Limonoids from the Seeds of the Marine Mangrove *Xylocarpus granatum*

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Five new limonoids, granaxylocarpins A−E (**1**−**5**), were isolated from the seeds of the Chinese marine mangrove *Xylocarpus granatum*. Granaxylocarpins A (**1**) and B (**2**) are mexicanolide-type limonoids with a 9,10-*seco* skeleton, and granaxylocarpin C (**3**) possesses an 8α,30α-epoxy ring and a rare 1,29-oxygen bridge. The structures of these limonoids were characterized on the basis of extensive spectroscopic methods and single-crystal X-ray diffraction analysis performed on **4**. The structure of xyloccensin U (**4a**) was revised as **4b** by comparison with granaxylocarpin D (**4**). The cytotoxicity of these isolates was evaluated against the P-388 and A-549 tumor cell lines.

Limonoids are highly oxygenated nortriterpenoids with their structural features either containing or being derived from a precursor with a 4,4,8-trimethyl-17-furanylsteroid skeleton.[1a] Naturally occurring meliaceous limonoids usually have a *β*-furyl ring at C-17 of the D-ring, as well as oxygenated groups at C-3, C-7, C-16, C-17, and C-30.[1] *Xylocarpus granatum* Koenig (Meliaceae), a marine mangrove plant, is distributed mainly along the seashore along the Indian Ocean and in Southeast Asia. Previous investigations on this plant have led to the isolation of about 30 limonoids mainly belonging to the phragmalin and mexicanolide structural types.[2−5] Recently, four new 9,10-*seco* limonoids have been isolated by our group from *X. granatum* collected from Hainan Island of the People's Republic of China.[6] In continuation of our studies on the chemical diversity of this plant, five new limonoids, granaxylocarpins A−E (**1**−**5**), were isolated from the seeds of *X. granatum*. Granaxylocarpins A (**1**) and B (**2**) are mexicanolide-type limonoids with a 9,10-*seco* skeleton, and granaxylocarpin C (**3**) possesses an 8α,30α-epoxy ring and a rare 1,29-oxygen bridge. The structure of a previously reported limonoid, xyloccensin U (**4a**), was also revised by comparison with the spectroscopic data of **4**. Herein, details of the isolation, structure elucidation, and cytotoxicity of compounds **1**−**5** are presented.

Granaxylocarpin A (**1**), a colorless oil, was assigned a molecular formula of $C_{34}H_{44}O_{12}$, as established by the HREIMS ($[M]^+$ at *m*/*z* 644.2844, calcd 644.2833) and NMR data. The IR spectrum displayed absorption bands at 3435 and 1736 cm^{-1}, indicating the presence of hydroxy and ester functionalities. The NMR data (Tables 1 and 2) and HSQC spectrum showed signals for a methoxy [δ_H 3.67 (3H, s), δ_C 51.9], two ketone carbonyls (δ_C 208.1 and 209.1), four methyls [δ_H 0.94 (3H, s), 0.95 (3H, d, J = 6.2 Hz), 0.89 (3H, s), and 1.23 (3H, s); δ_C 18.7, 11.6, 24.7, and 20.6], and an acetyl [δ_H 2.04 (3H, s), δ_C 21.4 and 171.0], together with a *β*-furyl ring [δ_H 7.51 (s), 6.42 (d, J = 1.1 Hz), and 7.41 (d, J = 1.1 Hz); δ_C 119.6, 141.4, 109.8, and 143.1]. The aforementioned data of **1** resembled those reported for xylogranatin B (**1a**)[6] except for the absence of a tigloyl group. Instead, the typical resonances of a 2-methylbutanoate group [δ_H 2.28 (m), 1.36 (qd, J = 7.3,7.3 Hz), 1.68 (m), 0.89 (3H, t, J = 7.3 Hz), 1.07 (3H, d, J = 7.2 Hz); δ_C 175.3, 40.6, 26.0, 11.4, and 15.6] were observed in both the ^1H and ^{13}C NMR spectra (Tables 1 and 2). The HMBC correlations from H-3, H-2′, H-3′, and H-5′ to C-1′ confirmed that the 2-methylbutanoyloxy group is attached to C-3 (Figure S2, Supporting Information). The significant ROESY correlations of OH-8/H-2, H-2/H-10, H-2/Me-29, H-10/Me-29, H-12*β*/H-30, H-12*β*/H-17, and Me-18/H-22 (Figure 1), as well as the ^1H and ^{13}C NMR data similar to those of xylogranatin B (**1a**), suggested that **1** shares the same relative configuration as **1a** in the limonoid core. The

