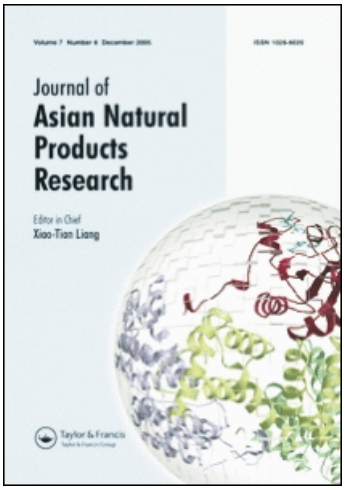

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MANUIFOLIN Q, AN UNUSUAL 4-ARYL-SUBSTITUTED ISOFLAVAN FROM *MAACKIA TENUIFOLIA*

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Manuifolin Q (**1**), an unusual 4-aryl-substituted isoflavan, was isolated from the roots of *Maackia tenuifolia*. Its absolute configuration was determined as (3*R*,4*R*)-3,4-*trans*-7,2′-dihydroxy-4′-methoxy-4-[(2,4-dihydroxy-5-(1,1-dimethyl-2-propenyl)]-phenyl-isoflavan, on the basis of spectroscopic analysis.

Keywords: Manuifolin Q; Isoflavan; *Maackia tenuifolia*; Leguminosae

INTRODUCTION

Maackia tenuifolia (Hemsl.) Hand-Mazz. (Leguminosae) is known as "*GuangYeMaAnShu*" and its roots have been used as an anti-tumor drug and fungicide in Chinese folk medicine [1]. Previous studies on this plant resulted in the isolation of some new isoflavonoids [2–5]. As part of a continuing investigation of the chemical constituents of *M. tenuifolia*, we examined the CH_2Cl_2-soluble fraction of the 95% ethanol extract of the roots, and obtained manuifolin Q (**1**), a new isoflavan that has an unusual 4-aryl-substituted isoflavan skeleton. Although 4-aryl-substituted flavans or their oligomers are common in natural plants, to our knowledge, 4-aryl-substituted isoflavans have not been reported from natural sources, except for (4–5′) bi-isoflavans [6,7]. In this paper, we report the isolation and structure elucidation of manuifolin Q.

RESULTS AND DISCUSSION

Manuifolin Q (**1**) was obtained as a colorless oil. Its molecular formula $C_{27}H_{28}O_6$ was deduced by HR-EIMS. The ^{1}H NMR spectrum displayed signals due to two 1,2,4-trisubstituted benzene rings [δ 7.17 (1H, d, $J = 8.5$ Hz), 6.43 (1H, d, $J = 2.5$ Hz) and 6.29 (1H, dd, $J = 8.5$, 2.5 Hz); and δ 6.62 (1H, d, $J = 8.2$ Hz), 6.33 (1H, d, $J = 2.5$ Hz) and 6.31

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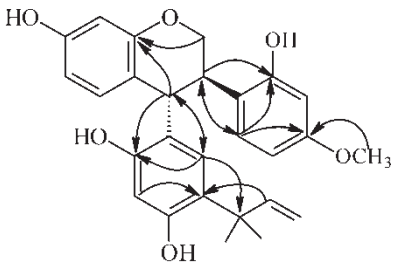

FIGURE 1 Key HMBC correlations of **1** (H → C).

(1H, dd, $J = 8.2, 2.5$ Hz)], a 1,2,4,5-tetrasubstituted benzene ring (δ 6.72 and 6.41, each s), a 1,1-dimethyl-2-propenyl group [δ 1.30 (6H, s), 6.16 (1H, dd, $J = 17.6, 10.6$ Hz), 4.88 (1H, d, $J = 17.6$ Hz) and 4.84 (1H, d, $J = 10.6$ Hz)], and a methoxyl group [δ 3.67 (3H, s)]. Moreover, the remaining four ^{1}H signals [δ 4.24 (1H, dd, $J = 10.8, 3.8$ Hz), 4.18 (1H, dd, $J = 10.8, 6.0$ Hz), 3.65 (1H, m) and 4.56 (1H, d, $J = 7.0$ Hz)], which constitute an AA'MX system rather than an AA'MXX' one, indicated a 4-substituted heterocyclic isoflavan.

In the ^{13}C NMR spectrum, apart from two olefinic carbons [δ 148.8 (d) and 109.6 (t)] due to the 1,1-dimethyl-2-propenyl group, 18 carbons in the aromatic region were assigned to three benzene rings, of which six should be connected to an O-atom as their chemical shifts are higher than 150 ppm. Three aliphatic signals at δ 67.9 (t), 38.9 (d), and 37.4 (d) were attributed to the heterocyclic carbons.

The above discussions show that **1** possesses a 4-aryl-substituted isoflavan framework with four hydroxyls, one methoxyl, and a 1,1-dimethyl-2-propenyl as substituent groups linked to three benzene rings. The positions of those groups were indicated by the HMBC experiments (Fig. 1). Both C-7″ and C-2″ were correlated with H-6″ while C-5″ was correlated with both H-3″ and H-8″, which showed that the 1,1-dimethyl-2-propenyl group should be located at C-5″ of D ring. The methoxyl positioned at C-4′ of the B ring was elucidated by HMBC correlations between C-4′ and H (-OMe), and H-6′ (Fig. 1). All other NMR data were assigned unambiguously on the basis of the HMBC and HMQC spectra.

