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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 HAND.-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 HAND.-MAZZ., the only species of the family Rhoipteleaceae, we have reported the structural elucidation of triterpenes,1) triterpene esters2) from the barks, diarylheptanoids,3) ellagitannins,4) euphane-type triterpene bidesmosides and tridesmosides,5) and dammmarane-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 EtO, 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 EtO 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 [M]+ at m/z 235 in EI-MS and the result of elemental analysis, suggesting that 1 is an alkaloid. Its 1H-NMR spectrum displayed the signals due to a 1,2,3-trisubstituted benzene ring [δH 7.50 (1H, d, J=2, 8 Hz), 7.36 (1H, dd, J=8, 9 Hz), 7.11 (1H, dd, J=2, 9 Hz)], an N-methyl [δH 2.62 (3H, s)] and a methoxyl group [δH 3.87 (3H, s)]. These besides, the signals arising from a carboxylic carbon, a methine, a methyne [δC 175.4 (d, C-2)] and three methylenes [δC 54.8 (t, C-5), 31.0 (t, C-3), 22.6 (t, C-4)] were confirmed by the 13C-NMR and DEPT spectra. The correlations (Fig. 1) of the methylenes and methine in the 1H-1H COSY spectrum and their chemical shifts suggested the presence of a 2-substituted pyrrolidine ring in compound 1.7) The HMBC correlations shown in Fig. 1 determined the positions of the carboxylic acid group and methoxyl group in C-2’ and C-6’, respectively, in the benzene ring. Furthermore, the HMBC correlations from H-2 signal to C-1’, C-2’ and C-6’ signals confirmed the linkage of 2-substituted pyrrolidine ring to the benzene ring at C-1’ position. Thus, the plain structure of 1 was concluded to be as shown in Fig. 1. The absolute configuration of C-2 of 1 was determined to be R on the basis of observation of a negative Cotton effect at 246 nm in the CD spectrum.7)

Compound 2 was also isolated from the fruits as colorles crystals, mp 221—223 °C and showed a positive reaction to ninhydrin reagent by heating. Its molecular formula of C₁₃H₁₃NO₂ was deduced from the data of EI-MS spectrum (molecular ion peak at m/z 205 [M]+) and elemental analysis. The 1H- and 13C-NMR data of 2 were very similar to those of 1, exhibiting a 2-substituted pyrrolidine ring, a carboxylic acid group, 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. From the above evidence, compound 2 was assigned to 2R-dihydroshihunine.

Compound 3 was isolated from the branches as a white amorphous powder which showed an [M]+ ion peak at m/z...
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 [\(\delta_H 6.89\) (1H, d, \(J = 5.8\) Hz, H-19), 6.69 (1H, d, \(J = 8\) Hz, H-18)] and a 1,3,4-trisubstituted benzene ring [\(\delta_H 6.84\) (1H, d, \(J = 5.8\) 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 [\(\delta_H 5.93\) (1H, s, 15-OH)] and an alcoholic hydroxyl [\(\delta_H 1.25\) (1H, s, 9-OH)] which were exchangeable with D\(_2\)O, and two methoxyl groups [\(\delta_H 4.00, 3.98\) (each 3H, s)] were also confirmed in the \(^1\)H-NMR spectrum. The \(^1\)H- and \(^{13}\)C-NMR spectral data mentioned above are very similar to those of platycarynol 8) (5) isolated from \(\text{Platycarya strobilacea}\) (Juglandaceae), suggesting that 3 is a diphenyl ether-type diarylheptanoid. The correlations of the aliphatic protons in the \(^1\)H–\(^1\)H 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 (\(\delta_H 3.98\)), between phenolic hydroxyl and methoxyl (\(\delta_H 4.00\)) 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)-\(\alpha\)-methoxy-\(\alpha\)-(trifluoromethyl)-phenylacetic acid (MTPA) and (S)-MTPA, respectively. By applying the modification of Mosher’s method\(^9\) to the MTPA esters (3b, c) of 3a, the positive and negative \(\Delta\delta (\delta_c - \delta_s)\) values shown in Fig. 3 unequivocally indicated a 9\(R\) 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 [\(\delta_H 8.32\) (1H, dd, \(J = 1, 8\) Hz), 8.16 (1H, dd, \(J = 2, 8\) Hz), 7.61 (1H, dt, \(J = 1, 8\) Hz), 7.53 (1H, dt, \(J = 1, 8\) Hz)], a singlet aromatic signal (\(\delta_H 7.11\)) and a methoxyl group (\(\delta_H 3.98\)). The \(^{13}\)C-NMR spectral data indicated the presence of an ester carbonyl (\(\delta_C 172.2\)), a methoxyl group (\(\delta_C 52.6\)) 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 \(\text{Juglans mandshurica}\) (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 chilanthia (Rhoipteleaceae). Compounds 1 and 2 belong to pyrrolidine-type alkaloids. Interestingly, compound 2 possesses an antipodal structure of 2S-dihydroshihunine which was isolated from Banisteriopsis cappi (Malpighiaceae). Compound 3 has the same skeleton as 5 which was isolated from Platy- 
carya striobilia (Juglandaceae) in our previous paper. Compound 4 is considered to be biogenetically-related to 
juglone which is widely distributed in Juglandaceous plants.

Chemotaxonomic studies on the Rhoipteleaceae based on 
our extensive and detailed investigations on the chemical 
constituents of Rhoiptelea chilanthia DIEL ET HAND-MAZZ. 1—6 have 
suggested the relationships of the order Rhoipteleales (comprising 
Rhoipteleaceous) to the Juglandales (comprising 
Juglandaceae), Fagales (comprising Betulaceae and 
Fagaceae) and Myricales (comprising Myricaceae). The 
existence of 3 and 4 reported in the present paper further 
support the affinity of a systematic position between the 
Rhoipteleales and Juglandales, and suggested the Juglandales is 
probably the most closely related order to the 
Rhoipteleales.