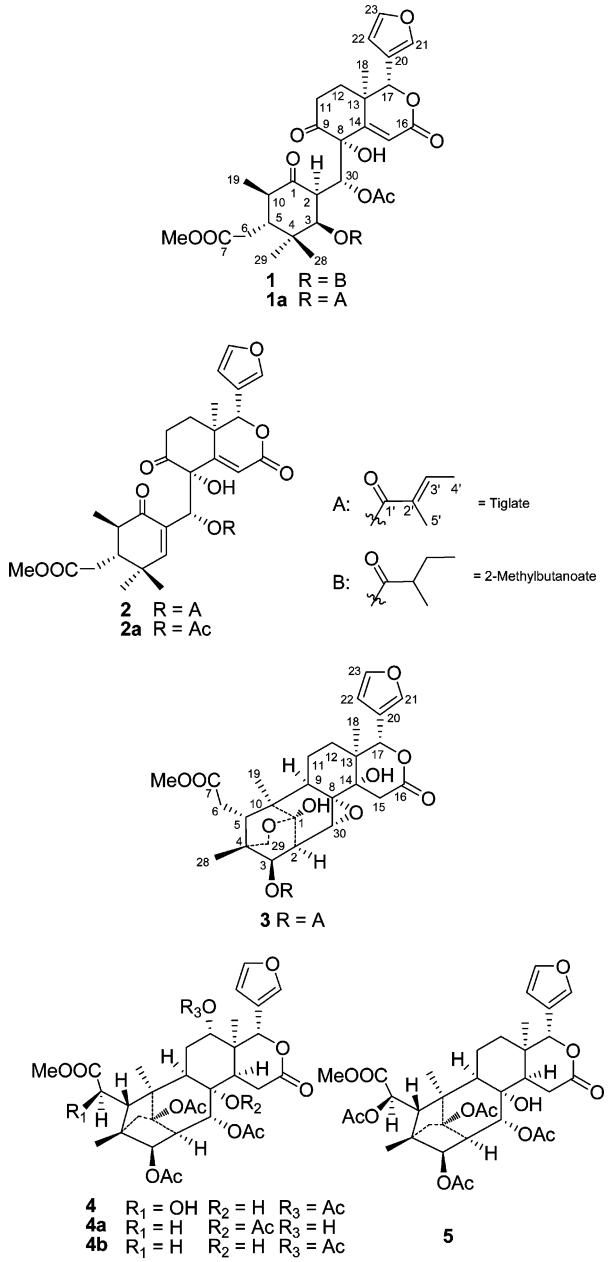

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Table 1. ^{1}H NMR Spectroscopic Data for Granaxylocarpins A−E (**1**−**5**)[a]

