Sindurol and Nephthoside: New Tetraprenyltoluquinols from the Soft Coral *Sinularia dura* and *Nephthea* sp.

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Four new tetraprenyltoluquinols (**2**−**5**) have been isolated from the Indo-Pacific soft corals *Sinularia dura* and *Nephthea* sp. Sindurol (**2**), isolated from the *Sinularia*, is a 1,3,5-trialkylated 2,8-dioxabicyclo[3.2.1]octane, and nephthoside (**4**), obtained from the *Nephthea*, is a new substituted hydroquinone D-arabinose glycoside. Compounds **3** and **5** are closely related to nephthoside (**4**). The structure determination of all new compounds was based mainly on 1D- and 2D-NMR spectroscopy and mass spectrometry, as well as some chemical transformations.

In our continuing search for bioactive metabolites from marine invertebrates, we encountered two Indo-Pacific soft corals, *Sinularia dura* Pratt (Alcyoniidae) and *Nephthea* sp. (Nephtheidae), whose lipophilic (EtOAc) extract was cytotoxic. Investigation of these extracts yielded several polyprenylhydroquinones. Among Octocorallia the genus *Nephthea* of the family Nephtheidae comprises of a large variety of species. The current literature is not adequate for identification of *Nephthea* material to a species level; a study based on a diverse collection from numerous Indo-Pacific reefs including Sodwana Bay, South Africa, is ongoing.

Polyprenylquinones and hydroquinones are an important subclass among the various marine terpenoids of mixed biogenesis.[2,3] Linear prenyl derivatives and particularly polyprenyltoluquinols are less common. The most common sources are marine plants of the order Fucales[3,4] and the brown algae. Less common sources are marine invertebrates such as sponges of the genera *Ircinia*[5] and *Toxiclona*,[6] alcyonaceans,[7] gorgonaceans,[8] and ascidians.[9]

From the crude extract of *S. dura* (Pratt, 1903) (family Alcyoniidae) collected in Sodwana Bay, Durban, South Africa[10] were isolated two major compounds. One of these turned out to be the known cembranoid epoxypukalide (**1**) isolated earlier from *S. polydactyla*,[11] and the second, designated sindurol (**2**), was determined to be a new tetraprenyltoluquinol derivative.

Sindurol (**2**) is an optically active glass, $[\alpha]_D = -45°$, and has a molecular formula of $C_{31}H_{44}O_9$ (*m*/*z* 560, EIMS), which was established by the HREIMS of the M − H_2O ion. The IR (3400, 1745, and 1230 cm^{-1}) and the UV spectra [λ_{max}(MeOH) 280 nm, ϵ 3580][11] indicated the presence of hydroxyl, ester, and hydroquinone functionalities. The ^{1}H- and ^{13}C-NMR spectra (Table 1) displayed signals assignable to five singlet methyls, two vinyl protons, two acetates, six methylenes, one oxygenated methylene, two oxygenated methines, three oxygenated nonprotonated C-atoms, and an alkylated toluquinol moiety. The NMR data as well as the *m*/*z* 69 fragment in the mass spectrum suggested the presence of a terminal isoprene unit. This unit could readily be further extended, on the basis of COSY and HMBC homo- and heterocorrelations (Table 1), to partial structure A.

A: $(CH_3)_2C{=}CHCH_2CH_2C(CH_3){=}CHCH(CH_2{-})O{-}$ $(C_{11}H_{18}O)$

The second suggested part, an alkylated toluquinol system, was unequivocally confirmed by the *m*/*z* 137 fragment, $CH_3C_6H_2(OH)_2CH_2^+$ ($C_8H_9O_2$, HREIMS), in the mass spectrum of **1** (see also below for compound **3**). Because of the almost identical chemical shift of C-1′ and C-4′ (δ_C 147.6 s and 147.7 s), the HMBC experiment could not distinguish between the two possible isomeric *meta*- or *para*-dialkylated hydroquinols. However, the sharp singlets of the two aromatic protons (δ_H 6.52 and 6.53 ppm) indicated that they, and therefore also the two alkyl groups, were *para*. Unequivocal proof for this was obtained from the clear differences in the carbon chemical shifts of C-1′ to C-6′ in the two possible *para* and *meta* isomers (Table 2). Clearly, the differences between C-1′ and C-4′ of the *para* isomer are minimal, while the differences for C-2′, -5′, and -6′ are significant.

