Renealtins A and B, New Diarylheptanoids with a Tetrahydrofuran Ring from the Seeds of *Renealmia exaltata*

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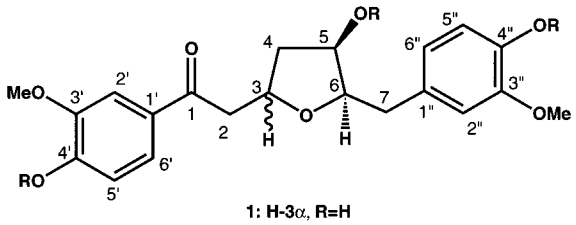
Two new diarylheptanoids, renealtins A (**1**) and B (**2**), have been isolated from the seeds of the Brazilian medicinal plant *Renealmia exaltata* ("Pacová-catinga", Zingiberaceae), and their structures were elucidated by spectroscopic data. Renealtins A (**1**) and B (**2**) are the first example of naturally occurring diarylheptanoids containing a tetrahydrofuran ring.

Brazilian medicinal plants have proven to be a rich source of compounds that might be useful for the development of new pharmaceutical agents.[1] In our search for structurally unique compounds from Brazilian medicinal plants, labdane-derived diterpenoids[2] and nitorogen-containing clerodane diterpenoids[3,4] have been isolated from the leaves of *Echinodorus macrophyllus*. Recent investigations on extracts from the seeds of the Brazilian medicinal plant *Renealmia exaltata* ("Pacová-catinga") led to the isolation of three new labdane diterpenoids, pacovatinins A−C.[5] Further investigation on extracts from the seeds of *R. exaltata* resulted in the isolation of renealtins A (**1**) and B (**2**), two new diarylheptanoids containing a tetrahydrofuran ring. In this paper we describe the isolation and structure elucidation of **1** and **2**.



The seeds of *R. exaltata* L.f. (Zingiberaceae) were extracted with MeOH. The MeOH extracts were partitioned between hexane and 90% MeOH, and the MeOH layer was partitioned between EtOAc and H_2O. The EtOAc-soluble portions were subjected to silica gel column chromatography ($CHCl_3$−MeOH, 4:1) followed by reversed-phase C_{18} column chromatography (MeOH−H_2O, 1:1) and then reversed-phase C_{18} HPLC (MeOH−H_2O, 1:1) to afford renealtins A (**1**, 0.000095%) and B (**2**, 0.000095%).

The molecular formula, $C_{21}H_{24}O_7$, of renealtin A (**1**) was established by HRFABMS [*m/z* 411.1420 $(M + Na)^+$, Δ 0.0 mmu]. The IR spectrum suggested the presence of hydroxy (3423 cm^{-1}) and unsaturated ketone (1629 cm^{-1}) groups, while UV absorptions at 305 and 279 nm implied that **1** possessed a conjugated benzene ring. The gross structure of **1** was deduced from detailed analysis of ^1H and ^{13}C NMR data (Table 1) aided with 2D NMR experiments ($^1H-^1H$ COSY, HMQC, and HMBC) (Figure 1). The ^{13}C NMR data indicated that the molecule possessed one ketone, two benzene rings, three oxymethines, two methoxy groups, and three methylenes. Since nine of 10 unsaturations were accounted for, **1** was inferred to contain one more ring. The $^1H-^1H$ COSY (Figure 1) spectrum indicated connectivities of C-2 to C-7, C-5′ to C-6′, and C-5″ to C-6″. The coupling

Table 1. ^1H and ^{13}C NMR Data of Renealtins A (**1**) and B (**2**) in CD_3OD

	1		**2**	
position	$^1H^a$	$^{13}C^a$	$^1H^a$	$^{13}C^a$
1		198.36		199.83
2a	3.55 (dd, 6.9,15.6)	48.86	3.24 (m)	45.13
2b	3.10 (dd, 5.8,15.6)		2.94 (dd, 5.8,15.7)	
3	4.33 (m)	75.81	4.73 (m)	75.56
4a	2.53 (m)	41.29	2.18 (m)	38.45
4b	1.78 (m)		1.89 (m)	
5	4.16 (m)	73.10	4.13 (m)	72.86
6a	3.73 (m)	86.00	3.97 (m)	84.83
7a	2.87 (dd, 6.0,13.7)	34.69	2.79 (dd, 6.0,13.7)	35.55
7b	2.81 (dd, 7.2,13.7)		2.70 (dd, 7.2,13.7)	
1′		130.11		130.10
2′	7.58 (d, 1.9)	110.48	7.47 (d, 1.9)	111.62
3′		147.75		148.82
4′		152.56		153.80
5′	6.88 (dd, 8.2)	114.04	6.81 (d, 8.2)	115.33
6′	7.63 (dd, 8.2,1.9)	123.89	7.54 (d, 8.2,1.9)	124.64
1″		131.10		132.66
2″	6.80 (m)	112.24	6.80 (d, 1.9)	113.72
3″		147.55		148.46
4″		144.88		145.92
5″	6.66 (brd)	114.40	6.66 (brd)	115.50
6″	6.66 (brd)	121.23	6.66 (brd)	122.06
3′-OMe	3.90 (s)	55.44	3.80 (s)	56.10
3″-OMe	3.72 (s)	55.55	3.72 (s)	56.10

[a] δ in ppm.

