Triprenylated Flavonoids from *Dorstenia psilurus* and Their α-Glucosidase Inhibition Properties

Turibio K. Tabopda,*[,†] Joseph Ngoupayo,[†] Patrice K. Awoussong,[†] Anne-Claire Mitaine-Offer,[‡] Muhammad S. Ali,[§] Bonaventure T. Ngadjui,[†] and Marie-Aleth Lacaille-Dubois[‡]

Organic Chemistry Department, University of Yaoundé I, P.O. Box 8664, Yaoundé, Cameroon, HEJ Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Pakistan, and Laboratoire de Pharmacognosie, Faculté de Pharmacie, Université de Bourgogne, UMIB UPRES EA 3660, 7 Boulevard Jeanne d'Arc, B.P. 87900, 21079 Dijon Cedex, France

Received August 16, 2008

Six new unusual C-4′-prenylated flavonols, dorsilurins F−K (**1**−**6**), together with six known compounds were isolated from the roots of *Dorstenia psilurus*, and their structures were elucidated on the basis of spectroscopic evidence. The isolated compounds exhibited moderate to low α-glucosidase inhibitory activity. Dorsilurin F (**1**), with three unmodified prenyl groups, was the most active, while dorsilurin K (**6**), with only one unmodified prenyl group, was the least active compound. Furthermore, NMR data of dorsilurin C (**7**), isolated some years ago from the same plant, have been revised.

The genus *Dorstenia* Linne (Moraceae) is represented by approximately 170 species worldwide.[1] It is largely made up of undergrowth and herbaceous perennials with succulent and scrambling rhizomes.[2] This genus contains many plants that are used as antisnakebite, anti-infection, and antirheumatic remedies in the medicinal plant therapy of many countries in Africa and Central and South America.[3,4] This genus is recognized as a rich source of prenylated and geranylated flavonoids and coumarins.[4] As part of our studies on Cameroonian *Dorstenia* species, we have already reported the isolation and characterization of some prenylated flavonoids.[5−14] Our previous phytochemical studies on the roots of *Dorstenia psilurus* led to the isolation and characterization of prenylated flavonoids dorsilurins A−E.[9,10] In continuing this study, we report here the isolation, structure elucidation, and α-glucosidase inhibition properties of six additional prenylated flavonoids named dorsilurins F−K (**1**−**6**) from a methanol extract of the roots of *D. psilurus*. We also revised the NMR data of dorsilurin C.

A methanolic extract of roots of *D. psilurus* was further extracted with *n*-hexane followed by $CHCl_3$. The $CHCl_3$-soluble fraction was subjected to repeated column chromatography on Sephadex LH-20 and silica gel to afford six additional prenylated flavonoids (**1**−**6**). Compounds **1**−**6** exhibited IR absorptions at ca. 3410 (O−H), 1650 (conjugated C═O), 1610 (C═C), and 1570 (C═C) cm^{-1}, as well as a positive Shinoda test and UV absorption maxima at 260−295 and 336−373 nm, which indicated their flavonoid character.[15] Their ^{13}C NMR spectra displayed characteristic resonances for a flavonol C ring at ca. δ 152 (C-2), 139 (C-3), and 179 (C-4) ppm. The absolute configuration of compounds **2**, **3**, and **4** was then determined by applying the modified Mosher's method[16] to the (*S*)- and (*R*)-MTPA (α-methoxy-α-trifluoromethyl)phenylacetic acid esters obtained by reacting **2**, **3**, and **4** with the corresponding (−)- and (+)-MTPA chloride. In fact, the Δδ values ($\delta_S - \delta_R$) depicted in Figure 2 permitted assignment of C-2′′′′ absolute configuration because the protons on the left-hand side of the MTPA plane shown in Figure 3 had all negative numbers as a consequence of the shielding effect exerted by the phenyl ring of the esterifying acid.

Compound **1** was obtained as a yellow, amorphous powder. The molecular formula $C_{30}H_{34}O_6$ was deduced from the HREIMS ([M^+] *m*/*z* 490.2347) and spectroscopic data. The ^1H NMR spectrum of **1** showed a downfield resonance at δ_H 13.15, attributed to a hydrogen-bonded hydroxy proton (5-OH), and only three aromatic ^1H NMR signals of an ABX-type ring B at δ_H 6.47 (1H, d, *J* = 2.3 Hz, H-2′), 6.55 (1H, d, *J* = 8.6 Hz, H-5′), and 7.65 (1H, dd, *J* = 2.3, 8.6 Hz, H-6′), suggesting fully substituted A and C rings. The observed chemical shifts of the ring B protons are consistent with an uncommon 3′-hydroxy-4′-alkyl substitution[17] instead of the more common 3′-alkyl-4′-hydroxy pattern at δ 7.17 (1H, br s, H-2′), 6.82 (1H, d, *J* = 9.0 Hz, H-5′), and 7.19 (1H, br d, *J* = 9.0 Hz, H-6′).[9] The ^1H NMR spectrum of **1** also showed the presence of three prenyl groups at C-4′, C-6, and C-8. The prenyl group at C-4′ showed NOE interactions between the olefinic proton at C-2′′′′ (δ 5.39) and the aromatic proton at C-5′ (δ 6.55) and between the *ortho*-coupled aromatic protons at C-5′ (δ 7.65) and C-6′ (δ 7.65) in the NOESY spectrum. The HMBC spectrum (Figure 1) indicated correlations from the methylene protons at C-1′′′′ (δ 3.37) to C-3′ (δ 158.4), C-5′ (δ 125.5), and C-3′′′′ (δ 130.5). Additional HMBC correlations were observed from H-2′ (δ 6.47) and H-6′ (δ 7.65) to C-2 (δ 150.3) and C-4′ (δ 125.7) and from H-5′ (δ 6.55) to C-1′ (δ 125.5) and C-3′ (δ 158.4). Most of the ^1H and ^{13}C NMR data of the A- and C-rings parts of compound **1** (see Tables 1 and 2) are superimposable on those of dorsilurin C isolated from the same plant,[10] confirming the presence of a flavonol with two prenyl moieties on the A ring. The presence of prenyl groups was confirmed from the ^1H NMR signals [δ_H 3.44 (2H, br d, *J* = 6.7 Hz, H-1′′′), 3.56 (2H, br d, *J* = 6.7 Hz, H-1′′), 3.37 (2H, d, *J* = 7.8 Hz, H-1′′′′), 5.26 (1H, t, *J* = 7.3 Hz, H-2′′′), 5.26 (1H, t, *J* = 7.3 Hz, H-2′′), 5.39 (1H, t, *J* = 7.8 Hz, H-2′′′′), 1.95 (12H, s, H-4′′, H-4′′′, H-5′′, H-5′′′), 1.74 (3H, s, H-4′′′′), and 1.72 (3H, s, H-5′′′′)].