position	1	2	3	4	5
2	3.63 (dd, 9.1, 2.1)		3.03 (dd, 10.2, 2.7)	2.98 (dd, 11.4, 2.7)	2.99 (dd, 11.4, 2.6)
3	5.33 (d, 2.1)	7.0 (s)	5.11 (d, 10.2)	5.20 (d, 11.4)	5.27 (d, 11.4)
5	2.20 (m)	2.26 (m)	2.85 (brd, 10.7)	2.88 (s)	3.23 (s)
6α	2.24 (m)	2.25 (m)	2.40 (dd, 16.8, 10.7)	4.24 (s)	5.38 (s)
6*β*	2.44 (m)	2.45 (m)	2.30 (m)		
9			2.25 (dd, 11.8, 5.5)	2.19 (dd, 13.8, 8.8)	1.88 (m)
10	2.38 (m)	2.28 (m)			
11α	2.63 (m)	2.55 (m)	1.77 (m)	2.01 (m)	1.75 (m)
11*β*	3.41 (ddd, 13.6, 13.7, 13.6)	3.08 (dd, 19.8, 7.0)	1.77 (m)	1.84 (ddd, 14.6, 4.0, 4.0)	1.86 (m)
12α	1.57 (dd, 9.4, 3.6)	1.63 (dd, 13.7, 7.3)	1.75 (m)	5.01 (brs)	1.41 (m)
12*β*	2.56 (m)	2.66 (ddd, 13.2, 13.2, 7.0)	1.67 (m)		1.88 (m)
14				2.40 (d, 8.6)	2.02 (brd, 8.9)
15	6.11 (s)	6.08 (s)	α 2.98 (brd, 16.8) *β* 2.60 (d, 16.8)	α 2.64 (dd, 19.4, 8.6) *β* 3.33 (d, 19.4)	α 2.73 (dd, 19.4, 8.9) *β* 3.35 (brd, 19.4)
17	5.25 (s)	5.36 (s)	5.27 (s)	5.72 (s)	5.71 (s)
18	0.94 (s)	0.96 (s)	0.93 (s)	0.99 (s)	0.98 (s)
19	0.95 (d, 6.2)	1.03 (d, 5.5)	1.03 (s)	1.37 (s)	1.16 (s)
21	7.51 (s)	7.55 (s)	7.63 (s)	7.41 (brs)	7.42 (s)
22	6.42 (d, 1.1)	6.46 (d, 1.5)	6.46 (brs)	6.32 (d, 1.0)	6.35 (s)
23	7.41 (d, 1.1)	7.45 (d, 1.5)	7.39 (t, 1.6)	7.43 (t, 1.0)	7.43 (s)
28	0.89 (s)	1.19 (s)	0.62 (s)	0.92 (s)	1.00 (s)
29	1.23 (s)	1.13 (s)	α 3.87 (d, 10.0) *β* 3.49 (brd, 10.0)	2.38 (2H, brs)	α 2.45 (brd, 10.6) *β* 2.25 (brd, 10.6)
30	5.79 (d, 9.1)	6.60 (s)	3.34 (d, 2.8)	5.41 (d, 2.7)	5.41 (d, 2.6)
MeO-7	3.67 (s)	3.69 (s)	3.69 (s)	3.82 (s)	3.75 (s)
OAc-30	2.04 (s)			2.02 (s)	2.04 (s)
2′	2.28 (m)			OH-6 2.97 (s)	OAc-1 2.13 (s)
3′	a 1.36 (qd, 7.3, 7.3) b 1.68 (m)	6.95 (qq, 6.6, 0.7)	7.0 (qq, 7.0, 1.5)	OH-8 4.42 (s) OAc-1 2.07 (s)	OAc-3 2.12 (s) OAc-6 2.18 (s)
4′	0.89 (t, 7.3)	1.83 (d, 6.6)	1.75 (dd, 7.0, 1.5)	OAc-3 2.07 (s)	OH-8 4.27 (s)
5′	1.07 (d, 7.2) OH-8 4.11 (s)	1.84 (s) OH-8 3.88 (s)	1.86 (3H, brs) OH-1 3.95 (s) OH-14 2.70 (s)	OAc-12 2.13 (s)	

[a] Recorded at 400 MHz in $CDCl_3$, δ_H in ppm, J in Hz.

