.7 Hz, Glc H-1), 4.38 (1H, d, *J* = 4.2 Hz, H-1), 4.05 (1H, *m*, H-2), 3.85 (3H, s, Ar−OMe), 3.83 (9H, s, Ar−OMe × 3), 3.80 (1H, m) and 3.70 (1H, m) (Glc H-6), 3.28 (3H, s, 1-OMe), 2.74 (1H, dd, *J* = 7.6, 17.0 Hz) and 2.53 (1H, dd, *J* = 5.3, 17.0 Hz) (H-3); ^{13}C NMR ($CDCl_3$) δ 149.30 (s, C-4″), 148.90 (s, C-4′ and C-3″), 148.62 (s, C-3′), 129.68 (s, C-1′), 124.69 (d, C-6″), 120.41 (d, C-6′), 114.40 (d, C-2′), 114.31 (s, C-1″), 111.05 (d, C-5″), 110.92 (d, C-2″), 110.70 (d, C-5′), 102.68 (d, Glc C-1), 84.84 (s, C-4), 84.31 (d, C-1), 82.55 (s, C-5), 79.93 (d, C-2), 76.22 (d, Glc C-5), 75.61 (d, Glc C-3), 73.11 (d, Glc C-2), 70.13 (d, Glc C-4), 62.19 (t, Glc C-6), 57.24 (q, 1-OMe), 55.98 (q), 55.90 (2C, q) and 55.85 (q) (4 × Ar−OMe), 21.89 (t, C-3); FABMS (pos.) *m*/*z* [M + Na]$^+$ 571 (100), [M]$^+$ 548 (4), 413 (24), 391 (16), 181 (25), 176 (41), 91 (55), 77 (55), 69 (75), 55 (100); HRFABMS (pos.) *m*/*z* [M + H]$^+$ 549.2438 (calcd for $C_{28}H_{37}O_{11}$ 549.2335).

Tetra-*O*-methylcurculigine (4a): amorphous powder; R_f 0.19 [MeOH−$CHCl_3$ (1:9)]; $[\alpha]^{20}_D$ −21.7° [*c* 0.6, $CHCl_3$−MeOH (1:1)]; IR ν_{max} 3400 (br s), 2950, 1665, 1590, 1510, 1420, 1280, 1160, 1080, 1020 cm^{-1}; UV λ_{max} (log ϵ) 228 (4.40), 274 (4.12), 301 (3.88) nm; CD (*c* 1.81 × 10^{-5} M) ($\Delta\epsilon$) 326 (+0.19), 314 (0), 310 (+0.05), 302 (+0.06), 295 (−0.09), 286 (+0.15), 271 (−0.39), 266 (−0.34), 259 (−0.53), 246 (−0.17), 233 (−1.34), 209 (+0.44); ^{1}H and ^{13}C NMR, see Tables 2 and 3; FABMS (neg.) *m*/*z* (rel int.) [M − H]$^-$ 551 (4), 537 (3), 377 (4), 303 (4), 287 (13), 229 (7), 197 (33), 179 (8), 153 (21), 139 (20), 107 (100).

Tetra-*O*-methylisocurculigine (5a): amorphous powder; R_f 0.19 [MeOH−$CHCl_3$ (1:9)]; $[\alpha]^{20}_D$ −6.0° [*c* 0.5, $CHCl_3$−MeOH (1:1)]; UV λ_{max} (log ϵ) 228 (4.33), 274 (4.05), 300 (3.81) nm; IR ν_{max} 3400 (br s), 2950, 1665, 1590, 1510, 1420, 1280, 1020 cm^{-1}; CD (*c* 1.81 × 10^{-5} M) ($\Delta\epsilon$) 322 (+0.37), 313 (+0.14), 308 (+0.23), 302(+0.09), 294 (+0.29), 275 (−0.28), 267 (−0.29), 252 (+0.15), 248 (+0.08), 240 (+0.49), 229 (−0.07), 208 (−2.65); ^{1}H and ^{13}C NMR, see Tables 2 and 3; FABMS (neg.) *m*/*z* (rel int.) [M − H]$^-$ 551 (4), 537 (3), 377 (6), 303 (4), 287 (18), 229 (12), 197 (36), 179 (9), 153 (12), 139 (26), 107 (100), 105 (15).