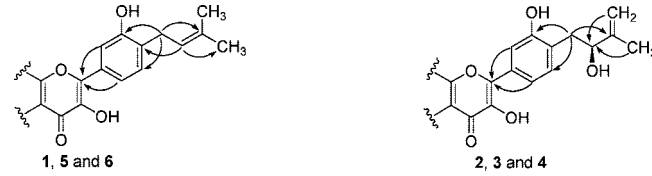
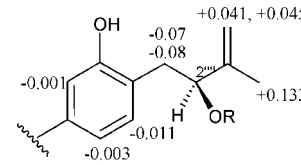


Figure 1. Selected HMBC correlations of **1**−**6**.



8 R = S (−)–MTPA
9 R = R (+)–MTPA

Figure 2. Differences of the proton chemical shifts ($\Delta\delta = \delta_S - \delta_R$) of MTPA Mosher ester derivatives of compounds **2**, **3**, and **4**.

* To whom corrspondence should be addressed. Tel: +237-77976633. Fax: +237-22221873. E-mail: ttabopda@yahoo.fr.
† University of Yaoundé I.
‡ Université de Bourgogne.
§ University of Karachi.

10.1021/np800509u CCC: $40.75
Published on Web 12/05/2008

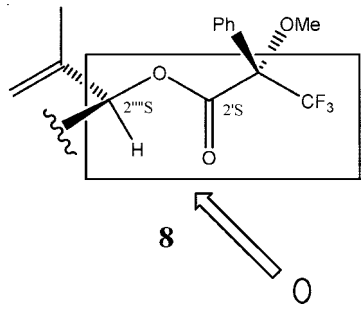


Figure 3. MTPA plane for the (*S*)-MTPA esters used to assign the absolute configuration at C-2′′′′ for **2**, **3**, and **4**.

HMBC correlations were observed between the allylic methylene signals at δ_H 3.44 (H_2-1′′′) and oxygenated carbons at δ_C 157.3 (C-9) and 161.0 (C-7), between δ_H 3.56 (H_2-1′′) and δ_C 161.0 (C-7) and 158.2 (C-5), and between δ_H 3.37 (H_2-1′′′′) and δ_C 158.4 (C-3′) and 125.5 (C-5′), indicating the presence of prenyl moieties at positions C-8, C-6, and C-4′, respectively. Thus, the structure of compound **1** was established as 6,8,4′-triprenyl-5,7,3′-trihydroxyflavonol, a new naturally occurring prenylated flavonoid assigned the name dorsilurin F.

Dorsilurin G (**2**) was obtained as a yellow, amorphous powder. The molecular formula $C_{30}H_{34}O_7$ was deduced from the HREIMS ([M^+] *m*/*z* 506.2309). A hydrogen-bonded hydroxy group was deduced from the presence of a signal at δ_H 12.80 (5-OH) in the ^{1}H NMR spectrum. In the aromatic region, dorsilurin G (**2**) displayed only three proton NMR signals. The three aromatic proton signals form an ABX system [δ_H 6.45 (1H, d, J = 2.2 Hz, H-2′), 7.71 (1H, d, J = 8.6 Hz, H-5′), and 6.55 (1H, dd, J = 2.2, 8.6 Hz, H-6′)] located in ring B. The ^{1}H NMR spectrum of this compound showed the presence of two prenyl groups [δ_H 3.44 (2H, br d, J = 6.8 Hz, H-1′′′), 3.49 (2H, br d, J = 6.7 Hz, H-1′′), 5.25 (1H, t, J = 7.5 Hz, H-2′′′), 5.26 (1H, t, J = 7.4 Hz, H-2′′), 1.94 (6H, s, H-5′′, H-5′′′), 1.96 (3H, s, H-4′′′), 1.97 (3H, s, H-4′′)] and a 2-hydroxy-3-methylbut-3-enyl group [δ_H 2.88 (1H, dd, J = 7.9, 15.1 Hz, H-1′′′′a), 3.04 (1H, dd, J = 5.7, 15.1 Hz, H-1′′′′b), 4.33 (1H, d, J = 7.9 Hz, H-2′′′′), 1.85 (3H, s, H-4′′′′), 4.91, 5.07 (s, 1H each, H-5′′′′a, H-5′′′′b)]. The EIMS spectrum displayed characteristic fragment ion peaks at *m*/*z* 288 and 218, resulting from a Retro-Diels−Alder (RDA) fragmentation of ring C. The ion peak at *m*/*z* 288 suggested the presence of two hydroxy and two prenyl groups on the A ring. This was confirmed by the C/H NMR data of ring A, which were quite similar to those of compound **1**. This finding, together with the observed chemical shifts of the protons of ring B superimposable on those of compound **1**, suggested that the 2-hydroxy-3-methylbut-3-enyl group is located at C-4′. An extensive analysis of ^{13}C/DEPT NMR data and comparison with the values of compound **1** allowed full assignment of all the protons and carbons (Tables 1 and 2). The structure of this new derivative, named dorsilurin G, was determined as 6,8-diprenyl-4′-(2*S*-hydroxy-3-methylbut-3-enyl)-5,7,3′-trihydroxyflavonol (**2**).

