TRICHILININS B AND C, TWO NEW LIMONOIDS FROM *MELIA TOOSENDAN*

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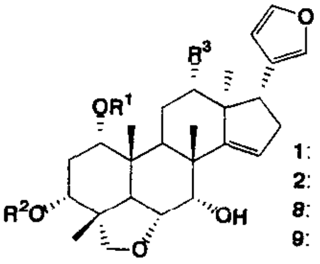
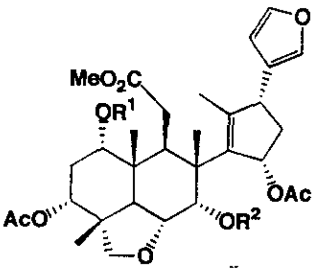
Abstract—Two new limonoids, trichilinins B and C, were isolated along with four nimbolidins and salannin from the root bark of *Melia toosendan*.

Meliaceae plants are a rich source of limonoids and attracting considerable interest, because the limonoids from them showed several interesting biological activities, in which an insect antifeedant activity has been well studied.[1] We have isolated several types of limonoids as insect antifeedant from a typical plant *Melia azedarach* Linn and a related plant *M. toosendan*: i.e. meliacarpinins,[2,3] trichilins[4-6] and azedarachins.[7,8]

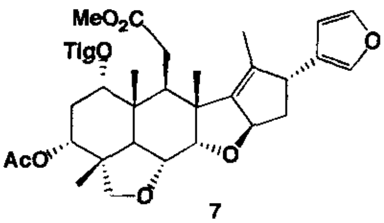
In the continuous study of limonoids from *M. toosendan*, we isolated two new limonoids, named trichilinins B (1) and C (2), along with four nimbolidins (3)-(6)[9] and salannin (7)[10] from the hexane extract of the dried root bark.



	R¹	R²	R³
1:	Tig	Ac	OAc
2:	Ac	Tig	H
8:	H	H	H
9:	H	Ac	OAc



	R¹	R²
3:	Ac	Tig
4:	Ac	COCHMe₂
5:	Tig	Tig
6:	Tig	COCHMe₂



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Their structures were elucidated by spectroscopic means and the trichilinins were considered to be biogenetic precursors of ring-C cleaved limonoids such as 3-7. We report here the isolation and structures of trichilinins B(1) and C(2) and the antifeedant activity of the isolated limonoids against the larvae of *Spodoptera eridania* (Boisduval).

Trichilinin B (1), $[\alpha]_D^{19}$ +56° (c 0.13, MeOH), exhibited following spectral data. Negative FABms: m/z 609$[M-H]^-$; HRFABms: m/z 551.3002$[M+H-AcOH]^+$(Δ-0.7mmu); uv: 221nm (ε 11400); ir: 3600-3220, 1738, 1712 and 1655 cm^{-1}. The ms and ^{13}C nmr (Table 2) data revealed the molecular formula as $C_{35}H_{46}O_9$ (13 unsaturations). In the ^1H nmr spectrum, the presence of four tertiary methyls and a β-furyl moiety were observed along with a trisubstituted olefinic proton signal at δ 5.69 (dd, J=3.3 and 1.5 Hz, 15-H) and a typical AB quartet at δ3.60(J=7.6 Hz, 28β-H) and 3.63(br, J=7.6 Hz, 28α-H), weakly coupled to 4β-Me signal. One methine proton at δ4.21(d, J=2.9 Hz, 7-H) under hydroxyl, coupling with a methine proton at δ4.16(dd, J=12.5 and 2.9 Hz, 6-H) linked to an ether oxygen, was also observed along with three protons under acyloxy groups at δ4.66 (dd, J=2.9 and 2.6 Hz, 1-H), 4.93(dd, J=2.9 and 2.6 Hz, 3-H) and 5.05(dd, J=9.2 and 7.0 Hz, 12-H).

These data strongly suggested that 1 was a hexacyclic structure similar to vilasinin (8)[11] and trichilinin (9),[12] and the ^1H nmr spectrum of 1 was very similar to that of 9 except for the addition of one tigloyl group. The substitution pattern around the A-ring with 1α-tigloyloxy and 3α-acetoxyl groups, was deduced from the long range coupling between 1β- and 3β-H signals and the high field shift to δ1.08(dt, J=14.3 and 7.0 Hz) of the 11α-H signal, attributable to a shielding effect of the 1α-tigloyl group,[10] compared to δ1.49 in 9. The presence of 1α-tigloyl was also confirmed by a nOe enhancement of the 9-H signal by irradiation at the 2'-methyl signal of tig-