On the basis of the ^{1}H-^{1}H COSY and mainly the HMBC experiments (Figure 1 and Table 1) the toluquinol moiety could further be extended to partial structure B.

B: $CH_3C_6H_2(OH)_2CH_2CH(OAc)C(O{-})CH_2OAc$ $(C_{15}H_{18}O_7)$

With parts A (11 carbon atoms) and B (15 carbon atoms) assigned, this left five C-atoms to be accounted for. These must include one carbon bearing two oxygens (C-4) (δ_C 102.3 ppm), one of the five methyls (Me-19) (which because of its low-field proton resonance (δ_H 1.58s), and the fact that it is not a vinyl methyl must be attached to an oxygenated carbon atom (C-7) (δ_C 84.5s)), and an ethylene group (C-5 and -6) [(δ_C 23.5 t and 26.3 t, and δ_H 1.44 m (1H) and 2.11 m (3H)]. Since sindurol (**2**) contains 10 degrees of unsaturation, of which eight were accounted for by partial structures A

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Table 1. ^{13}C and ^{1}H NMR Data (125 and 500 MHz) Including CH-Correlations of Sindurol (**2**)[a,b]

position	δ_C	δ_H	HMBC (H to C)	position	δ_C	δ_H	HMBC (H to C)
1	28.7 t	2.83 dd (14, 11)[c], 3.17 dd (14, 2)	1′, 2′, 3′, 2	17	17.6 q	1.59 s	13, 14, 15
				18	16.5 q	1.71 s	10, 11, 12
				19	22.5 q	1.58 s	4, 7, 8
2	72.7 d	5.70 dd (11, 2)	1, 20, Ac, 2′	20	66.3 t	4.36 d (11)	2, 5, OAc
3	75.5 s					4.14 d (11)	
4	102.3 s			2-OAc	170.1 s		
				2-OAc	20.8 q	1.90 s	*C*OCH$_3$
5	23.5 t	1.44 m, 2.11 m	3, 19	20-OAc	171.1 s		
6	26.3 t	2.11 m		20-OAc	21.0 q	2.14 s	*C*OCH$_3$
7	84.5 s			1′	147.7 s		
8	46.9 t	1.92 m, 2.19 dd (14, 6)	4, 7, 9, 10	2′	121.9 s		
9	75.1 d	5.01 ddd (10, 9, 6)	4, 8, 11	3′[d]	116.9 d	6.52 s	1, 2
10	126.0 d	5.26 d (9)	8, 12, 18	4′	147.6 s		
11	139.5 s			5′	123.5 s		
12	39.5 t	2.03 m	10, 11, 17	6′[d]	118.2 d	6.53 s	2′, 4′, 7′
13	26.5 t	1.88 m, 2.11 m	10, 16	7′	15.5 q		5′, 6′
14	123.9 t	5.10 brt (7)					
15	131.0 s						
16	25.6 q	1.68 s	14, 15, 17				

[a] $CDCl_3$, Bruker ARX 500 instrument, chemical shifts refer to TMS ($\delta_H = 0$) and $CDCl_3$ ($\delta_C = 77.0$). [b] Assignments aided by HMQC, HMBC, HOMO-COSY, TOCSY, and NOESY experiments. [c] *J* values in Hz. [d] May be interchangeable.

Table 2. Comparison of the Carbon Chemical Shifts of the Aromatic Ring in Compounds **2**−**4** and **m**[a]

compd	C-1′	2′	3′	4′	5′	6′	substitution
2	147.7	121.9	116.9	147.6	123.5	118.2	(*para*)
3	147.8	124.3	116.2	147.4	125.3	118.1	(*para*)
4	149.6	125.0	117.0	148.4	126.3	118.3	(*para*)
m	149.4	131.9	115.5	145.9	114.0	127.8	(*meta*)

[a] **m** = 2′-substituted tetraprenyl-6′-methylhydroquinone.[12]

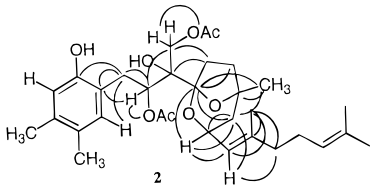


Figure 1. Major CH correlations (HMBC) for compound **2**.

and B, *vide supra*, the remaining connecting portion has to be bicyclic.