Dorsilurin H (**3**) was assigned the molecular formula $C_{30}H_{34}O_7$ by HREIMS. In the HMQC spectrum, the signals observed at δ_H 6.45 (d, J = 2.2 Hz), 6.53 (dd, J = 2.2, 8.5 Hz), and 7.69 (d, J = 8.5 Hz) were correlated with ^{13}C NMR signals at δ_C 109.7 (C-2′), 122.1 (C-6′), and 125.7 (C-5′), respectively, indicating the presence of a 3′-hydroxy-4′-alkyl disubstituted B ring. The ^{1}H NMR spectra of dorsilurin H (**3**) also showed the presence of a prenyl group [δ_H 3.51 (2H, dd, J = 2.4, 8.0 Hz, H-1′′′); 5.21 (1H, t, J = 8.0 Hz, H-2′′′); 1.93 (6H, s, H-4′′′, H-5′′′)], a 2,2-dimethyldihydropyrano group [δ_H 1.87 (2H, t, J = 6.8 Hz, H-3′′); 2.72 (2H, t, J = 6.8 Hz, H-4′′); 1.33 (6H, s, H-5′′, H-6′′)], and a 2-hydroxy-3-methylbut-3-enyl group [δ_H 2.87 (1H, dd, J = 7.6, 14.9 Hz, H-1′′′′a); 3.01 (1H, dd, J = 5.6, 14.9 Hz, H-1′′′′b); 4.31 (1H, d, J = 7.6 Hz, H-2′′′′); 1.86 (3H, s, H-4′′′′); 4.89 (1H, s, H-5′′′′a); 5.05 (1H, s, H-5′′′′b)]. The EIMS of compound **3** showed fragment ion peaks at *m*/*z* 218 and 288, resulting from RDA fragmentation, suggesting the presence of a prenyl and a 2,2-dimethyldihydropyrano group on the A ring and 2-hydroxy-3-methylbut-3-enyl group on the B ring. From the HMBC spectrum (Figure 1), the 2-hydroxy-3-methylbut-3-enyl group was located at C-4′. The presence of the 2,2-dimethyldihydropyrano moiety was also evident from the EIMS, which displayed the typical fragment at *m*/*z* 491 [M − 15]$^+$.[18] The location of the 2,2-dimethyldihydropyran ring fused to the C-5 and C-6 positions was assigned by the HMBC experiment, revealing correlations from the protons at C-4′′ (δ_H 2.72) to carbons at C-5 (δ_C 156.3) and C-7 (δ_C 162.0) and from the ^{1}H NMR, in which no hydrogen-bonded hydroxy group was observed. Thus, on the basis of these observations, the structure of dorsilurin H (**3**) was characterized as 5,6-(2,2-dimethyldihydropyrano)-7,3′-dihydroxy-8-prenyl-4′-(2S-hydroxy-3-methylbut-3-enyl)flavonol.

The molecular formula of dorsilurin I (**4**) was determined as $C_{30}H_{34}O_7$ by HREIMS (*m*/*z* 506.2309). The ^{1}H NMR spectrum of **4** showed a downfield resonance at δ_H 13.05, attributed to a hydrogen-bonded hydroxy proton (5-OH), three signals for the aromatic protons of an ABX-type ring B, one prenyl group, one 2,2-dimethyldihydropyrano, and one 2-hydroxy-3-methylbut-3-enyl group. The EIMS of compound **4** is similar to that of compound **3**. The fragment ion peaks at *m*/*z* 218 and 288 suggested that the prenyl and the 2,2-dimethyldihydropyrano groups are located on ring A, while the 2-hydroxy-3-methylbut-3-enyl group is located at C-4′. All the ^{1}H and ^{13}C NMR chemical shifts of ring B and the 2-hydroxy-3-methylbut-3-enyl group assigned from 2D NMR spectra were superimposable with those of compounds **2** and **3**, confirming the substitution pattern of ring B. Two possibilities were considered regarding the position of the prenyl group, one with an angular 2,2-dimethyldihydropyran ring or an alternative structure with a linear 2,2-dimethyldihydropyrano and a prenyl substituent at C-8. The ^{13}C chemical shift of C-6 (δ_C 108.9) strongly favors the attachment of the prenyl group at C-6, indicating that the annulation of the 2,2-dimethyldihydropyran ring was at C-7/C-8. Furthermore, the HMBC experiment reveals correlations from protons at C-1′′ (δ_H 3.45) to C-5 (δ_C 157.7) and C-7 (δ_C 161.4) and from hydrogen-bonded hydroxy proton (δ_H 13.05, 5-OH) to C-5 (δ_C 157.7), C-6 (δ_C 108.9), and C-10 (δ_C 102.4). The structure of dorsilurin I (**4**) was determined to be 7,8-(2,2-dimethyldihydropyrano)-5,3′-dihydroxy-6-prenyl-4′-(2*S*-hydroxy-3-methylbut-3-enyl)flavonol.

Compound **5** (dorsilurin J) was assumed to have the molecular formula $C_{30}H_{34}O_6$ from the HREIMS data. Its NMR data are similar to those of dorsilurin H (**3**). However, its ^{1}H and ^{13}C NMR data revealed the presence of two prenyl groups and one 2,2-dimethyldihydropyrano instead of one prenyl, one 2,2-dimethyldihydropyrano, and one 2-hydroxy-3-methylbut-3-enyl group as in compound **3**. The EIMS of **5** showed RDA fragment ion peaks at *m*/*z* 202 and 288, suggesting the presence of a prenyl group on the B ring. On the basis of these findings, compound **5** was concluded to have a prenyl and a 2,2-dimethyldihydropyrano group on the A ring. The annulation of the 2,2-dimethyldihydropyran ring at the C-5/C-6 positions was deduced from the absence of the hydrogen-bonded hydroxy proton in the ^{1}H NMR spectra and by direct comparison of ^{1}H and ^{13}C NMR data with those of dorsilurin H (**3**). From the foregoing data, compound **5** was characterized as 5,6-(2,2-dimethyldihydropyrano)-7,3′-dihydroxy-8,4′-diprenylflavonol.