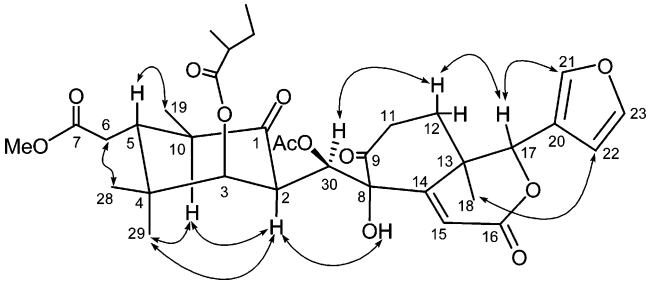

Figure 1. Key ROESY (↔) correlations of **1**.

similar CD curves of the two compounds further confirmed this conclusion (Figure S1, Supporting Information). Therefore, the structure of granaxylocarpin A (**1**) was assigned as 2′,3′-dihydroxylograngatin B.

Granaxylocarpin B (**2**), a colorless oil, was assigned a molecular formula of $C_{32}H_{38}O_{10}$ from the molecular ion peak at *m*/*z* 582.2473 (calcd 582.2465) in the HREIMS, which was in agreement with the 1D NMR data (Tables 1 and 2). The UV, IR, and NMR data of **2** showed a close similarity to those of xylogranatin C (**2a**),[6] with the only difference being due to the presence of a C-30 tigloyloxyl group in **2** [δ_H 6.95, (qq, J = 6.6, 0.7 Hz), 1.83 (3H, d, J = 6.6 Hz), and 1.84 (3H, s); δ_C 166.8, 127.7, 139.9, 14.7, and 12.1], instead of a C-30 acetoxyl substituent in xylogranatin C. The attachment of the tigloyloxyl at C-30 in **2** was confirmed by the HMBC correlation of H-30/C-1′ (Figure S3, Supporting Information). The relative configuration of **2** was assigned to be the same as that of xylogranatin C by comparing their NMR data and CD spectrum (Figure S1, Supporting Information). Therefore, the structure of granaxylocarpin B (**2**) was assigned as a 30-*O*-tiglate analogue of xylogranatin C.

Granaxylocarpin C (**3**), a white powder, gave a molecular formula of $C_{32}H_{40}O_{11}$, as established on the basis of HRESIMS ([M + Na]$^+$ at *m*/*z* 623.2427), accounting for 13 degrees of unsaturation. The IR spectrum revealed the presence of hydroxyl (3458 cm^{-1}) and ester (1732 cm^{-1}) groups. The ^{13}C NMR data (Table 2) showed that six degrees of unsaturation came from three carbon−carbon double bonds and three carbonyls. The remaining degrees of unsaturation thus required the presence of seven rings in **3**. The characteristics of a *β*-furyl ring [δ_H 7.63 (s), 6.46 (brs), and 7.39 (t, J = 1.6 Hz); δ_C 120.2, 141.3, 110.3, and 142.8], an 8,30-epoxy ring [δ_H 3.34 (d, J = 2.8 Hz); δ_C 60.6 and 63.6], a tigloyl [δ_H 7.0 (qq, J = 7.0, 1.5 Hz), 1.75 (3H, dd, J = 7.0, 1.5 Hz), 1.86 (3H, brs); δ_C 167.5, 127.2, 140.5, 14.6, and 12.1], a methoxy [δ_H 3.69 (3H, s); δ_C 52.1], and a 1,29-oxygen bridge [δ_H 3.87 (d, J = 10.0 Hz), 3.49 (brd, J = 10.0 Hz); δ_C 96.7 and 67.2] were also determined from its ^{1}H and ^{13}C NMR spectra (Tables 1 and 2). The aforementioned data indicated that the structure of **3** is closely related to that of xyloccensin L, a limonoid isolated from the same plant.[2] The only difference was the presence of a C-14 hydroxyl in **3**, which was revealed by the HMBC correlations of OH-14/C-14 (δ_C 72.0), C-8, C-13, and C-15 (Figure 2a). The relative configuration of **3** was assigned as being identical to that of xyloccensin L by a ROESY experiment (Figure 2b), in which the hydroxyl at C-14 showed an α-orientation as judged by the correlation between OH-14 and Me-18. Compound **3** is only the second limonoid with a 1,29-oxygen bridge to have been reported and was established as 14α-hydroxyxyloccensin L.

