Alkaloids, Diarylheptanoid and Naphthalene Carboxylic Acid Ester from Rhoiptelea chiliantha

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Two pyrrolidine alkaloids (1, 2) were isolated from the fruits of Rhoiptelea chiliantha DIEL et HAN-D.-MAZZ. (Rhoipteleaceae). A diphenyl ether-type diarylheptanoid (3), and a naphthalene carboxylic acid methyl ester (4) which is biogenetically-related to juglone were isolated from the branches of the same plant. Their chemical structures were elucidated on the basis of spectroscopic analysis and chemical evidence.

Key words Rhoiptelea chiliantha; Rhoipteleaceae; pyrrolidine alkaloid; diarylheptanoid; chemotaxonomy

In a series of papers on our chemical and chemotaxonomical studies of Rhoiptelea chiliantha DIEL et HAN-D.-MAZZ., the only species of the family Rhoipteleaceae, we have reported the structural elucidation of triterpenes,1) triterpene esters2) from the barks, diarylheptanoids3) ellagitannins,4) euphane-type triterpene bidesmosides and tridesmosides,5) and dammarane-type triterpene glycosides6) from the fruits and leaves. In a continuation of this investigation, we chemically studied the branches whose constituents have not yet been examined, and also further separated the composition of the fruits. Herein, we describe the structural elucidation of two pyrrolidine alkaloids (1 and 2) from the fruits, a diphenyl ether-type diarylheptanoid (3) and a naphthalene carboxylic acid methyl ester (4) which is biogenetically-related to juglone from the branches.

Results and Discussion

The MeOH extracts of the air-dried fruits and branches of Rhoiptelea chiliantha were separately partitioned between H2O and Et2O, the remaining H2O layers were further extracted with EtOAc. The H2O layer of the fruits was subjected to column chromatography over MCI-gel CHP 20P, Bondapak ODS and silica gel to afford compounds 1 and 2. The Et2O layer of the branch was chromatographed over silica gel and MCI-gel CHP 20P to yield compound 3. The H2O layer of the branches was chromatographed over Sephadex LH-20 and silica gel to afford compound 4.

Compound 1 was isolated from the fruits as colorless needles, mp 178—180°C. It showed a pink spot on TLC by heating. Its molecular formula C13H17NO3 was deduced from the data of EI-MS spectrum (m/z 235 in EI-MS and the molecular ion peak at m/z 205 [M]+) and elemental analysis. The 1H- and 13C-NMR data of 1 were very similar to those of dihydroshihunine, an N-methyl group and a benzene ring. However, the presence of a 1,2-disubstituted benzene ring in 2 instead of a trisubstituted one in 1, and the absence of methoxyl group in 2 indicated that there is no methoxyl group in C-6 of the benzene ring. By comparing the NMR data of 2 with those of dihydroshihunine isolated from Banisteriopsis cappi (Malpighiaceae),7) 2 was determined to possess a plain structure the same as dihydroshihunine. But the sign of the optical rotation of 2 (−257.4°) is opposite to that (+234.7°) of 2S-dihydroshihunine, suggesting 2 has a 2R configuration. Additionally, the appearance of a negative Cotton effect at 244 nm in the CD spectrum of 2 also confirmed this conclusion.

Compound 3 was isolated from the branches as a white amorphous powder which showed an [M]+ ion peak at m/z 259.4. 