Compound **6** was assigned the molecular formula $C_{30}H_{34}O_6$ from HREIMS ([M]$^+$ at *m*/*z* 490.2343). The ^{1}H and ^{13}C NMR spectrum of this compound exhibited the presence of a prenyl and two 2,2-dimethyldihydropyrano moieties. The absence of a signal in the ^{1}H NMR spectrum, attributable to a hydrogen-bonded hydroxy proton, led to the assumption that a free hydroxy group was not present at C-5. The aromatic region in the ^{1}H NMR spectrum of **6**

Table 1. ^{1}H NMR Data of Compounds **1**−**6** (300 MHz in $CDCl_3$)

position	1	2	3	4	5	6
2′	6.47 (d, 2.3)	6.45 (d, 2.2)	6.45 (d, 2.2)	6.46 (d, 2.2)	6.47 (d, 2.3)	6.46 (d, 2.3)
5′	6.55 (d, 8.6)	6.55 (d, 8.6)	6.53 (d, 8.5)	6.53 (d, 8.5)	6.55 (d, 8.6)	6.55 (d, 8.5)
6′	7.65 (dd, 2.3, 8.6)	7.71 (dd, 2.2, 8.6)	7.69 (dd, 2.2, 8.5)	7.70 (dd, 2.2, 8.5)	7.64 (dd, 2.3, 8.6)	7.64 (dd, 2.3, 8.5)
1″	3.56 (br d, 6.7)	3.49 (br d, 6.7)		3.45 (br d, 6.8)		
2″	5.26 (t, 7.3)	5.26 (t, 7.4)		5.23 (t, 7.5)		
3″			1.87 (t, 6.8)		1.88 (t, 6.8)	1.87 (t, 6.8)
4″	1.95 (s)	1.97 (s)	2.72 (t, 6.8)	1.70 (s)	2.72 (t, 6.8)	2.73 (t, 6.8)
5″	1.95 (s)	1.94 (s)	1.33 (s)	1.81 (s)	1.31 (s)	1.36 (s)
6″			1.33 (s)		1.31 (s)	1.36 (s)
1‴	3.44 (br d, 6.7)	3.44 (br d, 6.8)	3.51 (dd, 2.4, 8.0)		3.51 (dd, 2.3, 7.9)	
2‴	5.26 (t, 7.3)	5.25 (t, 7.5)	5.21 (t, 8.0)		5.23 (t, 7.9)	
3‴				1.88 (t, 6.8)		1.90 (t, 6.9)
4‴	1.95 (s)	1.96 (s)	1.93 (s)	2.74 (t, 6.8)	1.94 (s)	2.74 (t, 6.9)
5‴	1.95 (s)	1.94 (s)	1.93 (s)	1.53 (s)	1.93 (s)	1.55 (s)
6‴				1.53 (s)		1.55 (s)
1⁗	3.37 (d, 7.8)	2.88 (dd, 7.9, 15.1)	2.87 (dd, 7.6, 14.9)	2.88 (dd, 7.7, 14.5)	3.36 (d, 8.0)	3.37 (d, 7.8)
		3.04 (dd, 5.7, 15.1)	3.01 (dd, 5.6, 14.9)	3.05 (dd, 5.7, 14.5)		
2⁗	5.39 (t, 7.8)	4.33 (d, 7.9)	4.31 (d, 7.6)	4.33 (d, 7.7)	5.37 (t, 8.0)	5.38 (t, 7.8)
3⁗						
4⁗	1.74 (s)	1.85 (s)	1.86 (s)	1.85 (s)	1.73 (s)	1.75 (s)
5⁗	1.72 (s)	4.91 (s)	4.89 (s)	4.90 (s)	1.72 (s)	1.73 (s)
		5.07 (s)	5.05 (s)	5.05 (s)		
5-OH	13.15	12.80	-	13.05		

Table 2. ^{13}C NMR Data of Compounds **1**−**7** (75 MHz in $CDCl_3$)

position	1	2	3	4	5	6	7
2	150.3	149.6	150.2	150.0	150.2	149.9	153.0
3	137.1	137.5	137.1	137.2	137.1	137.2	138.9
4	179.3	179.2	179.7	179.5	179.6	179.7	179.4
5	158.2	158.0	156.3	157.7	156.5	155.8	159.0
6	110.4	109.8	106.5	108.9	106.1	106.1	112.3
7	161.0	160.9	162.0	161.4	161.8	161.7	164.2
8	105.5	105.4	104.9	104.7	105.0	104.4	107.4
9	157.3	157.2	158.7	159.9	158.7	160.0	158.0
10	105.3	105.3	104.6	102.4	104.9	102.3	105.8
1′	125.5	125.3	125.5	125.4	125.1	125.5	126.1
2′	110.0	110.3	109.7	110.1	109.5	109.9	109.6
3′	158.4	158.5	158.5	158.9	157.7	158.7	159.6
4′	125.7	125.4	125.5	125.8	125.3	125.5	125.9
5′	125.5	125.6	125.7	125.6	125.5	125.7	126.1
6′	122.3	122.3	122.1	122.2	122.6	122.4	123.4
1″	21.4	21.3		22.0			22.2
2″	122.3	122.4	77.0	122.8	76.9	76.7	122.2
3″	130.7	130.8	32.9	131.6	33.0	33.0	132.5
4″	25.3	25.3	18.1	25.5	17.8	17.7	25.8
5″	17.8	17.7	26.9	17.5	27.0	27.1	18.6
6″			26.9		27.0	27.1	
1‴	21.5	21.5	22.1		22.1		22.5
2‴	122.7	122.8	123.1	77.0	122.9	76.9	122.9
3‴	131.1	130.9	132.0	33.1	132.0	33.1	132.5
4‴	25.5	25.7	24.9	17.9	25.1	17.6	18.6
5‴	18.0	17.9	17.8	26.6	18.1	27.0	25.8
6‴				26.6		27.0	
1⁗	22.3	30.7	30.6	30.5	21.8	21.8	
2⁗	121.9	77.4	77.4	77.6	122.2	122.3	77.4
3⁗	130.5	148.1	148.0	147.8	131.0	130.7	115.3
4⁗	25.4	110.4	110.5	110.5	25.3	25.4	127.9
5⁗	17.9	19.0	18.9	18.9	17.7	17.8	27.7
6⁗							28.0