1-*O*-Methylcurculigine Tetra-*O*-methyl Ether (7a): amorphous powder; R_f 0.33 [MeOH−$CHCl_3$ (1:9)]; $[\alpha]^{23}_D$ −9.0° (*c* 1.0, MeOH); UV λ_{max} (log ϵ) 229 (4.19), 274 (3.90), 304 (sh, 3.68) nm; IR ν_{max} cm^{-1}: 3400 (br s), 2950, 1665, 1590, 1520, 1420, 1280, 1035, 1020, 810, 770; CD (*c* 1.77 × 10^{-5} M) ($\Delta\epsilon$) 304 (+0.16), 298 (+0.23), 294 (+0.18), 286 (+0.47), 284 (+0.46), 278 (+0.52), 265 (+0.21), 253 (+0.34), 232 (−0.64), 212 (+0.75); ^{1}H and ^{13}C NMR, see Tables 2 and 3; FABMS (neg.) *m*/*z* (rel int.) [M]$^-$ 566 (7), 552 (9), 377 (6), 321 (5), 301 (5), 287 (18), 285 (9), 229 (22), 219 (7), 210 (10), 197 (52), 195 (20), 179 (16), 171 (19), 155 (21), 153 (35), 139 (100), 105 (48), 89 (22).

1-*O*-Methylisocurculigine Tetra-*O*-methyl Ether (8a): amorphous powder; R_f 0.33 [MeOH−$CHCl_3$ (1:9)]; $[\alpha]^{23}_D$ +1.4° (*c* 0.7, MeOH); IR ν_{max} 3500 (br s), 2950, 1665 (C=O), 1590, 1520, 1410, 1280, 1120, 660 cm^{-1}; UV λ_{max} (log ϵ) 229 (4.19), 274 (3.91), 307 (sh, 3.68) nm; CD (*c* 1.77 × 10^{-5} M) ($\Delta\epsilon$) 306 (−0.03), 294 (−0.29), 288 (−0.15), 277 (−0.20), 267 (−0.18), 262 (−0.21), 243 (0), 234 (+0.44), 225 (+0.28), 219 (0), [214 (+0.24), 208 (−0.42)]; ^{1}H and ^{13}C NMR, see Tables 2 and 3; FABMS (neg.) *m*/*z* (rel int.) [M]$^-$ 566 (8), 551 (22), 377 (8), 287 (34), 269 (8), 229 (43), 197 (100), 179 (34), 139 (87), 87 (43).

Curcapital (9): amorphous powder; R_f 0.28 [MeOH−H_2O (1:1), RP_8]; IR ν_{max} 3300 (br s), 1630, 1560, 1520, 1475, 1420, 1250, 1020, 870, 830, 790, 680 cm^{-1}; UV λ_{max} (log ϵ) 221 (4.38), 250 (4.63), 276 (4.55), 309 (sh, 4.15), 376 (4.25) nm; ^{1}H and ^{13}C NMR, see Table 4; FABMS (neg.) *m*/*z* (rel int.) [M − H]$^-$ 309 (30), [M − 2H]$^-$ 308 (12), 279 (5), 203 (7), 171 (23), 137

(18), 113 (100), 89 (18), 87 (20), 77 (14), 75 (20), 64 (20); HRFABMS (neg.) *m/z* [M − H]$^-$ 309.0412 (calcd for $C_{17}H_9O_6$ 309.0399).