Fig. 1. Selected 1H–1H COSY and HMBC Correlations of Compound 1

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358 in the EI-MS spectrum. Taking the $^{13}$C-NMR data and the result of elemental analysis into account, the molecular formula of 3 was established to be C$_{21}$H$_{26}$O$_{5}$. In the $^{13}$C-NMR spectrum, the signals due to two aromatic nuclei and seven aliphatic carbons along with two methoxyl groups were observed, indicating that 3 is a diarylheptanoid. Analysis of the aromatic signals in the $^1$H-NMR spectra suggested the presence of a 1,2,3,4-tetrasubstituted benzene ring [δ$_{H}$ 6.89 (1H, d, J = 58 Hz), 6.69 (1H, d, J = 8 Hz, H-18)] and a 1,3,4-trisubstituted benzene ring [δ$_{H}$ 6.84 (1H, d, J = 58 Hz, H-3), 6.70 (1H, dd, J = 2, 8 Hz, H-4), 5.72 (1H, d, J = 2 Hz, H-6)]. In addition, a phenolic hydroxyl [δ$_{H}$ 5.93 (1H, s, 15-OH)] and an alcoholic hydroxyl [δ$_{H}$ 1.25 (1H, s, 9-OH)] which were exchangeable with D$_2$O, and two methoxyl groups [δ$_{H}$ 4.00, 3.98 (each 3H, s)] were also confirmed in the 1H-NMR spectrum. The $^1$H- and $^{13}$C-NMR spectral data mentioned above are very similar to those of platycarynol (8) isolated from Platycarya strobilacea (Juglandaceae), suggesting that 3 is a diphenyl ether-type diarylheptanoid. The correlations of the aliphatic protons in the 1H–1H COSY spectrum displayed the connectivities from C-7 to C-13 (Fig. 2), revealing the location of a hydroxyl group at C-9 position. The NOE correlations between H-13 and phenolic hydroxyl, and between H-6 and H-8 which were observed in the NOE spectrum of 3 revealed the linkage of C-7 to C-5 of benzene ring A and C-13 to C-14 of benzene ring B (Fig. 2). Furthermore, the NOE correlations between H-3 and methoxyl (δ$_{H}$ 3.98), between phenolic hydroxyl and methoxyl (δ$_{H}$ 4.00) indicated the positions of methoxyls and hydroxyl in benzene rings. Hence, the linkage diphenyl ether is determined to be between C-1 and C-17. From the above evidence, the plain structure of 3 was determined to be as shown in Fig. 2.

To determine the absolute configuration of the secondary hydroxyl group at C-9, 3 was methylated with CH$_2$N$_2$ to give 3a which was further esterified by (R)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid (MTPA) and (S)-MTPA, respectively. By applying the modification of Mosher’s method$^{10}$ to the MTPA esters (3b, c) of 3a, the positive and negative $\Delta\delta$ (δ$_{S}$ – δ$_{R}$) values shown in Fig. 3 unequivocally indicated a 9R configuration in compound 3.

The negative Cotton effect at 241 nm and the positive one at 218 nm in the CD spectrum suggested the chiral plane of 3 is expressed as $S$ configuration which is the same as that of (+)-galeon, a diarylheptanoid isolated from the Myrica plant.$^{10}$

Compound 4 was isolated as a light yellow powder from the branches. Its molecular formula was determined to be C$_{12}$H$_{10}$O$_{4}$ by high resolution EI-MS. The $^1$H-NMR spectrum displayed the signals derived from a 1,2-disubstituted benzene ring [δ$_{H}$ 8.32 (1H, dd, J = 1, 8 Hz), 8.16 (1H, dd, J = 1, 8 Hz), 7.61 (1H, dt, J = 1, 8 Hz), 7.53 (1H, dt, J = 1, 8 Hz)], a singlet aromatic signal (δ$_{H}$ 7.11) and a methoxyl group (δ$_{H}$ 3.98). The $^{13}$C-NMR spectral data indicated the presence of an ester carbonyl (δ$_{C}$ 172.2), a methoxyl group (δ$_{C}$ 52.6) and 10 aromatic signals, suggesting 4 is a naphthalene carboxylic acid methyl ester. Therefore, the remaining residues of 4 are deduced to be two hydroxyl groups. The carbonyl and these two hydroxyl groups were determined to be located in C-2, C-1 and C-4, respectively, of the naphthalene ring by the HMBC correlations shown in Fig. 4. A glucoside of hydroxynaphthalene carboxylic acid methyl ester related to 4 was reported to be present in Juglans mandshurica (Juglandaceae).$^{11}$