showed the presence of signals of only three protons of an ABX system located on the B ring. The EIMS of **6** showed ion peaks of RDA fragmentation of the C ring at *m*/*z* 202 and 288, suggesting that the prenyl group is located on the B ring. The NMR data comparison with those of compound **5** proved that the prenyl group was located at C-4′. Hence, the two 2,2-dimethyldihydropyrano groups are located on the A ring. It was evident at this point that the structure of compound **6** was derived from dorsilurin F (**1**) with three prenyl groups at C-6, C-8, and C-4′, with the former two cyclized (C-8/C-7−O− and C-6/C-5−O−) to form two 2,2-dimethyldihydropyrano rings. The ^{13}C NMR signals (Table 2) were fully assigned using DEPT spectra and by comparison of values with those reported for dorsilurin C isolated from the same plant.[10] Compound **6** was therefore characterized as 5,6−7,8-bis(2,2-dimethyldihydropyrano)-3′-hydroxy-4′-prenyl-flavonol.

Table 3. IC_{50} Values for Enzyme Inhibitory Activity of Compounds **1**−**7**

compound	α-D-glucosidase (yeast) IC_{50} (μM) ± SD	β-D-glucosidase (sweet almonds) IC_{50} (μM) ± SD	β-D-mannosidase (jack bean) IC_{50} (μM) ± SD
dorsilurin F (**1**)	4.13 ± 0.12	117.33 ± 0.15	192.09 ± 0.63
dorsilurin G (**2**)	7.51 ± 0.17	431.14 ± 1.91	231.99 ± 0.18
dorsilurin H (**3**)	24.01 ± 0.46	671.03 ± 0.44	[a]
dorsilurin I (**4**)	21.49 ± 0.71	431.14 ± 1.91	[a]
dorsilurin J (**5**)	16.91 ± 0.68	316.55 ± 0.83	518.27 ± 0.88
dorsilurin K (**6**)	43.95 ± 0.46	[a]	[a]
dorsilurin C (**7**)	11.17 ± 0.15	422.21 ± 0.42	358.21 ± 0.17
1-deoxynojirimycin	426.00 ± 8.14		

[a] No inhibition at 800 μM concentration.

In this work, we also revised the NMR data of dorsilurin C (**7**) as indicated in Table 2 and in the Experimental Section.

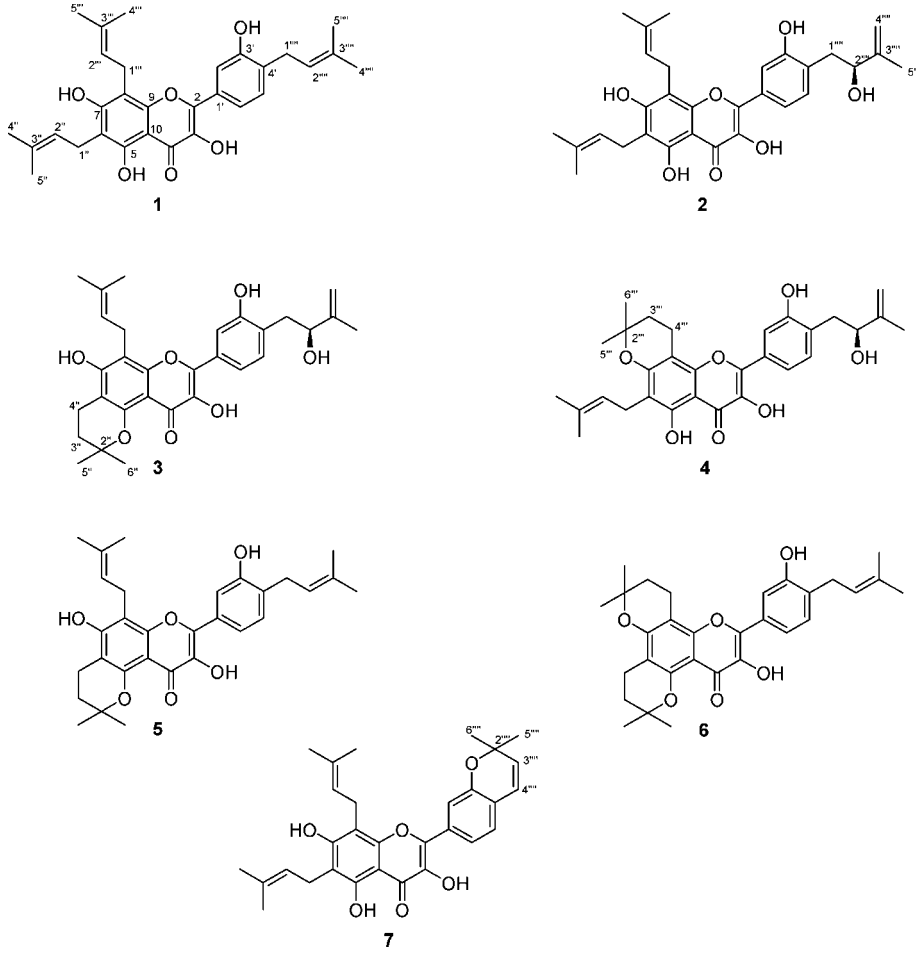
The genus *Dorstenia* is known to elaborate various flavonoids classes. These metabolites, especially the prenylated flavonoids, are fairly distributed in the genus. However, 3′-hydroxy-4′-alkyl-flavonoids are relatively rare.

