LIMONOIDS FROM *MELIA TOOSENDAN* (MELIACEAE) AND THEIR ANTIFEEDANT ACTIVITY

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Abstract - Twenty two new limonoids have been isolated along with nineteen known limonoids from a Meliaceae plant *Melia toosendan* and their antifeeding activity was tested against the larvae of *Spodoptera* insects. The structures, ^{13}C NMR data and antifeedant activity of the isolated compounds are summarized.

INTRODUCTION

Limonoids are tetranortriterpenoids with a 4,4,8-trimethylfuranylsteroid skeleton derived from euphane (H-20β) or tirucallane (H-20α) triterpenoids, and, in general, have intense bitter taste. Meliaceae plants are a rich source of limonoids. Limonoids from the neem tree *Melia azadirachta indica* and the bead tree *M. azedarach* have been well studied, because of their marked insect antifeedant property and a variety of the structures.[1,2] We have also reported the isolation and antifeedant activity of limonoids from *M. azedarach*.[3-9] *M. toosendan* is native to China and a very similar large tree to *M. azedarach*, and, in China, an extract of the bark is used as an anthelmintic. The isolation of two limonoids, toosendanin (12)[10,11] and *iso*-chuanliansu (27),[11] have been reported from the bark. In our continuing studies on bioactive limonoids, we found that *M. toosendan* contained several types of limonoids possessing insect antifeedant activity, and isolated forty one limonoids from samples of the root and stem bark and the fruits collected in China: one protolimonoid (1); two meliacins, azadirone (2) and acetyltrichilenone (3); four C-28/C-6 bridged ethers, trichilinins (7)-(10); thirteen C-19/C-29 bridged acetals with 14,15-epoxide, amoorastatines (11) and (12), azedarachins (13)-(16), trichilins (19)-(25), and five related 15-keto compounds, amoorastatones (26) and (27), and neoazedarachins (28)-(30); twelve ring C-seco compounds, nimbolinins (34)-(36), ohchinolides (37) and (38), nimbolidins (39)-(43), salannin (44) and ohchinolal (45); three azadirachtin-type higher oxidized C-seco compounds, meliacarpinins (46)-(48); and one novel spiro limonoid, spirosendan (49). These limonoids included twenty two new compounds and almost all of the compounds showed antifeedant activity against the larvae of *Spodoptera* insects.

1. LIMONOIDS FROM *M. TOOSENDAN*

Commonly, after formation of the basic limonoid skeleton, a variety of oxidation and skeletal rearrangement may occur. The D ring is often oxidized to a lactone (D-seco limonoids) and the subsequent oxidation and rearrangement of the A ring lead to formation of the typical rutaceous limonoids such as limonin. But, many of limonoids from Meliaceae exist as intact apo-euphol or ring C-seco compounds. Although some mechanisms have been proposed,[12-14] the biosynthesis of ring C-seco limonoids is less clear. The types of limonoids from *M. toosendan* were very similar with those from *M. azedarach*, a typical Meliaceae plant observed in all over the world.

1.1 Isolation of limonoids

The stem and root bark were collected in December 1992 at Xiangtan in China. On the other hand, the fruits were gathered in July 1996 at Guangzou, China. The presence of limonoids in the extract was detected by the characteristic color with Ehrlich's reagent on TLC. The limonoids from *M. toosendan* were also very sensitive to traces of acid and gradually decomposed on a silica column. It was, therefore, necessary to use DCCC (droplet counter-current chromatography), flash chromatography, preparative TLC and careful HPLC techniques to separate the various congeners. Each of the air-dried stem and root bark gave 12 compounds of 11-16 and 20-25, and 33 compounds of 1-3, 7, 8, 11, 12, 14-16, 19, 25-33 and 37-49, respectively. From the fruits, 7 compounds of 9, 10, 12 and 34-37 were isolated.

1.2 Structures of the limonoids

Structures of the isolated limonoids were elucidated by spectroscopic means including 2D NMR and CD spectra, and chemical reactions.