Granaxylocarpin D (**4**), colorless prisms, exhibited a molecular formula of $C_{35}H_{44}O_{15}$ as determined by HREIMS at *m*/*z* 704.2674 [M]$^+$ (calcd 704.2680). The ^{1}H and ^{13}C NMR data (Tables 1 and 2) of **4** were closely comparable to analogous data of xyloccensin U (**4a**), a limonoid isolated previously from *X. granatum*.[3] Spectroscopic analysis revealed that the only structural difference between these two compounds is the C-6-OH group in **4**. This OH-6 group was assigned as *β*-oriented from the correlation between H-6 and H-11α in the ROESY spectrum. This was supported by the

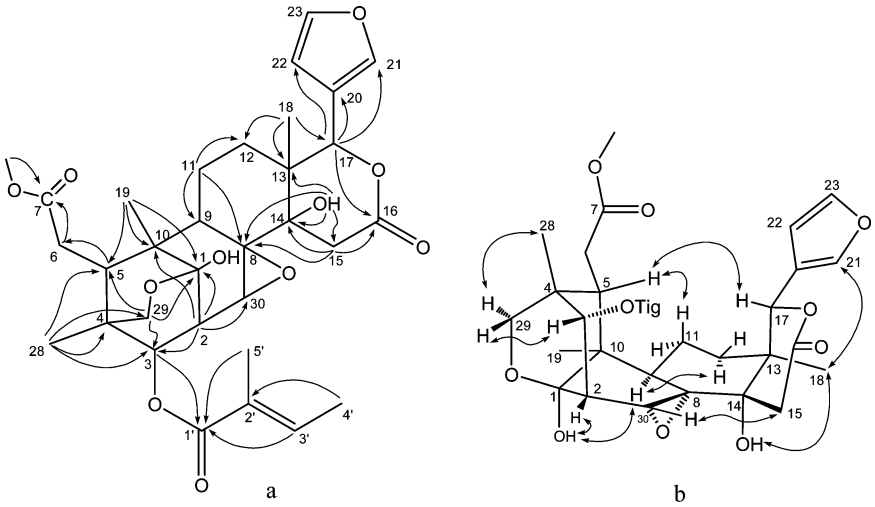

Figure 2. (a) Selected HMBC (H→C) correlations of **3**. (b) Key ROESY (H↔H) correlations of **3**.

Table 2. ^{13}C NMR Spectroscopic Data for Granaxylocarpins A−E (**1**−**5**)[a]