In our search for α-glucosidase inhibitors from Cameroonian plants, we evaluated the isolated compounds for their possible glycosidase enzyme inhibitory activity against α-glucosidase, β-glucosidase, and α-mannosidase. Compound **1**, with three unmodified prenyl groups, showed the best α-glucosidase inhibitory activity (IC_{50} 4.13 μM), while compound **6**, with only one unmodified prenyl group, showed the worst α-glucosidase inhibitory activity (IC_{50} 43.95 μM). Thus, it would appear that α-glucosidase inhibitory activity increased with the number of unmodified prenylated groups present. These compounds showed very weak enzyme inhibitory activities against β-glucosidase and α-mannosidase. From *Dorsilurus psilurus*, all flavonoids isolated to date are triprenylated, which may explain the α-glucosidase inhibitory and antihypertensive activities of extracts of *D. psilurus*.[19] These preliminary experiments will provide the basis for further examination of the suitability of *D. psilurus* as a spice supplement that contributes toward the treatment and prevention of diabetes.

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter, and UV spectra were recorded on a Bio-TeK spectrophotometer. Melting points were determined on a

Chart 1



Büchi 535 melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO 302-A spectrophotometer in $CHCl_3$. The EIMS (70 eV) was measured on a Varian AAT 311A mass spectrometer, and HREIMS were recorded on a JEOL HX110 mass spectrometer. 1D and 2D NMR spectra were run on a Bruker AMX 300 MHz NMR spectrometer. The chemical shifts are given in ppm (δ), relative to TMS as internal standard, and coupling constants are in Hz. Column chromatography was carried out on silica gel (70−230 mesh, Merck). TLC was performed on Merck precoated aluminum silica gel 60 F_{254} sheets. The plates were checked under UV light (254 and 366 nm) and developed with vanillin and H_2SO_4 in EtOH. A molecular device spectrophotometer was used for measurement of enzyme inhibition.

Plant Material. The roots of *D. psilurus* were collected from Kumba in the South West Province of Cameroon in June 2006 and identified by Victor Nana, of the National Herbarium in Yaounde. A voucher specimen (1649/SRF/CAM) is deposited at the National Herbarium, Yaounde, Cameroon.

Extraction and Isolation. The dried, powdered roots of *D. psilurus* (400 g) were refluxed with MeOH (3 × 1 L). This MeOH extract was concentrated to dryness and gave a residue (47 g), which was suspended in H_2O and partitioned with *n*-hexane (3 × 300 mL). The residual H_2O solution was concentrated in vacuo to give a residue, which was partitioned between H_2O and $CHCl_3$. After concentration, the $CHCl_3$ fraction was subjected to column chromatography over silica gel (230−400 mesh), eluted with a gradient of *n*-hexane−EtOAc followed by EtOAc−MeOH to afford 60 fractions (200 mL each). These fractions were pooled into nine fractions (F-1 to F-9) according to their similarity on TLC (*n*-hexane−EtOAc, 3:1 and 1:1). Fraction F1 (1.8 g), examined by TLC (*n*-hexane−EtOAc, 9:1), contained mainly mixtures of hydrocarbons and phytosterols. Recrystallization gave β-sitosterol (275 mg). Recristallization of fraction F2 yielded stearyl ferulate (113 mg). Fractions F3−F4 (2.5 g) was crystallized from a mixture of *n*-hexane−EtOAc to afford psoralen (930 mg). Fraction F5 (1.3 g) was subjected to repeated chromatographic separation on silica gel using $CHCl_3$−MeOH−H_2O (65:35:10, lower phase) as eluent. Dorsilurins J (**5**, 39 mg) and K (**6**, 13 mg) were obtained. Under the same conditions, fractions F6 (237 mg) and F7 (118 mg) yielded dorsilurins I (**4**, 58 mg) and F (**1**, 39 mg) respectively. Fraction F8 was purified on preparative TLC using $CHCl_3$−MeOH (6:4) to yield dorsilurins G (**2**, 41 mg, R_f = 0.43) and H (**3**, 67 mg, R_f = 0.51).

Preparation of Mosher Ester Derivatives of 2, 3, and 4. To two solutions of compounds **2**, **3**, or **4**, respectively (10 mg), in CH_2Cl_2 (2 mL) containing dicyclohexylcarbodiimide (DCC) and dimethylaminopyridine (DMAP) were added (*S*)-(−)-MTPA and (*R*)-(+)-MTPA, respectively. Each mixture was stirred at room temperature for 6 h, and the products were purified by preparative TLC using *n*-hexane−EtOAc (3:2) as eluant.

Dorsilurin F (1): yellow, amorphous powder; UV (MeOH) λ_{max} (log ϵ) 250 (4.50), 280 (4.59), 361 (4.32) nm; IR (KBr) ν_{max} 3444−3412 (OH), 1647 (C═O), 1603, 1554, 1471, 1420, 1356, 1307, 1261 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m*/*z* 490 $[M]^+$ (39), 435 (100), 380 (58), 379 (12), 288 (43), 202 (29), 189 (43), 177 (100), 147 (71), 130 (8), 55 (12); HREIMS *m*/*z* 490.2347 (calcd for $C_{30}H_{34}O_6$, 490.2356).