In the HR-EIMS the characteristic fragment ions *m/z* 299.1269 (**A1**, 100) and 150.0687 (**B**, 8) were ascribed to an RDA cleavage, which further supported the above assignments. The possible fragmentation pattern according to HR-EIMS data and the manner of cleavage of [4,5′]-bi-isoflavans [6] is shown in Fig. 2.

The absolute configuration of **1** was determined as (3*R*,4*R*)-3,4-*trans* on the basis of CD curve analysis. Its CD spectrum displayed a negative Cotton effect at 240 nm and a positive one in the range 260–300 nm, which is in agreement with those of compound **2**, an analogue whose stereochemistry as (3*R*,4*R*)-3,4-*trans* has been unambiguously elucidated through direct synthesis from known chiral reagents [6]. Therefore, **1** was formulated as (3*R*,4*R*)-3,4-*trans*-7,2′-dihydroxy-4′-methoxy-4-[(2,4-dihydroxy-5-(1,1-dimethyl-2-propenyl)]-phenyl-isoflavan (Fig. 3).

EXPERIMENTAL

General Experimental Procedures

The UV spectrum was taken on a Shimadzu UV-250 instrument and the CD spectrum on a JASCO J-715 spectropolarimeter in MeOH. Optical rotation was measured using a Perkin-Elmer 241 MC polarimeter in MeOH. The IR spectrum was recorded on a Nicolet Magna 750 FTIR (KBr) spectrophotometer. EIMS and HR-EIMS data were provided by a MAT-95

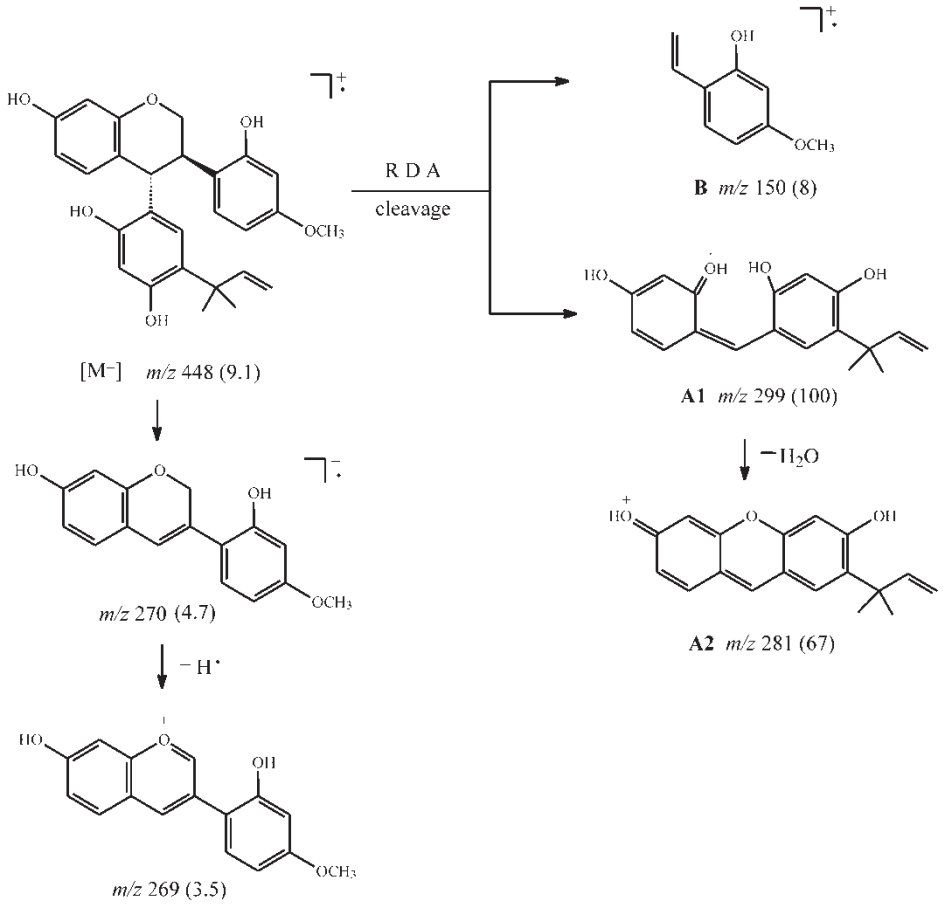

FIGURE 2 Possible EIMS fragmentation pattern of **1**.

spectrometer. NMR spectra were recorded on a Bruker AM-400 instrument with DMCO-d_6 as solvent, using the residual Me_2CO peak (δ_H: 2.07; δ_C: 29.5) as reference for the chemical shifts (δ), J in Hz). Silica gel (200–300, 400 mesh) and precoated plates of silica gel ($HSGF_{254}$) (Qingdao Haiyang Chemical Group Co., Qingdao, China) were used for column chromatography (CC) and for TLC, respectively.