Table 1. ^1H Nmr data for 1 and 2

H	1	2
1	4.66 dd(2.9, 2.6)	4.77 dd(3.0, 2.6)
2α	2.14 dt(16.7, 2.7)	2.12 m
β	2.21 dt(16.7, 2.9)	2.23 m
3	4.93 dd(2.9, 2.6)	4.96 dd(3.3, 2.6)
5	2.75 d(12.5)	2.81 d(12.5)
6	4.16 dd(12.5, 2.9)	4.19 dd(12.8, 2.9)
7	4.21 d(2.9)	4.26 d(2.9)
9	2.80 dd(12.3, 7.6)	3.18 dd(13.5, 5.9)
11α	1.08 dt(14.3, 7.0)	2.22 m
β	2.13 m	2.28 m
12	5.05 dd(9.2, 7.0)	2.18 m 2.36 m
15	5.69 dd(3.3, 1.5)	5.71 dd(3.3, 1.8)
16α	2.55 ddd(16.1, 10.9, 1.5)	2.59 ddd(15.7, 10.7, 1.8)
β	2.45 ddd(16.1, 7.9, 3.0)	2.51 ddd(15.6, 7.8, 3.3)
17	3.01 dd(10.6, 7.7)	3.46 dd(10.6, 7.7)
18	1.03 s	1.02 s
19	0.94 s	0.96 s
21	7.20 br s	7.35 br s
22	6.23 d(1.1)	6.56 br s
23	7.32 dd(1.5, 1.3)	7.35 br s
28α	3.63 br d(7.6)	3.66 br d(7.7)
β	3.60 d(7.6)	3.63 d(7.7)
29	1.21 br s	1.23 br s
30	1.11 s	1.07 s
Ac	1.88 s 1.90 s	1.93 s
Tig 2'-Me	1.83 br s	1.79 br d(1.1)
3'	6.96 qq(7.2, 1.5)	6.95 qq(7.2, 1.5)
3'-Me	1.75 dd(7.3, 1.1)	1.70 dd(7.2, 1.4)

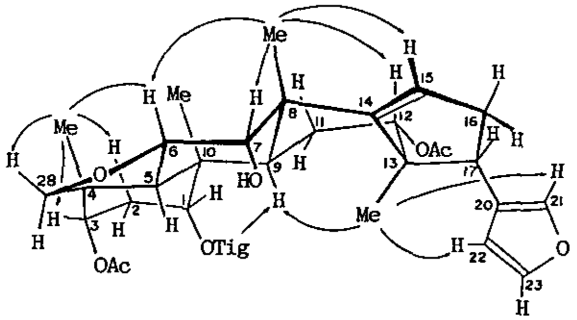

Figure 1. Selected nOe connectivities for 1.

Table 2. ^{13}C Nmr data for 1

C		C	
1	71.9 d	19	15.2 q
2	27.4 t	20	124.5 s
3	73.9 d	21	140.3 d
4	42.4 s	22	111.7 d
5	39.6 d	23	142.1 d
6	72.4 d	28	78.0 t
7	71.7 d	29	19.7 q
8	45.4 s	30	15.3 q
9	34.3 d	Ac	20.9 q
10	39.5 s		21.3 q
11	24.2 t		170.2 s
12	77.2 d		170.9 s
13	51.4 s	1'	166.5 s
14	157.4 s	2'	128.7 s
15	122.7 d	2'-Me	11.9 q
16	36.6 t	3'	138.0 d
17	50.3 d	3'-Me	14.4 q
18	26.9 q		

loyl. The α configuration of the 12-OAc group was apparent from the couplings of the 12β-H signal and also from the high field shift of the acetyl signal to δ 1.88 in 1 from δ 2.13 in 9, attributable to the effect of the 1α-tigloyl group. Another stereochemistry of 1 was comfirmed by nOe experiments (Figure 1).

The ^{1}H nmr spectrum of trichilinin C (2), $[\alpha]_D^{19}$ +22° (c 0.09, MeOH); $C_{33}H_{44}O_7$, was superimposable on that of 1 except for the lack of one acetoxyl group and some differences in the chemical shifts. The fact that the 12-OAc group in 1 is missing in 2, was apparent from the presence of 12-methylene signls at δ 2.18 and 2.36. On the other hand, the substitution pattern of the A-ring with 1-acetoxyl and 3-tigloyloxy groups was deduced from the large low field shifts of the 11α- and 9-H signals from δ 1.08 and 2.80 in 1 to δ 2.22 and 3.18 in 2. These shifts would result in the cancellation of the effect due to 1α-tigloyl and a conformational change of the ring C, which was deduced from a large low field shift of the 17-H signal.