Dorsilurin G (2): yellow, amorphous powder; $[\alpha]^{20}_D$ −106.3 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ); 253 (4.51), 275 (4.33), 381 (4.52) nm; IR (KBr) ν_{max} 3450−3400 (OH), 1641 (C═O), 1600, 1551, 1465, 1420, 1350, 1310, 1260 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m*/*z* 506 $[M]^+$ (21), 451 (71), 396 (37), 288 (62), 218 (17), 205 (38), 189 (61), 177 (100), 147 (75), 134 (81), 71 (91), 55 (21); HREIMS *m*/*z* 506.2309 (calcd for $C_{30}H_{34}O_7$, 506.2303).

Dorsilurin H (3): yellow, amorphous powder; $[\alpha]^{20}_D$ −86.9 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 273 (4.22), 378 (4.52) nm; IR (KBr) ν_{max} 3450−3400 (OH), 1641 (C═O), 1605, 1550, 1470, 1420, 1350, 1310, 1260, 1220 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m*/*z* 506 $[M]^+$ (23), 491 (39), 436 (30), 365 (11), 293 (37), 288 (37), 273 (60), 218 (21), 177 (100), 147 (58), 72 (8), 71 (91), 55 (21); HREIMS *m*/*z* 506.2311 (calcd for $C_{30}H_{34}O_7$, 506.2303).

Dorsilurin I (4): yellow, amorphous powder; $[\alpha]^{20}_D$ −96.1 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) (4.34), 277 (4.22), 375 (4.38) nm;

IR (KBr) ν_{max} 3450−3400 (OH), 1640 (C═O), 1601, 1552, 1470, 1420, 1350, 1260, 1220 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m/z* 506 $[M]^+$ (23), 491 (39), 436 (30), 365 (11), 293 (37), 288 (37), 273 (60), 218 (21), 177 (100), 147 (58), 72 (8), 71 (91), 55 (21); HREIMS *m/z* 506.2311 (calcd for $C_{30}H_{34}O_7$, 506.2303).

Dorsilurin J (5): yellow, amorphous powder; UV (MeOH) λ_{max} (log ϵ) 205 (4.27), 280 (4.31), 375 (4.40) nm; IR (KBr) ν_{max} 3440−3405 (OH), 1643 (C═O), 1600, 1549, 1461, 1423, 1330, 1260 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m/z* 490 $[M]^+$ (41), 475 (17), 420 (22), 365 (42), 294 (12), 288 (27), 233 (51), 202 (23), 177 (100), 147 (77), 55 (21); HREIMS *m/z* 490.2345 (calcd for $C_{30}H_{34}O_6$, 490.2356).

Dorsilurin K (6): yellow, amorphous powder; UV (MeOH) λ_{max} (log ϵ) 271 (4.40), 371 (4.22) nm; IR (KBr) ν_{max} 3420−3400 (OH), 1650 (C═O), 1606, 1551, 1473, 1427, 1310, 1152 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m/z* 490 $[M]^+$ (53), 447 (22), 435 (81), 380 (17), 379 (43), 289 (34), 288 (8), 233 (37), 202 (11), 177 (100), 137 (63), 55 (91); HREIMS *m/z* 490.2349 (calcd for $C_{30}H_{34}O_6$, 490.2356).

Dorsilurin C (7): yellow gum; UV (MeOH) λ_{max} (log ϵ), 250 (4.55), 280 (4.61), 350 (4.22) nm; λ_{max} (MeOH+$AlCl_3$) (log ϵ): 207 (4.42), 245 (4.65), 275 (4.29), 380 (4.57) nm; λ_{max} (MeOH+$AlCl_3$+HCl) (log ϵ): 209 (4.36), 245 (4.62), 270 (4.32), 382 (4.58) nm; λ_{max} (MeOH+NaOAc) (log ϵ): 218 (4.50), 290 (4.65), 360 (4.37) nm; IR (KBr) ν_{max} 3480−3420 (OH), 1640 (C═O), 1600, 1550, 1475, 1420, 1350, 1310, 1260 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.75 (6H, br s, 2 × Me), 1.70, 1.84, 1.87, 1.98 (3H each, br s, 4 × Me olefinic), 3.44, 3.56 (2H each br d, J = 6.7 Hz, 2H-1‴, 2H-1″), 5.26 (2H, br t like m, H-2‴, H-2″), 5.43 (1H, br d like m, H-3⁗), 6.28 (1H, d, J = 9.5 Hz, H-4⁗), 6.3 (H, br s, OH), 6.43 (1H, d, J = 2.3 Hz, H-2′), 7.65 (1H, dd, J = 8.6, 2.3 Hz, H-6′), 6.55 (1H, d, J = 8.6 Hz, H-5′) and 13.05 (1H, br s, 5-OH); ^{13}C NMR data, see Table 2; EIMS *m/z* 488 $[M]^+$ (70), 473 ($[M - 15]^+$, 15) 433 ($[M - 55]^+$, 68), 389 (20), 378 (15), 377 (36), 321 (25), 288 (10), 200 (16), 189 (40), 128 (10), 55 (12); HREIMS *m/z* = 488.2193 (calcd for $C_{30}H_{32}O_6$ 488.2199).