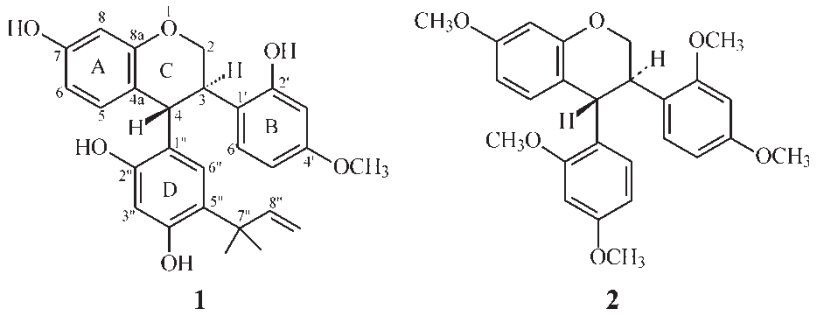

FIGURE 3 Structures **1** and **2**.

Plant Material

Roots of *Maackia tenuifolia* (Hemsl.) Hand-Mazz. (Leguminosae) were collected in Linan County, Zhejiang Province, China, and identified by Professor Shan-Hao Jiang. A voucher specimen (LMT 8503) has been deposited in the Herbarium of the Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

Extraction and Isolation

Powdered roots (37 kg) of *M. tenuifolia* were extracted with 95% EtOH and, after removing the ethanol, the solution was successively extracted with light petroleum, benzene, and CH_2Cl_2. The CH_2Cl_2 extract was concentrated under reduced pressure to give a brown gum (1 kg), 400 g of which was subjected to silica gel CC eluted with gradient light petroleum-EtOAc (8:1, 4:1, 2:1, 1:1, 0:1) and 95% EtOH to yield 200 fractions. The frs. 76–84 were chromatographed with $CHCl_3$–MeOH (1:1) over a Sephadex LH-20 column, and then further purified by silica gel CC with light petroleum–Me_2CO (2:1) and $CHCl_3$–MeOH (20:1) to give **1** (54 mg).

Manuifolin Q (**1**), $C_{27}H_{28}O_6$, a colorless oil; $[\alpha]_D^{23.5}$ −45.63 (*c* 0.26, MeOH), CD (*c* 0.01, MeOH) (°): $[\theta]_{300}$ +581, $[\theta]_{282}$ +1748, $[\theta]_{251}$ 0, $[\theta]_{238}$ −5245, $[\theta]_{221}$ −3715, $[\theta]_{213}$ 0, $[\theta]_{200}$ +14860, UV λ_{max} (MeOH) (nm) (log ϵ): 219 (4.56), 286 (4.05). IR ν_{max} (KBr) (cm^{-1}): 3415, 2967, 1622, 1596, 1506, 1471, 1444, 1292, 1160, 1116, 1032, 934, 842. EIMS (*m*/*z*): 448 (9.1, M^+), 299 (100), 281 (67), 270 (4.7), 269 (3.5), 150 (8). HR-EIMS: 448.1864 (M^+), calcd for $C_{27}H_{28}O_6$, 448.1885. ^{1}H NMR (400 MHz, DMCO-d_6, δ, ppm): 1.30 (6H, s, Me_2-C7″), 3.65 (1H, m, H-3), 3.67 (3H, s, —OCH_3), 4.18 (1H, dd, J = 10.8, 6.0 Hz, Ha-2), 4.24 (1H, dd, J = 10.8, 3.8 Hz, Hb-2), 4.56 (1H, d, J = 7.0 Hz, H-4), 4.84 (1H, d, J = 10.6 Hz, Ha-9″), 4.88 (1H, d, J = 17.6 Hz, Hb-9″), 6.16 (1H, dd, J = 17.6, 10.6 Hz, H-8″), 6.29 (1H, dd, J = 8.5, 2.5 Hz, H-5′), 6.31 (1H, dd, J = 8.2, 2.5 Hz, H-6), 6.33 (1H, d, J = 2.5 Hz, H-8), 6.41 (1H, s, H-3″), 6.43 (1H, d, J = 2.5 Hz, H-3′), 6.62 (1H, d, J = 8.2 Hz, H-5), 6.72 (1H, s, H-6″), 7.17 (1H, d, J = 8.5 Hz, H-6′). ^{13}C NMR (100 Hz, DMCO-d_6, δ): 27.2 ($CH_3 \times 2$, Me_2-C7″), 37.4 (CH-3), 38.9 (CH-4), 40.1 (C-7″), 54.9 (OCH_3), 67.9 (CH_2-2), 101.7 (CH-3′), 102.7 (CH-8), 104.0 (C-3″), 105.0 (CH-5′), 108.6 (CH-6), 109.6 (CH_2-9″), 116.5 (C-4a), 120.4 (C-1′), 121.8 (C-1″), 125.1 (C-5″), 128.8 (CH-6″), 128.9 (CH-6′), 131.4 (CH-5), 148.8 (CH-8″), 154.1 (C-2″), 154.8 (C-4″), 155.9 (C-8a), 156.2 (C-2′), 157.1 (C-7), 159.7 (C-4′).

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