Detailed examination of the HMBC correlations (the key correlations being those around the oxabicyclic system, Figure 1, Table 1) indicated the presence of a 1,3,5-trialkylated 2,8-dioxabicyclo[3.2.1]octane system. Sindurol (**2**) is thus a tetraprenyltoluquinol in which the two isoprene units next to the aromatic ring were oxidized and changed to form the substituted bicyclo heterocyclic system.

While the relative stereochemistry of the chiral centers C-4 and C-7 is determined from the geometry of the bicyclic system, the relative configuration of the third chiral center (C-9) was suggested from the coupling constants of H-9 (Table 1). A 10 Hz coupling between H-9 and one of the C-8 protons requires H-9 to be axial and the chain equatorial. Unequivocal proof for the dioxabicyclooctane structure, including the stereochemistry of C-9, came from a NOESY experiment. The major nontrivial correlations are represented in Figure 2.

Sindurol is unstable even in the cold, possibly due to an easy acetate migration. Regrettably, the small amounts of **2** available prevented further studies of the molecule, its absolute configuration, and its transformation product.

From the second soft coral investigated, *Nephthea* sp., three additional toluqinols (**3**, **4**, and **5**) have been

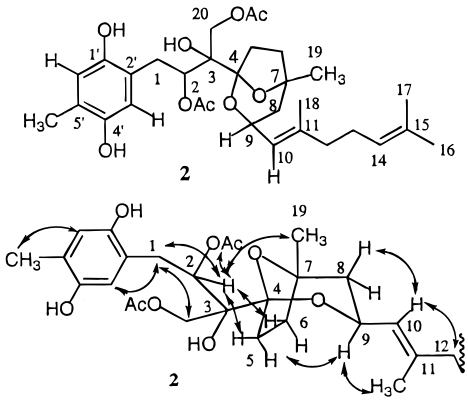
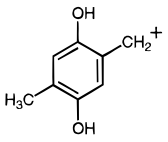
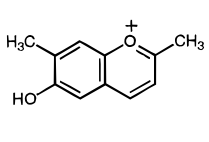


Figure 2. Major nontrivial NOE correlations for sindurol (**2**).

isolated. All three compounds have in common the same *all-trans* tetraprenyltoluquinol skeleton. Among the three, compound **3** represents the unsubstituted tetraprenyltoluqinol. Its structure was unequivocally determined on the basis of its HREIMS and the NMR spectra. The HREIMS gave, in addition to the molecular peak at *m*/*z* 396.3029 ($C_{27}H_{40}O_2$), diagnostic fragmentations for a polyprenyl chain (M − 69 and [M − 69] − 68) and two characteristic fragments at *m*/*z* 137 and 175 consistent with the following substructures:



m/*z* 137



m/*z* 175

Searching the literature for compounds with the molecular formula $C_{27}H_{40}O_2$ gave the 2′-tetraprenyl-6′-methylhydroquinone isomer, isolated from the brown seaweed *Stypopodium zonale*.[13,14] Comparison of the

Table 3. ^{13}C and ^{1}H NMR Data (125 and 500 MHz) Including CH Correlations of Nephthoside (**4**)[a,b]

position	δ_C	δ_H	HMBC (H to C)	position	δ_C	δ_H	HMBC (H to C)
1	29.9 t	3.31 d (7.0)	2, 3, 1′, 2′, 3′	1′	149.6 s		
				2′	125.0 s		
2	121.5 d	5.28 t (7.0)	1, 4/8/12, 20, 2′	3′	117.0 d	6.88 s	1, 1′, 4′, 5
3	138.8 s			4′	148.4 s		
4/8/12	39.67 t	2.02 m	18, 19	5′	126.3 s		
	39.7 t			6′	118.3 d	6.62 s	1′, 2′, 4′,
				7′	16.0 d	2.18 s	4′, 5′, 6′
5/9/13	26.6 t	2.10 m	4/8/12, 6/10	1″	98.4 d[d]	5.48 d (3.0)	3″,5″[c]
	26.8 t			2″	69.8 d	4.01 m	3″[c]
				3″	68.8 d	4.08 m	2″[c]
6, 10, 14	123.6 d	5.10 m	4/8/12, 5/9/13,	4″	70.8 d	4.03 m	2″[c]
	124.2 d		18/19, 16, 17	5″	63.0 t	3.82 dd (12.6, 1.6)	1″, 4″[c]
						3.97 d (12.6)	1″, 4″[c]
7, 11	135.6 s			1′-O*H*		4.95 brs	1′, 2′, 6′[c]
	134.9 s						
15	131.2 s						
16	25.7 q	1.68 s	14, 15, 17				
17	17.7 q	1.60 s	14, 15, 16				
18/19	16.0 q	1.60 s	4/8/12, 6/10				
	16.3 q						
20	16.06 q	1.77 s	2, 3, 4/8/12				