Experimental

General Melting points were determined on a micromelting point hot 
h stage apparatus (Yanagimoto) and are uncorrected. Optical rotations 
were measured with a JASCO J-725 apparatus. 1H- and 13C-NMR spectra were 
recorded with Varian Unity 
University, Nanjing, China. A voucher specimen has been de-

The fruits and branches of Rhoiptelea chilanthia have been 
gathered in Guangxi, China, in Oct., 1988. A voucher specimen has been de-

Preparation of MTP A Esters of 3a

A solution of 
CH2N2 in Et2O at room 
temperature. The reaction mixture was evaporated 
plus 
CHCl3). EI-MS 
CH3OD): 38.4 (t), 36.1 (t), 28.9 (t), 28.7 (t), 28.3 (t), 22.4 (t). CD (d), 115.9 (d), 114.1 (d), 112.0 (d), 71.8 (d, C-9), 61.7, 56.2 (each q, 2, 16-

Compound 3: A white amorphous powder, [α]D 35° +58.5° (c=0.3, CHCl3).

Anal. Caled for C13H17NO3·3/4 H2O: C, 62.76; H, 7.49; N, 5.63. Found: C, 62.80; H, 7.15; N, 5.54. EI-MS m/z: 235 (M+), 220 (M+), 195 (M–) 218.0561 (M+ 9). 1H-NMR (500 MHz, CDCl3): δ9 1.89 (3H, s, 16-OMe), 3.98 (3H, s, OMe). 13C-NMR (125 MHz, CDCl3): 115.9 (d), 114.1 (d), 112.0 (d), 71.8 (d, C-9), 61.7, 56.2 (each q, 2, 16-

Methylation of 3 A solution of 3 (142 mg in MeOH) was treated with 
CH2N2 in Et2O at room temperature. The reaction mixture was evaporated 
in vacuo, and the residue was separated with silica gel (hexane:EtOAc: 4: 1— 
1: 0) to give 3a (28.2 mg): a white amorphous powder, [α]D 35° +58.5° (c=0.9, CHCl3). EI-MS m/z: 372 (M+). 1H-NMR (200 MHz, CDCl3): δ9 6.95, 6.92 
(3H, s, OMe), 3.98 (3H, s, 16-OMe), 3.14 (1H, m, H-3a), 2.64 (1H, ddd, J=4, 10, 17 Hza), 2.55 (1H, ddd, J=4, 6, 17 Hzb), 2.38 (1H, ddd, J=4, 7, 13 Hz, H1b), 1.83 (1H, m, H-1a), 1.50 (3H, m, H-8, H-12b), 1.25 (3H, m, H-10a, 1a, 9-OH), 1.15 (1H, m, H- 
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Plant Material The fruits and branches of Rhoiptelea chilanthia were 
gathered in Guangxi, China, in Oct., 1988. A voucher specimen has been de-

Extraction and Isolation The MeOH extracts of the air-dried fruits 
(495 g) and branches (820 g) of Rhoiptelea chilanthia 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 give fr-1 (1.6 g), fr-2 (0.9 g) and fr-3 (13.7 g). Fraction-2 was 
subjected to Bondapak ODS (60—40% MeOH) and silica gel 
(hexane:EtOAc: 4: 1— 
1: 0) to give 3a (28.2 mg): a white amorphous powder, [α]D 35° +58.5° (c=0.9, CHCl3). EI-MS m/z: 372 (M+). 1H-NMR (200 MHz, CDCl3): δ9 6.95, 6.92 
(3H, s, OMe), 3.98 (3H, s, 16-OMe), 3.14 (1H, m, H-3a), 2.64 (1H, ddd, J=4, 10, 17 Hza), 2.55 (1H, ddd, J=4, 6, 17 Hzb), 2.38 (1H, ddd, J=4, 7, 13 Hz, H1b), 1.83 (1H, m, H-1a), 1.50 (3H, m, H-8, H-12b), 1.25 (3H, m, H-10a, 1a, 9-OH), 1.15 (1H, m, H- 

Preparation of MTP A Esters of 3a A solution of 3a (5 mg), dicyclo- 
hexylcarbodiimide (8 mg), 4-dimethylaminopyridine (6 mg) and (R) (+)-a- 
metoxy-α-(trifluromethyl)-phenylacetic acid (8 mg) in CH2Cl2, was 
allowed to react at room temperature for 18 h. The resulting mixture was puri-
fied over a micro-column (0.7×7 cm) of silica gel (hexane:EtOAc: 8: 1— 
1: 0) to afford (R)-MTPA ester 3b (3 mg). The use of (S) (−)-a-methoxy-
α-(trifluromethyl)-phenylacetic acid gave the (S)-MTPA ester 3c (3 mg).

Compound 4: A light yellow amorphous powder. HR-EL-MS m/z: 
218.0561 (M+): Caled for C13H17NO3·3/4 H2O: C, 62.76; H, 7.49; N, 5.63. Found: C, 62.80; H, 7.15; N, 5.54. EI-MS m/z: 235 (M+), 220 (M+), 195 (M–) 218.0561 (M+ 9). 1H-NMR (500 MHz, CDCl3): δ9 1.89 (3H, s, 16-OMe), 3.98 (3H, s, OMe). 13C-NMR (125 MHz, CDCl3): 115.9 (d), 114.1 (d), 112.0 (d), 71.8 (d, C-9), 61.7, 56.2 (each q, 2, 16-

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