(1) Protolimonoid (tetranortriterpenoid)

From the root bark, one known tetranortriterpenoid (1) was obtained, including the γ-lactone ring. Compound (1) is unusual and a possible precursor of limonoids. This is the second isolation in nature,[15] with only three other limonoids of this type having been reported.[15-17]

(2) Meliacins

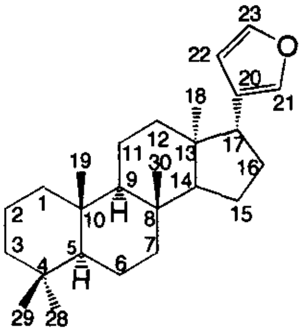
Two known intact apo-euphol limonoids of azadirone (2)[18] and acetyltrichilenone (3)[19] were isolated from the root bark. These compounds have been often found in Meliaceae. An epoxide rearrangement of a 14,15-epoxylimonoid to the 15-ketone by acid has been known. In 1967, Tayler *et al.* reported a ready isomerization of trichilenone (4) to neotrichilenone (6) by acid.[20] On the other hand, we found that alkaline treatment of acetyltrichilenone (3) also gave the 15-oxo compound (6) and the subsequent acetylation with Ac_2O and DMAP (4-dimethylaminopyridine) resulted in the formation of the epoxide, acetyltrichilenone (3).[21]

(3) Trichilinins

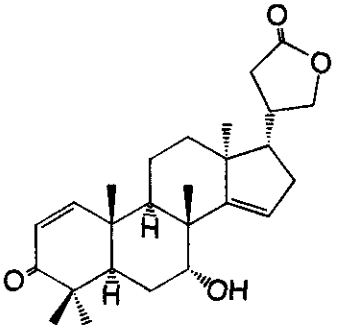
Four new meliacins, trichilinins B (7), C (8),[22] D (9) and E (10),[23] having a C-28/C-26 bridged ether linkage, were isolated from the root bark and the fruits. Although some limonoids of this type have been reported,[24,25] the C-12 oxygen function as in 7, 8 and 10 are at present unique and these compounds appear to be biosynthetic precursors of ring-C cleaved limonoids.

(4) C-19/C-29 bridged acetals

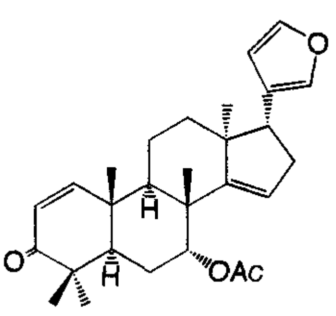
Aside from the highly oxidized ring C-seco limonoids such as azadirachtins[26,27] and meliacarpinins,[4,8] the most active antifeeding compounds appear to be intact apo-euphol limonoids with a C-19/C-29 lactol bridge. Several types of this class were isolated from the stem and root bark. Azedarachins and trichilins with a 14,15-epoxide and an 11-keto function are potent antifeedants, different from each other only in the oxidation pattern of the ring A. On the other hand, neoazedarachins are the 15-keto isomers of azedarachins. Stereochemistry at C-12 and 29 in these compounds was mainly determined from chemical shifts of the 12- and 3-H signals, and by NOE observation between the 12β-H and 17-H signals and the 4α-Me and 29-H signals, respectively.[5]



limonoid skeletone



1



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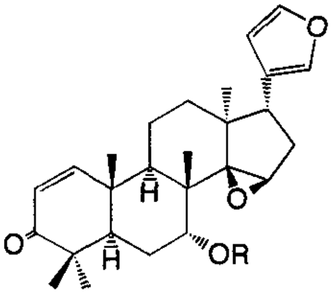
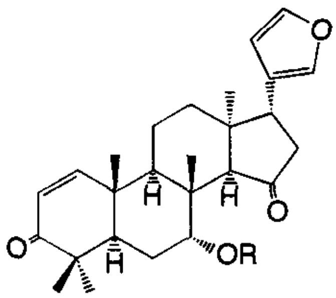