[a] $CDCl_3$, Bruker ARX 500 instrument, chemical shifts refer to TMS ($\delta_H = 0$) and $CDCl_3$ ($\delta_C = 77.0$). [b] Assignments aided by HMQC, HMBC, and homo-COSY experiments. [c] Correlations from the HMBC experiment of **6**. [d] Values of 93.4, 69.5, 69.5, 69.5, and 63.4 ppm for C-1″−5″, respectively, were measured for the C-1″-unsubstituted β-D-arabinose.[16]

Table 4. Comparison of NMR Data of Compound **6** and ***β*-Arabinose Tetraacetate**[15]

	6		β-D-arabinose tetraacetate[a]
position	δ_C	δ_H	δ_H
1″	95.9d	5.64 (d, J = 3.4 Hz)	6.27 (d, J = 3.3 Hz)
2″	68.0d	5.31 (dd, J = 10.8, 3.4 Hz)	5.21 (dd, J = 11.8, 3.3 Hz)
3″	67.3d	5.54 (dd, J = 10.8, 3.4 Hz)	5.32 (dd, J = 11.8, 3.0 Hz)
4″	68.9d	5.42 (dt, J = 3.4, 1.7 Hz)	5.35 (ddd, J = 3.0, 1.9, 1.0 Hz)
5″	61.1t	3.76 (dd, J = 13.0, 1.7 Hz)	3.79 (dd, J = 13.2, 1.9 Hz)
		4.06 (dd, J = 13.0, 1.7 Hz)	4.18 (dd, J = 13.2, 1.0 Hz)

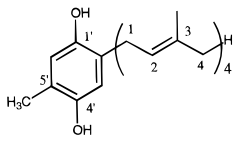
[a] For α-D-arabinose peracetate a $J_{H\text{-}1''/\text{-}2''}$ value of 6.4 Hz was measured.[15]

^{13}C-data of this *meta* (6′-methyl) isomer (**m**) and the *para* (5′-methyl) sindurol (Table 2) pointed clearly to **3** being a *para* isomer. The latter conclusion was further supported by the chemical correlation of **3** and **4**, for which the structure was established independently as discussed below. The corresponding quinone, tetraprenyltoluquinone, was previously isolated from an Australian *Nephthea* sp.[7]

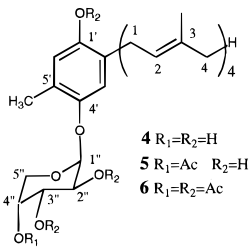
The major metabolite that was isolated from the Sodwana Bay *Nephthea* sp., nephthoside (**4**) (0.2% dry wt), was isolated as an optically active oil $[\alpha]_D = -114°$. Compound **4** was assigned a molecular formula $C_{32}H_{48}O_6$ from its HREIMS, which gave a molecular ion at m/z 528.3478. The ^{1}H- and ^{13}C-NMR spectra of nephthoside (**4**) (Table 3) indicated the presence of the same tetraprenyltoluquinol as in **3** and in addition the glycosidation of one of the phenol groups. The latter glycosidation created a larger difference in the chemical shifts of C-1′ and C-4′, enabling a distinction between the two in an HMBC experiment (Table 3), which established that C-1′ bears the free OH group and C-4′ (vicinal to the 5-methyl group for which correlations to C-4′ were observed) carries the substituted OH group.