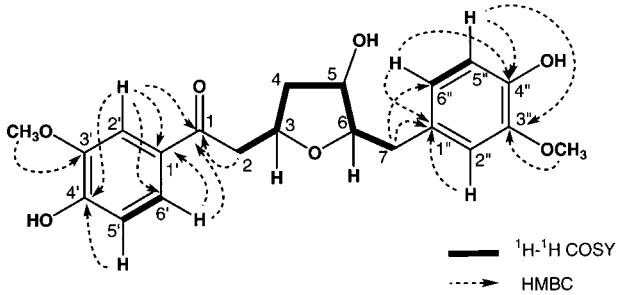


Figure 1. Selected 2D NMR data of renealtin A (**1**).

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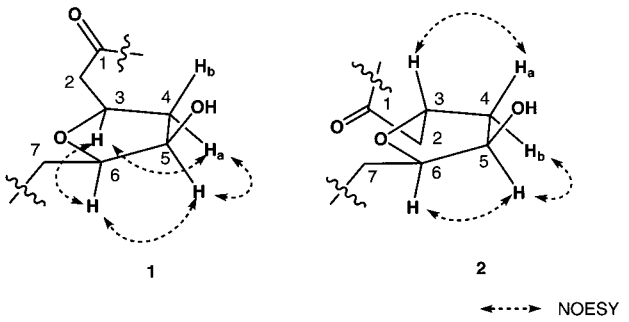

Figure 2. Selected NOESY correlations and relative stereochemistry of renealtins A (**1**) and B (**2**).

constants and chemical shifts (Table 1) of H-2′, H-5′, H-6′, H-2″, H-5″, and H-6″ suggested the presence of a 3′-methoxy-4′-hydroxybenzene ring and a 3″-methoxy-4″-hydroxybenzene ring. HMBC correlations of H_2-2 and H-2′ to C-1 (δ_C 198.36) and H_2-7 to C-1″ (δ_C 131.11) revealed connectivities between C-1′ and C-2 through a ketone carbonyl (C-1) and between C-1″ and C-7, respectively. Treatment of **1** with acetic anhydride in pyridine afforded the triacetate (**1a**), judging from its ^{1}H NMR and MS spectra. The proton signals at C-3 and C-6 in **1a** were not shifted as compared with those of **1**, indicating that **1a** possessed a tetrahydrofuran ring (C-3−C-6 and O-3) with a hydroxy group at C-5. Thus, the gross structure of renealtin A was elucidated to be **1**. NOESY correlations (Figure 2) of H-3/H-4a, H-3/H-6, H-4a/H-5, and H-5/H-6 indicated *syn* relationships both between H-3 and H-6 and between H-5 and H-6. Therefore, the relative stereochemistry of renealtin A (**1**) was assigned as shown in Figure 2.

Renealtin B (**2**) showed the molecular ion peak at *m*/*z* 411 $(M + Na)^+$ in the FABMS. HRFABMS analysis revealed the molecular formula to be $C_{21}H_{24}O_7$ [*m*/*z* 411.1408 $(M + Na)^+$, Δ −1.2 mmu], which was the same as that of renealtin A (**1**). ^{1}H and ^{13}C NMR data (Table 1) of **2** were quite similar to those of **1**. Detailed analysis of 2D NMR data (^{1}H−^{1}H COSY, HMQC, and HMBC) suggested that the gross structure of **2** was the same as that of **1**. NOESY correlations (Figure 2) of H-3/H-4a, H-4b/H-5, and H-5/H-6 indicated *anti* and *syn* relationships between H-3 and H-6 and between H-5 and H-6, respectively. Thus, renealtin B (**2**) was assigned to be the epimer at C-3 of renealtin A (**1**).

Renealtins A (**1**) and B (**2**) are the first example of diarylheptanoids containing a tetrahydrofuran ring, although some diarylheptanoids possessing a tetrahydropyran ring have been reported from *Alpinia blepharocalyx*[6] and *Zingiber officinale*.[7]

Experimental Section

General Experimental Procedures. Optical rotations were determined on a JASCO P-1030 polarimeter. UV and IR spectra were obtained on JASCO Ubest-35 and JASCO FT/IR-230 spectrometers, respectively. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-500 spectrometer. The 3.35 and 49.8 ppm resonances of residual CD_3OD were used as internal references for ^{1}H and ^{13}C NMR spectra, respectively. FAB mass spectra were measured on a JEOL HX-110 spectrometer using a glycerol matrix.