3 R= Ac

4 R= H



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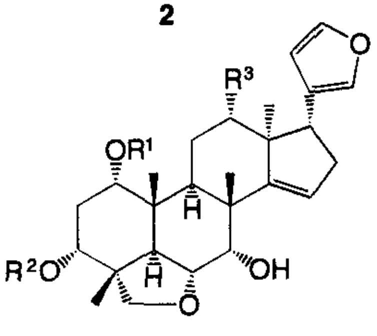
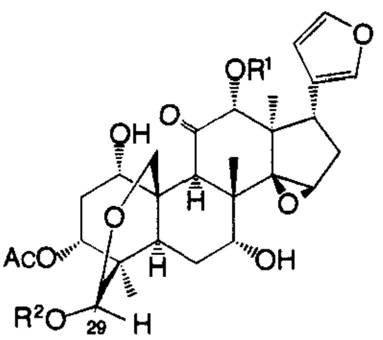
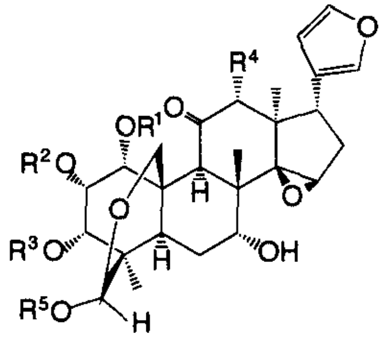
6 R= H



	R1	R2	R3
7*	Tig	Ac	OAc
8*	Ac	Tig	H
9*	Cin	H	OAc
10*	Bz	H	OAc



	R1	R2
11	H	H (and 29 epimer)
12	Ac	H (and 29-epimer)
13	H	$COCH(CH_3)CH_2CH_3$
14	Ac	$COCH(CH_3)CH_2CH_3$
15*	H	$COCH(CH_3)_2$
16	Ac	$COCH(CH_3)_2$
17	Ac	Ac
18	H	Bz



	R1	R2	R3	R4	R5
19	H	Ac	Ac	OH	$COCH(CH_3)CH_2CH_3$
20	H	Ac	Ac	OAc	$COCH(CH_3)_2$
21*	H	H	Ac	OAc	$COCH(CH_3)CH_2CH_3$
22*	H	H	Ac	H	$COCH(CH_3)CH_2CH_3$
23*	H	H	Ac	H	$COCH(CH_3)_2$
24*	H	Ac	H	H	$COCH(CH_3)CH_2CH_3$
25*	Ac	Ac	Ac	OAc	$COCH(CH_3)_2$

*New natural products

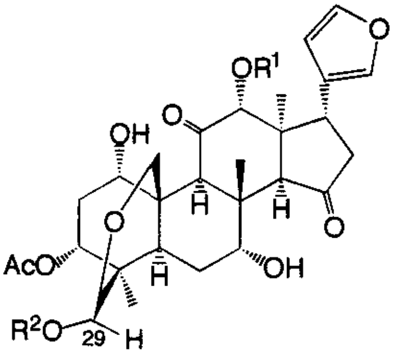
Three azedarachins, azedarachin A (13) and 12-*O*-acetylazedarachins A (14) and B (16), were first isolated from *M. azedarach* in 1994.[5] Azedarachin B (15) is a new compound from the root bark.[28] Two known 29-hemiacetals of 12α-hydroxyamoorastatin (11)[29] and its 12-acetate, toosendanin (12),[10,11] have been first isolated as 29-exo compounds by recrystalization from *Aphanamixis grandifolia* and *M. azedarach*, respectively, but each of them was elucidated by us as an equilibrium mixture of exo- and endo-isomer at C-29 in ratios of 5:2 to 5:4. Interestingly, acetylation and *p*-bromobenzoylation of both hemiacetals (11and12) afforded only 29-*exo* derivatives such as 17 and 18.[28]