Vilasinin and trichilinins appear to be biogenetic precursors of nimbolidins and salannin class ring-C cleaved limonoids, that is, a Grob type olefin-forming fragmentation[13] of a 12-hydroxy 14,15-epoxyvilasinin class compound and subsequent ether ring formation between C-7 and C-15 hydroxyl groups would yield nimbolidins and salannin.

Insect antifeedant activity of the isolated limonoids was tested by a leaf disk method[14] against the larvae of a Japanese pest insect *Spodoptera eridania* (Boisduval). Nimbolidins (3-6) showed the activity at 500 ppm, whereas trichilinins B (1) and C(2) and salannin (7) were all active at 1000 ppm. The activities of these compounds were not so strong compared to those of the azedarachins, 200~400 ppm, and trichilins, 200-400ppm, isolated from the same plant.

EXPERIMENTAL

^{1}H and ^{13}C Nmr were measured in $CDCl_3$ on a JEOL FX-400 spectrometer. Ir (KBr) and uv (in MeOH) were recorded on JASCO FT/IR 5300 and Shimadzu UV-210A spectrophotometers. Optical rotation was measured in MeOH using a JASCO J-20 A spectrometer.

Plant material. The root bark was collected in December 1992 at Xiangtan, China.

Extraction and isolation. The air-dried root bark (1.5 kg) was extracted with hexane (20 l), 15 ℃, 2 weeks, to yield 9.3 g of an extract, which was flash chromatographed on silica gel with a hexane-ether solvent system. Each limonoid fractions eluted with Et_2O was purified by prep-tlc using Et_2O to give three limonoid fracions. Each fraction was further separated and purified through hplc using μ-Bondapac C_{18} with 20-45% H_2O/MeOH as the solvent to give 1 (3.8 mg), 2 (0.9 mg), 3 (0.9 mg), 4 (6.6 mg), 5 (4.4mg), 6 (5.0 mg), and 7 (4.2 mg).

Trichilinin B (1). An amorphous powder, $C_{35}H_{46}O_9$; $[\alpha]_D^{19}$ +56° (c 0.13); uv 221 nm (ε 11400); ir 3600-3220, 1738, 1712 and 1655 cm^{-1}; negative FABms m/z 609[M-H]$^-$, HRFAB ms m/z 551.3002[M+H-Ac]$^+$ (Δ -0.7 mmu).

Trichilinin C (2). An amorphous powder, $C_{33}H_{44}O_7$; $[\alpha]_D^{19}$ +22° (c 0.09); uv 217 nm (ε 9000); FABms m/z 553[M+H]$^+$.

REFERENCES

1. D.E. Champagne, O. Koul, M.B. Isman, G.G.E. Scudder, and G.H.N. Towers, *Phytochemistry*, 1992, 31, 377.
2. M. Nakatani, R.C. Huang, H. Okamura, and T. Iwagawa, *Chem. Lett.*, 1993, 2125.
3. M. Nakatani, S. Arikawa, H. Okamuta, and T. Iwagawa, *Heterocycles*, 1994, 38, 327.
4. M. Nakatani, R.C. Huang, H. Okamura, H. Naoki, and T. Iwagawa, *Phytochemistry*, 1994, 36, 39.
5. M. Nakatani, J-Bo Zhou, T. Iwagawa, and H. Okamura, *Heterocycles*, 1994, 38, 2407.
6. J-Bo Zhou, H. Okamura, T. Iwagawa, and M. Nakatani, *Phytochemistry*, in press.
7. R.C. Huang, H. Okamura, T. Iwagawa, and M. Nakatani, *Bull. Chem. Soc. Jpn.*, 1994, 67, 2468.
8. R.C. Huang, H. Okamura, T. Iwagawa, and M. Nakatani, *Phytochemistry*, 1995, 38, 593.
9. M. Nakatani, J-Bo Zhou, N. Nakayama, H. Okamura, and T. Iwagawa, *Phytochemistry*, in press.
10. R. Henderson, R. McCrindle, A. Melera, and K.H. Overton, *Tetrahedron*, 1968, 24, 1525.
11. R.V. Pachapurkar, P.M. Kornule, and C.R. Narayanan, *Chem. Lett.*, 1974, 357.
12. M. Nakatani, T. Iwashita, K. Mizukawa, and T. Hase, *Heterocycles*, 1987, 26, 43.
13. C.A. Grob and P.W. Schiess, *Angew. Chem.*, *Int. Ed. Engl.*, 1967, 6, 1.
14. K. Wada and K. Munakata, *Agr. Food. Chem.*, 1968, 17, 471.

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