Plant Material. The seeds of *Renealmia exaltata* ("Pacová-catinga", Zingiberaceae) were purchased in São Paulo, Brazil, in March 2000. The plant was identified by Dr. G. Hashimoto (Centro de Pesquisas de História Natural, São Paulo, Brazil), and a voucher specimen has been deposited at the Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University.

Extraction and Separation. The seeds (420 g) were extracted with MeOH (500 mL × 3), and the extracts were partitioned between hexane (500 mL × 3) and 90% MeOH (500 mL). The MeOH layer was partitioned with EtOAc (500 mL × 3) and H_2O (50 mL). The EtOAc-soluble portions (4.2 g) were subjected to a silica gel column ($CHCl_3$−MeOH, 4:1) followed by a C_{18} column (Cosmosil ODS, MeOH−H_2O, 1:1) to give a fraction (135 mg). The fraction was subjected to a silica gel column (hexane−acetone, 1:1) followed by reversed-phase HPLC [Develosil ODS HG-5, Nomura Chemical, 1 × 25 cm; eluent, MeOH−H_2O (1:1); flow rate 2.5 mL/min] to give renealtins A (**1**, t_R 12.8 min, 0.4 mg) and B (**2**, t_R 13.6 min, 0.4 mg).

Renealtin A (1): yellow amorphous solid; $[\alpha]^{23}_D$ +22.4° (*c* 0.40, MeOH); UV (MeOH) λ_{max} (log ϵ) 305 (3.82), 279 (3.99), and 228 (4.25) nm; IR (KBr) ν_{max} 3423, 2925, and 1629 cm^{-1}; ^{1}H and ^{13}C NMR (Table 1); HMBC (H/C) 2/1 2/3 7/6 7/1″ 7/2″ 7/6″ 2′/1 2′/1′ 2′/3′ 2′/4′ 5′/4′ 5′/1′ 6′/1 6′/1′ 6′/2′ 6′/4′ 3′-OMe/3′ 2″/1″ 5″/3″ 5″/4″ 6″/1″ 6″/4″ 3″-OMe/3″; NOESY (H/H) 2a/3 2a/2′ 2a/6′ 2b/3 2b/2′ 2b/6′ 3/4a 3/6 4a/5 5/6 7/2″ 7/6″ 5′/6′ 2′/3′-OMe 2″/3″-OMe; FABMS *m*/*z* 411 $(M + Na)^+$; HRFABMS *m*/*z* 411.1420 $(M + Na)^+$ (calcd for $C_{21}H_{24}O_7Na$, 411.1420).

Renealtin B (2): yellow amorphous solid; $[\alpha]^{23}_D$ +73.5° (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ϵ) 304 (3.88), 279 (4.04), and 228 (4.29) nm; IR (KBr) ν_{max} 3430, 2925, and 1629 cm^{-1}; ^{1}H and ^{13}C NMR (Table 1); HMBC (H/C) 2/1 2/3 4/3 4/5 7/5 7/6 7/1″ 7/2″ 7/6″ 2′/1 2′/3′ 2′/4′ 2′/6′ 5′/1′ 5′/3′ 6′/1 6′/2′ 6′/4′ 2″/1″ 5″/6″ 6″/7 6″/1″ 6″/4″; NOESY (H/H) 2a/6′ 2b/6′ 3/4a 4b/5 4b/6 5/6 6/7a 6/7b 7a/2″ 7a/6″ 7b/2″ 7b/6″ 5′/6′ 2′/3′-OMe 2″/3″-OMe; FABMS *m*/*z* 411 $(M + Na)^+$; HRFABMS *m*/*z* 411.1408 $(M + Na)^+$ (calcd for $C_{21}H_{24}O_7Na$, 411.1420).

Acetylation of 1. To a solution of renealtin A (**1**) (0.05 mg) in pyridine (30 μL) at room temperature was added Ac_2O (30 μL). The mixture was stirred for 3 h, and the solvent was removed in vacuo to yield **1a** (0.06 mg): ^{1}H NMR (CD_3OD) δ_H 3.49 (1H, m, H-2a), 3.17 (1H, m, H-2b), 4.72 (1H, m, H-3), 2.64 (1H, m, H-4a), 1.78 (1H,m, H-4b), 5.23 (1H, m, H-5), 4.01 (1H, m, H-6), 2.87 (2H, m, H-7), 7.68 (1H,m, H-2′), 7.18 (1H, d, 8.7, H-5′), 7.66 (1H,m, H-6′), 6.85 (1H, m, H-2″), 6.86 (1H, m, H-5″), 6.74 (1H, m, H-6″) 3.88 (3H, s, 3′-OMe), and 3.70 (3H, s, 3″-OMe); FABMS *m*/*z* 537 $(M + Na)^+$.

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