Some of trichilins, first isolated from an African medicinal Meliaceae plant *Trichilia roka*,[30] have been also found from *M. azedarach* together with several new compounds.[3,31] From the stem and root bark of *M. toosendan*, five new compounds of trichilins I (21), J (22),[32] K (23), L (24)[33] and 1-*O*-acetyltrichilin H (25)[34] were isolated together with two known trichilins, B (19)[30] and H (20).[3] The 29-acetal acyl side chain in trichilins arising from *M. toosendan* is 2-methylpropanoyl or 2-methylbutanoyl similar to azedarachins, different from only 2-methylbutanoyl in trichilins from *T. roka*.[30,35]

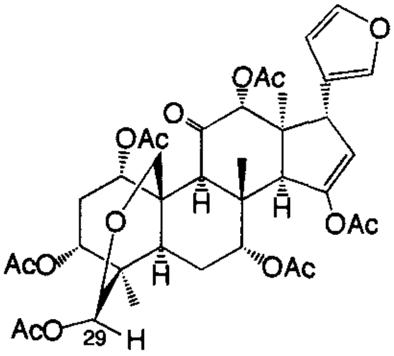
From the root bark, two new 15-keto-29-acyl acetals, neoazedarachins A (28) and B (29),[34] were isolated together with two known their hemiacetals, 12-hydroxyamoorastatone (26)[29] and *iso*-chuanliansu (27),[11] which have been, respectively, reported together with compounds (11) and (12). These neo-type compounds were smoothly derived from the corresponding 14,15-epoxy compounds by treatment with acid and their stereochemistry at C-14 was confirmed from the downfield shift of both 14α- and 7β-H signals, attributable to the effect of 7α-OH in a 1,3-diaxial relationship and to the anisotropic effect of the 15-keto group, respectively. Different from 11 and 12, acetylation of these hemiacetals (26) and (27) gave the acetate (31) as a mixture of 29- epimers. On the other hand, when treated with Ac_2O and DMAP, these hemiacetals afforded a pair of novel enol acetates (33) together with a pair of normal pentaacetates (32), which also readily changed to 33 by treatment with Ac_2O and DMAP.[21] Neoazedarachin D (30)[34] is the first natural 29-*endo* derivative found in C-19/C-29 bridged acetal limonoids.

(5) Ring C-seco limonoids

M. toosendan is also a rich source of ring C-seco limonoids and many types of new



	R1	R2
26	H	H
27	Ac	H
28*	H	$COCH(CH_3)CH_2CH_3$
29*	H	$COCH(CH_3)_2$
30*	H	CH_3 (*endo*)
31	Ac	Ac (and 29-epimer)
32	Ac	Ac 1,7-di-OAc (and 29-epimer)



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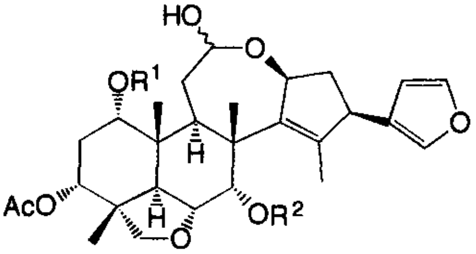
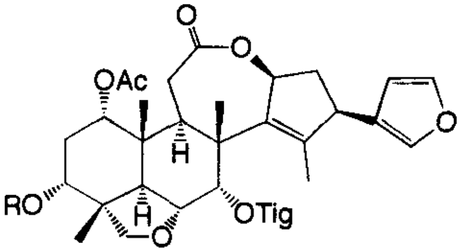
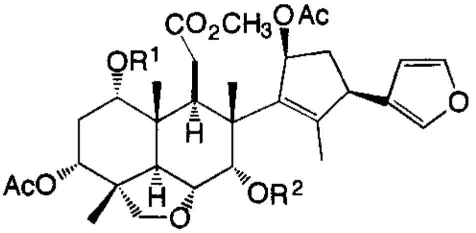


	R1	R2
34*	Ac	Bz
35*	H	Bz
36	H	Tig

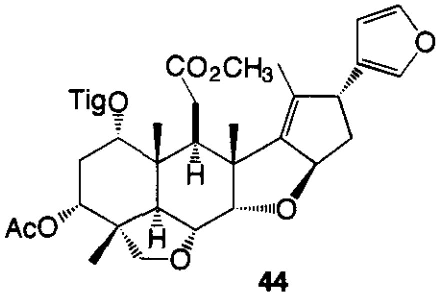


37 R= Ac

38* R= $COCH(CH_3)_2$



	R1	R2
39	Ac	Tig
40*	Ac	$COCH(CH_3)_2$
41*	Tig	Tig
42*	Tig	$COCH(CH_3)_2$
43*	$COCH(CH_3)CH_2CH_3$	Tig