Compound 4, a methyl ester of compound 6, may be an artifact produced in the course of plant extraction or isolation. Compound 6 is a biogenetically important intermediate in the biosynthesis of juglone from O-succinoylbenzoic acid$^{12}$ (Chart 1).
In conclusion, we have isolated four new compounds (1—4) from the fruits and branches of *Rhoiptelea chiliantha* (Rhoipteleaceae). Compounds 1 and 2 belong to pyrrolidine-type alkaloids. Interestingly, compound 2 possesses an antipodal structure of 2S-dihydroshikumine which was isolated from *Banisteriopsis cappi* (Malpighiaceae). Compound 3 has the same skeleton as 5 which was isolated from *Platyccarya strobilacea* (Juglandaceae) in our previous paper. Compound 4 is considered to be biogenetically-related to juglone which is widely distributed in Juglandaceae plants.

Chemotaxonomic studies on the Rhoipteleaceae based on our extensive and detailed investigations on the chemical constituents of *Rhoiptelea chiliantha* (Rhoipteleaceae) to the Juglandales (comprising Juglandaceae), Fagales (comprising Betulaceae and Fagaceae) and Myrtales (comprising Myricaceae). The existence of 3 and 4 reported in the present paper further supported the affiliation of a systematic position between the Rhoipteleaceae and Juglandales, and suggested the Juglandales is probably the most closely related order to the Rhoipteleaceae.

**Experimental**

**General** Melting points were determined on a micromelting point hot stage apparatus (Yanagimoto) and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. The CD spectra were measured on a JEOL JSM DX-303 spectrometer plus a JEOL JMS DX-303 spectrometer. FAB-MS were recorded on a JEOL JMS DX-303 spectrometer.

**Extraction and Isolation**

The fruits and branches of *Rhoiptelea chiliantha* (Rhoipteleaceae) were collected in Guangxi, China in Oct., 1988. A voucher specimen has been deposited in the Laboratory of Plant Chemotaxonomy, China Pharmaceutical University, Nanjing, China.

**Plant Material** The fruits and branches of *Rhoiptelea chiliantha* were collected in Guangxi, China, in Oct., 1988. A voucher specimen has been deposited in the Laboratory of Plant Chemotaxonomy, China Pharmaceutical University, Nanjing, China.

**Extraction and Isolation** The MeOH extracts of the air-dried fruits (495 g) and branches (820 g) of *Rhoiptelea chiliantha* were separately suspended in H2O, then successively extracted with Et2O and EtOAc. The water layer of the fruits was chromatographed over MCI-gel CHP 20P (0—100% MeOH) to afford fr.-1 (17.3 g), fr.-2 (2.9 g) and fr.-3 (4.0 g). Fraction-2 was subjected to Bondapak ODS (0—40% MeOH) and silica gel (100% MeOH) to give fr.-1 (1.6 g), fr.-2 (0.9 g) and fr.-3 (13.7 g). Fraction-2 was collected in MCI-gel CHP 20P (80—100% MeOH) to yield fr.-1 (1.5 g), fr.-2 (1.0 g) and fr.-3 (0.7 g). Fraction-2 was subjected to Sephadex LH-20 chromatography to afford fr.-1 (1.7 g), fr.-2 (2.9 g) and fr.-3 (4.0 g). Fraction-2 was separated by silica gel chromatography (CHCl3:MeOH: H2O, 9:1:0.2—8:2:0.2) to yield 162 mg.

Compound 1: Colorless needles, mp 178—180 °C, [a]25°dm3 —257.4° (c=0.2, CHCl3). Anal. Caled for C35H34O3N4: C, 72.82; H, 7.48; N, 6.68. Found: C, 72.82; H, 7.49; N, 6.68. The 1H- and 13C-NMR spectra were recorded on a Varian Unity 400 MHz spectrometer. The CD spectra were measured with a JASCO DIP-370 digital polarimeter. The optical rotations were measured with a JASCO DIP-370 digital polarimeter. The CD spectra were measured on a Varian Unity 400 MHz spectrometer plus a Varian Unity 400 MHz spectrometer. FAB-MS were recorded on a JEOL JMS DX-303 spectrometer.

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**References**