The NMR data of the unaccounted part of the molecule, $C_5H_9O_4$ (Table 3), were consistent with the presence of a β-arabinose moiety in **4** (Table 4).[15−16] The $^{1}H-^{1}H$ coupling constants were measured in part on **4** and in part on **6**, the peracetate of **4**.

Acid hydrolysis of **4** afforded the aglycon **3** identical to that isolated directly and arabinose. The strong negative rotation ($[\alpha]_D = -100°$) indicated that the arabinose belongs to the D-series (the $[\alpha]_D$s of all the other pentoses are in the range of ±30°).[17]



3



4 R_1=R_2=H
5 R_1=Ac R_2=H
6 R_1=R_2=Ac

The third metabolite (**5**), an oil, $C_{34}H_{50}O_7$ (HREIMS) had a proton NMR spectrum very similar to that of nephthoside (**4**), the only difference being an additional acetate group and the downfield shift of H-4″ (assigned by a $^{1}H-^{1}H$ COSY experiment) from δ 4.03 to δ 5.28 ppm. The latter shift as well as the HMBC correlation between H-4″ and the CO group of the acetate placed the latter acetate on C-4″. Acetylation of **5** gave the same tetracetate, **6**, as obtained from **4**, thereby confirming the structure of **5** as being 4″-acetoxynephthoside.

Noteworthy, as already mentioned by Bowden and Coll,[6] is the *para* dialkylation of the hydroquinone found in the soft corals compared to the *meta* dialkylation found in brown alga metabolites (e.g., *Cystoseira* sp.[3]). Prenylation *para* to the methyl group was also found, in addition to earlier reports of similar alkylation in a *Nephthea* sp.,[7] in a *Sinularia* sp.,[18] a *Gorgonia*,[8] and a *Stolonifer*.[2] The present work provides two additional such *para* prenylated compounds.

Sindurol (**2**) is cytotoxic to P388 mouse leukemia cells at a concentration of 1.2 μg/mL (IC_{50}), and the other three new natural compounds (**3**−**5**) were cytotoxic at a concentration of 2 μg/mL.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. Mass spectra (low resolution and high resolution) were recorded on a Fisons, Autospec Q instrument. ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AMX-360 and ARX-500 spectrometers. All chemical shifts are reported with respect to TMS ($\delta_H = 0$) and $CDCl_3$ ($\delta_C = 77.0$). Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter using a 1-cm microcell.

Biological Material. *Sinularia dura* (Pratt, 1903) (class Octocorallia, order Alcyonacea, family Alcyoniidae) (No. TASA-302) and *Nephthea* sp. (order Alcyonacea, family *Nephtheidae*) (No. TASA-296) were collected in Sodwana Bay, South Africa, by SCUBA at a depth of 10−20 m during the summer of 1993. In the collecting site, there was a single species of the genus *Nephthea*. The colonies are bushy, attaining a maximal length of 12 cm, and are cream to green in color. The polyps are grouped into catkins, and each polyp has a supporting bundle composed of prolonged sclerites. Voucher samples are deposited in the Zoological Department at Tel Aviv University.

Isolation Procedures. After collection, each of the soft corals was immediately frozen at −25 °C. The freeze-dried soft coral (60 g) was then extracted with EtOAc to give a brown gum (1.2 and 1.0 g for the *Sinularia* and *Nephthea*, respectively). Each of the crude gums was chromatographed first on a Sephadex LH-20 column, eluted with MeOH−$CHCl_3$−hexane (1:1:2), and then several times on Si gel columns eluted with hexane/EtOAc mixtures to afford (from *Sinularia*, sp.) **1** (50 mg, 0.09%)[10] and **2** (50 mg, 0.09%) and (from *Nephthea* sp.) **3** (20 mg, 0.05%), **4** (100 mg, 0.2%), and **5** (5 mg, 0.01%). Sindurol (**2**): oil; $[\alpha]_D$ −45° ($c = 0.01$, $CHCl_3$); IR ν_{max} (neat) 3400, 1745, 1230 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m/z* 560 (M^+, 2) 542 (5), 500 (4), 458 (6); HREIMS *m/z* 542.2880 (calcd for $C_{31}H_{42}O_8$ (542.2879).