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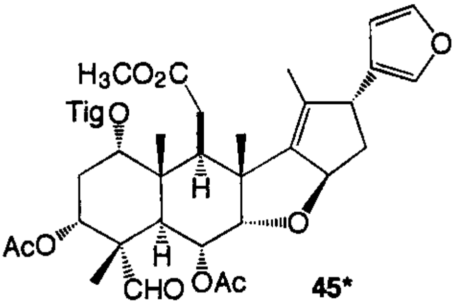
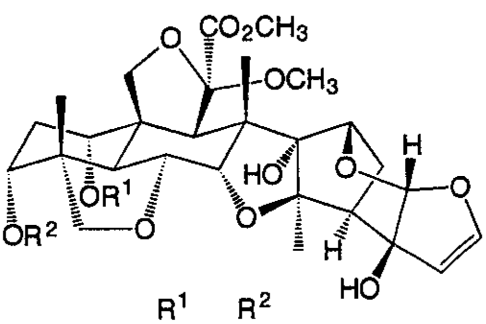
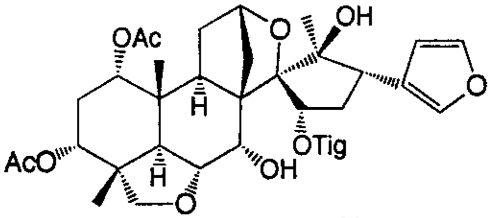
*New natural products



45*



	R^1	R^2
46	Cin	Ac
47	Ac	Tig
48	Tig	Ac



49*

*New natural products

compounds were isolated. Taylor proposed that cleavage of the C_{12}-C_{13} bond of limonoid is accompanied by the simultaneous opening of a 14,15-epoxide to generate 11-CHO and 15-OH functions and rotation about the C_8-C_{14} bond would allow the 15-OH to recyclize with the 11-CHO to form a lactol C ring.[36] The C-seco limonoids occurs only in the genus *Melia* and almost all of the types of C-seco limonoids found to date were isolated from *M. toosendan*.

Two new ring C lactols, nimbolinin A (34) and its 1-deacetyl compound (35),[23] and one new lactone, ohchinolide C (38),[37] were, respectively, isolated from the fruits and the root bark together with known 1-deacetylnimbolinin B (36)[38] and ohchinolide B (37),[39] isolated from *M. azedarach*. These lactols and lactones are rare in nature, with only each two other limonoids of the types having been reported.[38,40] Nimbolidins (39-43) and salannin (44)[41] are another types of the ring C-cleaved limonoids. Nimbolidins A (R^2= Bz in 39) and B (39) have been isolated from *M. azedarach*.[39] The stem and root bark of *M. toosendan* gave four new nimbolidins C (40)-F (43)[37,42] together with nimbolidin B (39) and salannin (44), the later of which is the most popular C-seco limonoid. 3-*O*-Acetylohchinolal (45),[37] a unique 28-CHO limonoid from the root bark, is the second compound in this type.[43]

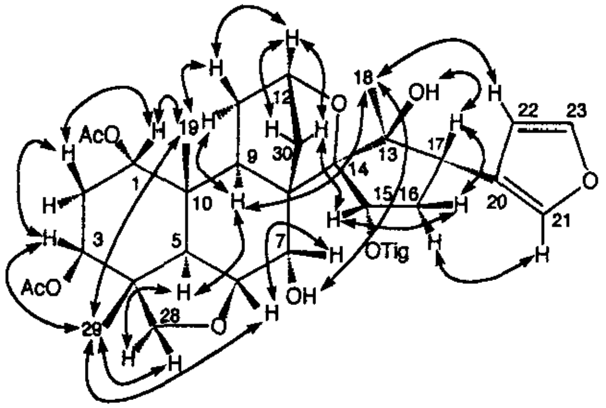
(6) Highly oxidized C-seco limonoids

Meliacarpinin A (46),[4] one of the most potent insect antifeedants, was isolated from *M.*