position	1	2	3	4	5
1	208.1	198.7	96.7	87.9	88.0
2	48.2	128.8	41.6	46.3	46.2
3	80.3	161.8	75.1	76.3	76.0
4	39.3	36.8	36.8	45.1	45.2
5	46.3	45.2	35.3	43.1	42.4
6	34.2	34.6	31.9	71.1	71.9
7	173.3	173.4	173.7	175.1	170.2
8	80.6	80.2	63.6	73.3	73.6
9	209.1	208.8	44.9	49.1	55.5
10	47.0	42.8	41.7	47.1	47.9
11	33.6	33.0	17.6	28.6	23.3
12	25.1	25.5	31.7	71.5	34.4
13	38.5	38.3	39.9	39.2	35.6
14	165.5	163.5	72.0	46.2	50.6
15	119.0	118.4	39.2	28.0	28.5
16	163.1	163.3	168.9	169.6	170.3
17	79.8	80.0	78.3	77.3	77.7
18	18.7	18.5	19.4	18.7	23.7
19	11.6	11.5	15.0	23.4	22.8
20	119.6	119.6	120.2	120.8	121.7
21	141.4	141.4	141.3	140.3	140.1
22	109.8	109.8	110.3	109.0	109.4
23	143.1	143.3	142.8	143.7	143.2
28	24.7	27.8	15.0	15.6	15.7
29	20.6	20.5	67.2	40.7	40.9
30	69.0	67.5	60.6	69.7	70.2
MeO-7	51.9	52.0	52.1	53.1	52.9
OAc-30	21.4			170.6	170.6
	171.0			21.3	21.4
1′	175.3	166.8	167.5	OAc-1 169.9	OAc-1 168.5
2′	40.6	127.7	127.2	20.9	22.1
3′	26.0	139.9	140.5	OAc-3 169.3	OAc-3 169.5
4′	11.4	14.7	14.6	21.1	21.2
5′	15.6	12.1	12.1	OAc-8 168.4	OAc-6 169.7
				22.0	21.0

[a] Recorded at 100 MHz in $CDCl_3$.

singlet resonances of H-5 and H-6, which indicated that the dihedral angle between them was approximately 90°.[3,4]

In the HMBC spectrum, a crucial correlation from an exchangeable proton signal at δ_H 4.42 to C-8 (δ_C 73.3) and C-14 (Figure S4, Supporting Information) revealed that one hydroxyl group is attached to C-8 in **4**. Consequently, an acetoxy group was located at C-12, although no HMBC correlation from H-12 to the acetoxy carbonyl was observed. A downfield-shifted proton signal at δ_H 5.01 (brs), assigned for H-12, also supported the presence of a C-12 acetoxy group. However, this assignment is contrary to that of xyloccensin U (**4a**), in which an *O*Ac-8 and an OH-12 were assigned only on the basis of the lack of a HMBC correlation from

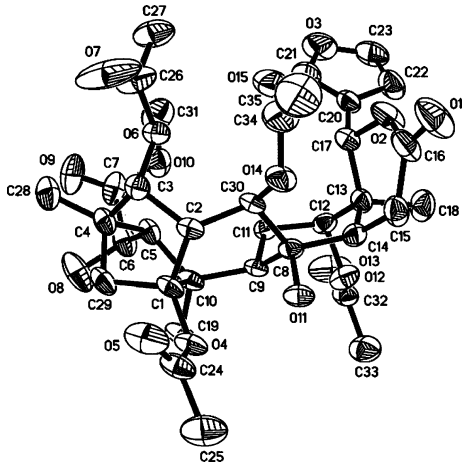

Figure 3. Single-crystal X-ray structure of **4**.

H-12 to the carbonyl of Ac.[3] To confirm the structure of **4**, a single-crystal X-ray diffraction analysis of **4** was performed (Figure 3),[7] which corroborated the structure proposed and verified the relative configuration of **4**. As the ^{1}H and ^{13}C NMR data of the central limonoid core of compound **4** and xyloccensin U[3] were almost identical, the structure of **4a** proposed previously for xyloccensin U was therefore revised as **4b** by analogous comparison. Therefore, the structure of granaxylocarpin D (**4**) was assigned as 6β-hydroxyxyloccensin U.