Compound **3**: oil; ν_{max} (neat) 3235 (OH), 2967, 2924, 2855, 1448, 1425, 1187 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.58 (1 H, brs), 6.53 (1 H, brs), 5.28 (1 H, t, J = 7 Hz), 5.09 (3 H, m), 4.68 (1 H, s), 4.32 (1 H, s), 3.27 (2 H, d, J = 7 Hz), 2.18 (3 H, s, Me-7′), 1.92−2.16 (12 H, m), 1.75 (3 H, s, Me-20), 1.68 (3 H, s, Me-16), 1.59 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 147.7 (s, C-1′), 147.3 (s, C-4′), 138.3 (s, C-3), 135.5, 135.0 (s, C-7/11) 131.3 (s, C-15), 125.2 (s, C-5′), 124.4 (s, C-2′), 124.2 (d, C-14), 123.7, 122.4 (d, C-6/10), 121.6 (d, C-2), 118.0 (d, C-6′), 116.1 (d, C-3′), 39.7 (t, C-4/8/12), 29.3 (t, C-1), 26.7, 26.6, 26.4 (t, C-5/9/13), 25.7 (q, C-16), 17.7 (q, C-17), 16.2 (q, C-20), 16.0 (q, C-18/19), 15.4 (q, C-7′); HREIMS *m/z* 396.3029 (calcd for $C_{27}H_{40}O_2$ 396.3028), EIMS (70 eV); *m/z* $[M]^+$ 396 (18), 192 (20), 177 (29), 175 (60), 149 (21), 137 (86), 135 (21), 121 (28), 109 (28), 95 (28), 81 (60), 69 (100).

Nephthoside (4): oil; $[\alpha]_D$ −114.3° ($c = 3.3$, $CHCl_3$); ν_{max} (neat) 3400 (OH), 2927 (CH, aliphatic), 1450, 1194, 1086, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz), see Table 3; ^{13}C NMR ($CDCl_3$, 90 MHz), see Table 3; HREIMS *m/z* 528.3478 (calcd for $C_{32}H_{48}O_6$ 528.3451); EIMS (70 eV) *m/z* $[M]^+$ 528 (6), 396 (79), 260 (13), 259 (16), 217 (12), 203 (17), 192 (38), 177 (52), 175 (69), 163 (16), 137 (100), 121 (32), 93 (22), 81 (56), 69 (92).

Nephthoside monoacetate (5), the third *Nephthea* metabolite: oil; $[\alpha]_D$ −83.3° ($c = 1.2$, $CHCl_3$); ν_{max} (neat) 3400 (OH), 2925 (CH, aliphatic) 1752 (C=O, ester), 1500, 1365, 1230, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz), δ 6.88 (1 H, brs, H-3′), 6.65 (1 H, brs, H-6′), 5.52 (1 H, d, J = 3.6 Hz, H-1″), 5.32 (1 H, t, J = 7.0 Hz, H-2), 5.28 (1 H, dt, J = 3.6, 1.7 Hz, H-4″), 5.12 (3 H, m, H-6/10/14), 4.93 (1 H, brs, H-1′-OH), 4.19 (1 H, dd, J = 10.0, 3.6 Hz, H-3″), 4.05 (1 H, dd, J = 13.0, 2.0 Hz, H-5″), 4.03 (1 H, dd, J = 10.0, 3.6 Hz, H-2″), 3.85 (1 H, dd, J = 13.0, 2.0 Hz, H-5″), 3.32 (2 H, d, J = 7.0 Hz, H-1), 2.22 (3 H, s, Me-7′), 2.20 (3 H, s, Ac-4″), 2.12 (6 H, m, H-5/9/13), 2.0−2.12 (6 H, m, H-4/8/12), 1.78 (3 H, s, Me-20), 1.70 (3 H, s, Me-16), 1.62 (3 H, s, Me-17), 1.62 (6 H, s, Me-18/19); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 170.9 (s, Ac-4″), 149.7 (s, C-1′), 148.4 (s, C-4′), 138.8 (s, C-3), 135.6, 134.9 (s, C-7/11) 131.3 (s, C-15), 126.4 (s, C-5′), 125.0 (s, C-2′), 124.4 (d, C-14), 123.6, 124.2 (d, C-6/10), 121.4 (d, C-2), 118.3 (d, C-6′), 116.9 (d, C-3′), 98.3 (d, C-1″), 71.1 (d, C-4″), 70.0 (d, C-2″), 69.2 (d, C-3″), 61.5 (t, C-5″), 39.7 (t, C-4/8/12), 29.9 (t, C-1), 26.7, 26.6, 26.5 (t, C-5/9/13), 25.7 (q, C-16), 21.1 (q, Ac-4″), 17.7 (q, C-17), 16.3 (q, C-20), 16.0 (q, C-18/19), 16.0 (q, C-7′); HREIMS *m/z* 570.3571 (calcd for $C_{34}H_{50}O_7$ 570.3558); EIMS (70 eV) *m/z* $[M]^+$ 570 (1), 428 (58), 410 (25), 396 (31), 275 (13), 191 (71), 175 (100), 157 (46), 137 (66), 121 (18), 115 (37), 97 (38), 81 (45), 69 (95).