Preparation of Tetramethyl-(1*R*)-1-*O*-methylnyasicoside (10a): (1*R*)-1-*O*-Methylnyasicoside (**10**) was *O*-methylated by reacting with freshly prepared ethereal CH_2N_2 in the usual manner, and the reaction mixture was separated on a Si gel column chromatograph (230−400 mesh, 4% MeOH in $CHCl_3$) to give **10a**: amorphous powder; $[\alpha]^{20}_D$ −1.0° (*c* 1.0, MeOH); IR ν_{max} 3400 (br, OH), 2940, 1510, 1460, 1420, 1260, 1240, 1140, 1080, 1020, 860, 820, 760 cm^{-1}; UV λ_{max} (log ϵ) 258 (4.35), 285 (3.88), 298 (sh, 3.70) nm; CD (1.82 × 10^{-5} M) ($\Delta\epsilon$) 312 (0), 285 (+2.63), 250 (+7.42), 234 (+0.88), 212 (+14.43); ^{1}H NMR ($CDCl_3$) δ 6.96 (1H, dd, J = 1.7, 8.3 Hz, H-6″), 6.90 (1H, d, J = 1.4 Hz, H-2′), 6.89 (1H, dd, J = 1.4, 8.1 Hz, H-6′), 6.88 (1H, d, J = 1.7 Hz, H-2″), 6.81 (1H, d, J = 8.1 Hz, H-5′), 6.74 (1H, d, J = 8.3 Hz, H-5″), 4.55 (1H, d, J = 7.6 Hz, Glc H-1), 4.40 (1H, d, J = 6.1 Hz, H-1), 4.02 (1H, ddd, J = 5.1, 5.3, 6.1 Hz, H-2), 3.85 (3H, s, Ar−OMe), 3.83 (9H, s, Ar−OMe × 3), 3.80 (1H, m) and 3.70 (1H, m) (Glc H-6), 3.24 (3H, s, 1-OMe), 2.68 (1H, dd, J = 5.1, 17.0 Hz) and 2.33 (1H, dd, J = 5.3, 17.0 Hz) (H-3); ^{13}C NMR ($CDCl_3$) δ 149.28 (s, C-4″), 149.02 (s, C-4′), 148.97 (s, C-3″), 148.60 (s, C-3′), 128.98 (s, C-1′), 124.73 (d, C-6″), 120.31 (d, C-6′), 114.40 (d, C-2′), 115.40 (s, C-1″), 110.04 (d, C-5″), 110.85 (d, C-2"), 110.81 (d, C-5′), 101.80 (d, Glc C-1), 84.37 (s, C-4), 84.37 (d, C-1), 82.78 (s, C-5), 78.83 (d, C-2), 76.16 (d, Glc C-5), 75.79 (d, Glc C-3), 72.93 (d, Glc C-2), 70.02 (d, Glc C-4), 62.02 (t, Glc C-6), 56.97 (q, 1-OMe), 56.00 (q), 55.90 (q), 55.87 (q) and 55.85 (q) (4 × Ar−OMe), 22.63 (t, C-3); FABMS (pos.) *m/z* [M + Na]$^+$ 571 (100), [M]$^+$ 548 (4), 437 (8), 459 (25), 371 (8), 329 (12), 289 (8), 176 (78), 154 (64), 136 (56), 77 (30).

Preparation of Tetra-*O*-methyltetrahydronyasicoside (11): A solution of tetramethylnyasicoside (**1a**) (48 mg) in MeOH (5 mL) was catalytically hydrogenated over 10% Pd/C (2 mg)−1 atm H_2 at room temperature for 1.5 h. After general workup, a colorless viscous product (**11**, 46 mg) was obtained: $[\alpha]^{20}_D$ −44.0° (*c* 1.0, MeOH); IR ν_{max} 3400 (br, OH), 2950, 1510, 1460, 1420, 1260, 1230, 1140, 1070, 1020, 800, 760 cm^{-1}; UV λ_{max} (log ϵ) 229 (4.35), 279 (3.90) nm; CD ($\Delta\epsilon$) 299 (0), 281 (0.03), 258 (0), 235 (−0.22), 218 (0); ^{1}H NMR (CD_3OD) δ 6.77 (1H, dd, J = 1.4 Hz, H-2′), 6.68 (1H, d, J = 1.4, 8.1 Hz, H-6′), 6.65 (1H, dd, J = 1.4, 8.0 Hz, H-6″), 6.62 (1H, d, J = 8.1 Hz, H-5′), 6.50 (1H, d, J = 1.4 Hz, H-2″), 6.47 (1H, d, J = 8.0 Hz, H-5″), 4.36 (1H, d, J = 7.4 Hz, H-1), 4.36 (1H, d, J = 7.6 Hz, Glc H-1), 3.87 (3H, s, OMe), 3.84 (m) and 3.70 (m) (Glc H-6), 3.80 (m, H-2), 3.73 (9H, s, OMe × 3), 3.40 (2H, m, Glc H-5,3), 3.35 (1H, m, Glc H-4), 3.30 (1H, m, Glc H-2), 2.30 (2H, m, H-5), 1.63 (1H, m) and 1.45 (1H, m) (H-3), 1.25 (2H, m, H-2); HRFABMS (neg.) [M]$^-$ *m/z* 538.2382 (calcd for $C_{27}H_{38}O_{11}$ 538.2414); FABMS *m/z* [M]$^-$ 538 (28), [M − H]$^-$ 537 (100), 523 (10), 321 (10), 213 (24), 229 (10), 153 (37).