Granaxylocarpin E (**5**), a white powder, was assigned a molecular formula of $C_{35}H_{44}O_{14}$ as established on the basis of the HRESIMS at *m*/*z* 711.2684 $[M + Na]^+$ (calcd for $C_{35}H_{44}O_{14}Na$, 711.2629) and NMR data. The ^{1}H and ^{13}C NMR data (Tables 1 and 2) of **5** were closely comparable to those of **4**. On comparison of the NMR data of **5** with those of **4**, a downfield-shifted proton resonance at δ_H 5.38 assignable to H-6 suggested the presence of an acetoxyl at C-6, which was confirmed by the HMBC correlations of H-6 with the acetyl carbonyl at δ_C 169.7 and C-7 at δ_C 170.2. One methylene carbon resonance at δ_C 34.4 correlated with H-17 and H-18 in the HMBC spectrum was attributed to C-12 (Figure S5, Supporting Information). The planar structure of **5** was therefore furnished, and the relative configuration was established as being the same as that of **4** from the ROESY spectrum. Therefore, the structure of granaxylocarpin E (**5**) was established as 6-acetyl-12-deacetoxy-granaxylocarpin D.

The cytotoxic activities of granaxylocarpins A−E (**1**−**5**) against the P-388 murine leukemia and A-549 human lung carcinoma cell lines were evaluated. Compounds **1** and **2** showed weak cytotoxic activities against the P-388 cell line (IC_{50} values of 9.3 and 4.9

μM, respectively), but were inactive against the A-549 cell line (IC_{50} values >10 μM). Compounds **3**−**5** were inactive against both the P-388 and A-549 cell lines.

Experimental Section

General Experimental Procedures. Melting points were measured on an SGW X-4 melting point instrument and are uncorrected. Optical rotations were determined on a Perkin-Elmer 341 polarimeter, and CD spectra were obtained on a JASCO 810 spectrometer. UV spectra were recorded on a Shimadzu UV-2550 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 577 spectrometer. NMR spectra were measured on a Bruker AM-400 spectrometer. EIMS and HREIMS (70 eV) were done on a Finnigan MAT 95 mass spectrometer, and ESIMS was carried out on a Finnigan LC Q^{DECA} instrument. Semipreparative HPLC was performed on a Waters 515 pump with a Waters 2487 detector (254 nm) and a YMC-Pack ODS-A column (250 × 10 mm, S-5 μm, 12 nm). All solvents used were of analytical grade (Shanghai Chemical Reagents Company, Ltd.). Silica gel (200−300 mesh, Qingdao Haiyang Chemical Co. Ltd.), C_{18} reversed-phase silica gel (150−200 mesh, Merck), MCI gel (CHP20P, 75−150 μm, Mitsubishi Chemical Industries Ltd.), and Sephadex LH-20 gel (Amersham Biosciences) were also used for column chromatography.

Plant Material. The seeds of *X. granatum* were collected from Cheng Mai County in Hainan Island, People's Republic of China, in August 2004, and the plant was identified by Prof. S.-M. Huang, Department of Biology, Hainan University, People's Republic of China. A voucher specimen has been deposited in Shanghai Institute of Materia Medica, Chinese Academy of Sciences (accession number Xg-2004-1Y).

Extraction and Isolation. The air-dried powder of the seeds of *X. granatum* (15.0 kg) was extracted with 95% EtOH at room temperature three times to give 412 g of crude extract, which was suspended in water (1.5 L) and then partitioned with ethyl acetate to give an ethyl acetate-soluble fraction (172 g). The ethyl acetate-soluble fraction was subjected to silica gel column chromatography eluted successively with a petroleum ether/acetone gradient (100:0 to 0:100) to obtain 15 fractions. Fractions 13 and 14 were combined and were subjected to column chromatography over silica gel, MCI gel, and Sephadex LH-20 to obtain two minor components, each of which was purified by semipreparative HPLC using CH_3CN/H_2O 70:30 (3 mL/min) to give compounds **1** (8 mg) and **2** (10 mg). Fraction 15 (16 g) was separated by column chromatography on silica gel and MCI gel to obtain three major components, which were further purified by semipreparative HPLC using CH_3CN/H_2O 60:40 (3 mL/min) to afford compounds **3** (32 mg), **4** (42 mg), and **5** (15 mg).