Acetylation of Nephthoside (4) and Nephthoside Acetate (5) to Tetraacetate 6. To a solution of 9 mg of nephthoside (**4**) or **5** was added a mixture of 1:1 dry pyridine and acetic anhydride (1 mL) and the resulting mixture allowed to stand overnight at room temperature. The solvent was then evaporated to give 8 mg of compound **6** as a colorless oil: $C_{40}H_{56}O_{10}$; $[\alpha]_D$ −112.1° ($c = 1.2$, $CHCl_3$); ν_{max} (neat) 2925, 1752, 1371, 1245, 1225, 1179, 1072, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.93 (1 H, brs, H-3′), 6.79 (1 H, brs, H-6′), 5.64 (1 H, d, J = 3.4 Hz, H-1″), 5.54 (1 H, dd, J = 10.8, 3.4 Hz, H-3″), 5.43 (1 H, dt, J = 3.4, 1.7 Hz, H-4″), 5.31 (1 H, dd, J = 10.8, 3.4 Hz, H-2″), 5.13 (1 H, t, J = 7.1 Hz, H-2) 5.09 (3 H, m, H-6/10/14), 4.06 (1 H, dd, J = 13, 1.7 Hz, H-5″), 3.76 (1 H, dd, J = 13.0, 1.7 Hz, H-5″), 3.15 (2 H, t, J = 7.1 Hz, H-1), 2.27 (3 H, s, Ac-1′), 2.22 (3 H, s, Me-7′), 2.17 (3 H, s, Me-Ac), 2.07−1.97 (12 H, m), 2.05 (3 H, s, Me-Ac), 2.03 (3 H, s, Me-Ac), 1.69 (6 H, s), 1.59 (9H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 170.3 (s, Ac), 170.3 (s, Ac), 170.1 (s, Ac), 169.8 (s, Ac), 152.7 (s, C-1′), 143.5 (s, C-4′), 137.2 (s, C-3), 135.2, 134.9 (s, C-7/11), 131.9 (s, C-15), 131.2 (s, C-5′), 126.4 (s, C-2′), 124.3 (d, C-2), 124.4, 124.3, 124.1 (d, C-6/10/14), 121.2 (d, C-6′), 115.7 (d, C-3′), 95.9 (d, C-1″), 68.9 (d, C-4″), 68.1 (d, C-2″), 67.3 (d, C-3″), 61.2 (t, C-5″), 39.7 (t, C-4/8/12), 28.7 (t, C-1), 26.8 (t, C-5/9/13), 25.7 (q, C-16), 20.9 (q, 2Ac), 20.7 (q, 2Ac), 17.7 (q, C-17), 16.2 (q, C-20), 16.0 (q, C-18/19), 15.8 (q, C-7′); EIMS *m/z* $[M]^+$ 728 (0.1%), 686 (1), 668 (1.5), 644 (2).

Hydrolysis of Nephthoside. Nephthoside (**4**) (16 mg) was refluxed for 6 h in a 1:4 solution of HCl; H_2O (5 mL). The solution was then neutralized with aqueous NH_4OH, the methanol removed under vacuum, and the residue partitioned between H_2O and $CHCl_3$. The

aqueous phase was freeze dried, and the ethanol soluble fraction was chromatographed on Sephadex LH-20 to give the monosaccharide D-arabinose, identified by its NMR data[15,16] and $[\alpha]_D$ −100° (c = 0.86, H_2O).[17]

References and Notes

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