Enzyme Inhibition Assay. The glycosidase inhibition assay was performed according to the slightly modified method of Matsu et al. (1996) as previously described.[20−22] α-D-Glucosidase (E.C.3.2.1.20), β-D-glucosidase (3.2.1.21), and α-D-mannosidase (3.2.1.24) were purchased from Wako Pure Chemical Industries Ltd. (Wako 076-02841). Briefly, α-glucosidase (500 units/mL) was incubated with *p*-nitrophenylglucopyranoside (p-NPG, final concentration: 0.7 mM) in the presence or absence of various concentrations of test compound in 50 mM phosphate buffer (pH 6.9) containing 1% v/v DMSO at 37 °C for exactly 10 min. After the incubation, an equal volume of stop solution (100 mM Na_2CO_3) was added, and the amount of released *p*-nitrophenol was measured in terms of the absorbance at 400 nm. The increment in absorption at 400 nm due to the hydrolysis of PNPG by glycosidase was monitored on a microplate spectrophotometer (Spectra Max, Molecular Devices). The absorbance of the reaction mixture was recorded at 400 nm at 1 min intervals in a temperature-controlled chamber at 37 °C. The linear reaction velocity (change in absorbance per minute) was calculated from the gradient of the linear portion of the reaction profile and used to determine the α-glucosidase activity. The concentration of the test compounds that inhibited the hydrolysis of PNP-G by α-glucosidase by 50% (IC_{50}) was determined by monitoring the effect of increasing the concentration of these compounds in the assays of the inhibition values. The IC_{50} values were then calculated using EZ-Fit enzyme kinetics program (Perrella Scientific Inc., Amherst, MA).

Acknowledgment. This study was supported by a grant from the French government. We are thankful to HEJ Research Institute of Chemistry and Dr. Panjwani Center for Molecular Medicine and Drug Research, University of Karachi, for spectra data and glycosidase bioassay.

References and Notes

(1) Mabberley, D. J. In *The Plant Book. A Portable Dictionary of Higher Plants*; Cambrige University Press: Cambridge, UK, 1987; p 192.
(2) Berg, C. C.; Human, M. E. E.; Weerdenburg, J. C. A. In *Flore du Cameroun*; Satabie, B., Ed.; MESRES: Yaounde, 1989; p 24.
(3) Bouquet, A. In *Féticheurs et Médecines Traditionnelles du Congo (Brazzaville)*; Memoires de l'Orstom: Paris, 1969; p 36.
(4) Abegaz, B. M.; Ngadjui, B. T.; Dongo, E.; Bezabih, M.-T. *Curr. Org. Chem.* **2000**, *4*, 1079–1090.
(5) Abegaz, B. M.; Ngadjui, B. T.; Dongo, E.; Tamboue, H. *Phytochemistry* **1998**, *49*, 1147–1150.
(6) Abegaz, B. M.; Ngadjui, B. T.; Dongo, E.; Ngameni, B.; Nindi, M. N.; Bezabih, M.-T. *Phytochemistry* **2002**, *59*, 877–883.
(7) Abegaz, B. M.; Ngadjui, B. T.; Folefoc, G. N.; Fotso, S.; Ambassa, P.; Bezabih, M.; Dongo, E.; Rise, F.; Petersen, D. *Phytochemistry* **2004**, *65*, 221–226.
(8) Ngadjui, B. T.; Abegaz, B. M.; Dongo, E.; Tamboue, H.; Kouam, F. *Phytochemistry* **1998a**, *48*, 349–354.
(9) Ngadjui, B. T.; Dongo, E.; Happi, E. N.; Bezabih, M.-T.; Abegaz, B. M. *Phytochemistry* **1998b**, *48*, 733–737.
(10) Ngadjui, B. T.; Tabopda, T. K.; Dongo, E.; Kapche, G. W. F.; Sandor, P.; Abegaz, B. M. *Phytochemistry* **1999a**, *52*, 731–735.
(11) Ngadjui, B. T.; Dongo, E.; Tamboue, H.; Kouam, F.; Abegaz, B. M. *Phytochemistry* **1999b**, *50*, 1401–1406.
(12) Ngadjui, B. T.; Dongo, E.; Kapche, G. W. F.; Tamboue, H.; Abegaz, B. M.; Connolly, J. D. *Phytochemistry* **1999c**, *51*, 119–123.
(13) Ngadjui, B. T.; Kouam, S. F.; Dongo, E.; Kapche, G. W. F.; Abegaz, B. M. *Phytochemistry* **2000**, *55*, 915–919.
(14) Ngameni, B.; Ngadjui, B. T.; Folefoc, G. N.; Watchueng, J.; Abegaz, B. M. *Phytochemistry* **2004**, *65*, 427–432.
(15) Mabry, T. J.; Markham, K. R.; Thomas, M. B. In *The Systematic Identification of Flavonoids*; Springer-Verlag; New York, 1970; pp 153−155.
(16) Ohtani, I.; Kusumi, T.; Ishitsuku, M. O.; Kakisawa, H. *Tetrahedron Lett.* **1989**, *30*, 3147–3150.
(17) Lin, M.; Li, J. B.; Li, S. Z.; Yu, D. Q.; Liang, X. T. *Phytochemistry* **1992**, *31*, 633–638.
(18) Takayama, M.; Fukai, T.; Hano, Y.; Nomura, T. *Heterocycles* **1992**, *33*, 405–434.
(19) Dimo, T.; Rakotonirina, A.; Tan, P. V.; Dongo, E.; Dongmo, A. B.; Kamtchouing, P.; Azay, J.; Abegaz, B. M.; Cros, G.; Ngadjui, B. T. *Phytomedicine* **2001**, *8*, 101–106.
(20) Tabopda, T. K.; Ngoupayo, J.; Liu, J.; Ali, M. S.; Khan, S. N.; Ngadjui, B. T.; Luu, B. *Chem. Pharm. Bull.* **2008**, *56*, 847–850.
(21) Tabopda, K. T.; Ngoupayo, J.; Liu, J.; Mitaine-Offer, A. C.; Tanoli, S. A. K.; Khan, S. N.; Ali, M. S.; Ngadjui, B. T.; Tsamo, E.; Lacaille-Dubois, M. A.; Luu, B. *Phytochemistry* **2008**, *69*, 1726–1731.
(22) Ngoupayo, J.; Noungoue, D. T.; Lenta, B. N.; Tabopda, K. T.; Khan, S. N.; Ngouela, S.; Ali, M. S.; Tsamo, E. *Nat. Prod. Commun.* **2007**, *2*, 1141–1144.

NP800509U