Granaxylocarpin A (1): colorless oil; $[\alpha]^{20}_D$ +47.0 (*c* 0.09, CH_3CN); UV (CH_3CN), no maxima above 210 nm; CD (CH_3CN) λ_{max} ($\Delta\epsilon$) 200 (−3.81), 221 (+3.42), 240 (−5.54), 277 (±4.60) nm; IR (KBr) ν_{max} 3435, 2974, 1736, 1464, 1375, 1229, 1140, 1051 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; EIMS *m*/*z* 644 $[M]^+$ (5), 482 (12), 383 (18), 262 (60), 239 (58), 165 (100), 137 (36); HREIMS *m*/*z* 644.2844 (calcd for $C_{34}H_{44}O_{12}$, 644.2833).

Granaxylocarpin B (2): colorless oil; $[\alpha]^{20}_D$ −34.0 (*c* 0.16, CH_3CN); UV (CH_3CN) λ_{max} (log ϵ) 222 (4.33) nm; CD (CH_3CN) λ_{max} ($\Delta\epsilon$) 212 (+14.6), 241 (−22.39), 275 (+4.23 nm; IR (KBr) ν_{max} 3396, 2962, 1724, 1674, 1653, 1439, 1269, 1151, 1020 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; EIMS *m*/*z* 582 $[M]^+$ (3), 482 (38), 464 (36), 262 (10), 165 (15), 83 (100); HREIMS *m*/*z* 582.2473 (calcd for $C_{32}H_{38}O_{10}$, 582.2465).

Granaxylocarpin C (3): white powder; $[\alpha]^{20}_D$ −47 (*c* 0.170, CH_3OH); UV (CH_3CN) λ_{max} (log ϵ) 214 (3.75) nm; IR (KBr) ν_{max} 3458, 2953, 1732, 1705, 1649, 1462, 1267 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; positive ESIMS *m*/*z* 623.2 $[M + Na]^+$ (100), 1223.3 $[2M + Na]^+$ (4); HRESIMS *m*/*z* 623.2427 $[M + Na]^+$ (calcd for $C_{32}H_{40}O_{11}Na$, 623.2468).

Granaxylocarpin D (4): colorless prisms; mp 221−222 °C; $[\alpha]^{20}_D$ −30 (*c* 0.185, CH_3OH); UV (CH_3CN) λ_{max} (log ϵ) 211 (3.81) nm; IR (KBr) ν_{max} 3512, 2955, 1747, 1375, 1236, 1061, 972 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; EIMS *m*/*z* 704 $[M]^+$ (8), 662 (62), 644 (98), 584 (100), 524 (63), 482 (48), 405 (46), 279 (37); HREIMS *m*/*z* 704.2674 (calcd for $C_{35}H_{44}O_{15}$, 704.2680).

Granaxylocarpin E (5): white powder; $[\alpha]^{20}_D$ −31 (*c* 0.110, CH_3OH); UV (CH_3CN) λ_{max} (log ϵ) 212 (3.62) nm; IR (KBr) ν_{max} 3520, 2937, 1736, 1373, 1225, 1063 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; positive ESIMS *m*/*z* 711.4 $[M + Na]^+$ (100); HRESIMS *m*/*z* 711.2684 $[M + Na]^+$ (calcd for $C_{35}H_{44}O_{14}Na$, 711.2629).

X-ray Crystallographic Study of Granaxylocarpin D (4). Described in the Supporting Information.

Cytotoxicity Assays. Cytotoxicity against the P-388 and A-549 cell lines was evaluated by using the MTT[8] and SRB[9] methods, respectively, according to the protocols described in previous literature and with pseudolaric acid B[10] as a positive control (IC_{50} = 0.74 μM against P-388 and 0.30 μM against A-549).

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Supporting Information Available: CD curves of **1**, **1a**, **2**, and **2a**; selected HMBC correlations of **1**, **2**, **4**, and **5** (figures); MS, IR, and 1D and 2D NMR spectra of **1**−**5**; CIF data for crystal study of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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