Preparation of Tetra-*O*-methylnyasicol 1,2-Acetonide (12): Tetra-*O*-methylnyasicol (34 mg),[6] obtained from nyasicol[2] by treating with CH_2N_2, was reacted with 2,2-dimethoxypropane (2.0 mL) and TsOH (2 mg) at 0 °C for 30 min, followed by additional stirring for 30 min at room temperature. The reaction mixture was then diluted with $CHCl_3$, washed with 5% $KHCO_3$ solution and H_2O, dried ($MgSO_4$), and evaporated in vacuo to yield an essentially pure **12** (36 mg), a colorless viscous liquid: $[\alpha]^{23}_D$ +84.3° (*c* 0.7, $CHCl_3$); UV λ_{max} (log ϵ) 221 (sh, 4.55), 237 (sh, 4.33), 258 (4.46), 286 (3.97), 297 (3.80) nm; CD (2.43 × 10^{-5} M) ($\Delta\epsilon$) 310 (0), 298 (0.11), 282 (0.26), 253 (0.77), 240 (0), 234 (−0.25), 224 (0); ^{1}H NMR ($CDCl_3$) δ 6.97 (1H, dd, J = 1.8, 8.2 Hz, H-6′), 6.96 (1H, d, J = 1.8 Hz, H-2′), 6.90 (1H, dd, J = 1.8, 8.2 Hz, H-6″), 6.82 (1H, d, J = 8.2 Hz, H-5′), 6.80 (1H, d, J = 1.8 Hz, H-2″), 6.73 (1H, d, J = 8.2 Hz, H-5″), 4.84 (1H, d, J = 8.3 Hz, H-1), 3.96 (1H, dt, J = 8.3, 4.9 Hz, H-2), 3.84 (9H, s, 3 × OMe), 3.82 (3H, s, 1 × OMe), 2.80 (1H, dd, J = 17.2, 5.2 Hz, H-3a), 2.69 (1H, dd, J = 17.2, 4.6 Hz, H-3b), 1.57 (3H, s, β-Me of acetonide), 1.54 (3H, s, β-Me of acetonide); HREIMS *m/z* [M]$^+$ 412.1886 (calcd for $C_{24}H_{28}O_6$ 412.1885); EIMS *m/z* [M]$^+$ 412 (2), 397 (3), 354 (7), 337 (25), 295 (8), 189 (9), 175 (100), 165 (37), 151 (33), 131 (18), 107 (11), 43 (11).

Hydration of Tetra-*O*-methylnyasicoside (1a) and Its 1-*O*-Methyl Derivative (10a). The mixture of **1a**[6] (36 mg), HgO (15 mg), concentrated H_2SO_4 (0.13 mL), and H_2O (3 mL)[7] was heated at 60° for 30 min. The reaction mixture was diluted with H_2O (10 mL) and passed over an Amberlite XAD-2 column (20 g) washed with H_2O and MeOH in order. The MeOH fraction (43 mg) was a mixture of **4a** and **5a**, which were separated as mentioned above to give each about 9 mg. Treatment of tetra-*O*-methyl-1-*O*-methylnyasicoside (**10a**) (38 mg) under similar conditions and fractionation via an Amberlite XAD-2 column yielded a mixture (36 mg) of **4a**, **5a**, and **7a**, which were separated on a Si gel column (10 g, 230−400 mesh) eluted with 4% MeOH in $CHCl_3$ to give **7a** (8 mg) and a mixture (6 mg) of **4a** and **5a**.

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References and Notes

(1) Lee, S. S.; Chang, W. L.; Chen, C. H. *Tetrahedron Lett.* **1996**, *37*, 4405−4408.
(2) Chang, W. L.; Su, M. J.; Lee, S. S. *J. Nat. Prod.* **1997**, *60*, 76−80.
(3) Chifundera, K.; Palazzino, G.; Messana, I.; Liu, P.; Galeffi, C.; Cannarsa, G. *Phytochemistry* **1994**, *35*, 1343−1348.
(4) Molecular modeling was performed by Systematic Search of Sybyl using Tripos Force Fields (TRIPOS, Inc.) to obtain the favored conformation of **2a** with minimum energy.
(5) Chifundera, K.; Messana, I.; Galeffi, C.; De Vicente, Y. *Tetrahedron* **1991**, *47*, 4369−4374.
(6) Galeffi, C.; G. Multari, G.; Msonthi, J. D.; Nicoletti, M.; Marini-Bettolo, G. B. *Tetrahedron* **1987**, *43*, 3519−3522.
(7) Stacy, G. W.; Mikulec, R. A. *Org. Synth.* **1955**, Coll. Vol. *4*, 13−15.
(8) Gaffield, W. *Tetrahedron* **1970**, *26*, 4093−4108.

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