azedarach in 1993. This limonoid and two other known related meliacarpinins C (47) and D (48)[8] were isolated from the root bark of *M. toosendan* and they are more highly oxidized natural products of the C-seco class similar to azadirachtins[27] from the Himarayan neem tree *M. azadirachta indica*. A large distinction between meliacarpinins and a series of azaditachtins is that the 4β-Me in meliacarpinins is oxidized to the carboxymethyl group in azadirachtins.

(7) Spiro limonoid

Spirosendan (49),[44] a new skeletal limonoid possessing a spiro-structure, was isolated from the root bark. The structure was elucidated by extending NMR studies including HSQC (^{1}H-detected single-bond heteronuclear multiple-quantum coherence) and HMBC (^{1}H-detected heteronuclear multiple-bond connectivity) spectra. The most unique point in structure is the presence of a C_{12}-C_{30} carbon linkage, which was also elucidated from the NOESY spectrum. Although some spiro limonoids have been reported,[45,46] this is, to the best of our knowledge, the first occurrence of this type of limonoid.



NOE correlation in spirosendan (**49**)

2. SELECTED ^{13}C NMR DATA OF THE ISOLATAD LIMONOIDS

Forty one limonoids have been isolated from *M. toosendan* and their structures were mainly elucidated by NMR spectroscopic methods. In particular, ^{13}C NMR was effective for the skeletal determination and the assignment of carbon signals of a new compound by comparison with the data of known compounds is simple and straightforward provided. But these data are scattered in the literature. Therefore, it would appear to be of value to provide an easy access to a list of ^{13}C NMR data of several types of limonoids.

Table 1. ^{13}C NMR data of the limonoids from *M. toosendan*

C	7	9	13	15	20	24	28	30	35
1	71.6	73.9	70.6	70.2	71.6	73.1	70.8	70.7	71.3
2	27.4	30.4	35.7	35.3	68.5	71.0	36.1	36.3	29.3
3	73.9	73.8	74.0	73.6	73.0	73.5	73.9	76.2	72.5
4	43.4	43.8	39.8	39.4	40.7	39.2	43.5	43.4	42.5
5	39.6	38.6	41.4	34.1	34.1	33.7	41.3	25.8	39.3
6	72.4	72.7	25.7	25.3	25.6	26.8	23.2	25.0	72.6
7	71.7	71.2	70.4	70.1	70.2	71.0	69.7	69.6	75.4
8	45.4	45.2	41.9	41.6	42.5	41.2	41.3	41.4	45.3
9	34.3	34.8	48.1	47.7	48.0	48.7	48.8	48.6	36.0
10	39.5	39.7	42.5	42.1	42.3	41.2	39.5	40.3	41.1
11	24.2	24.5	207.1	213.4	206.3	205.4	212.4	212.5	31.1
12	71.2	77.6	79.2	78.8	77.9	48.6	79.3	78.9	92.0
13	51.4	51.4	46.4	46.0	45.6	43.6	45.7	45.7	142.4
14	157.4	157.1	71.4	72.9	71.9	72.7	60.9	60.3	143.0
15	122.7	122.8	59.5	59.2	58.8	58.0	219.0	218.5	77.9
16	36.6	36.6	33.4	33.1	33.8	32.0	44.9	44.7	38.0
17	50.3	50.5	38.9	38.5	38.1	39.2	41.7	41.2	46.7
18	26.9	26.8	23.1	22.7	22.4	21.7	21.7	21.2	16.4
19	15.2	15.3	65.0	64.6	64.1	64.3	64.2	57.8	16.2
20	124.5	124.4	121.1	123.5	122.5	123.3	124.2	124.1	128.1
21	140.3	140.2	142.6	142.3	142.4	143.3	143.4	143.0	138.9
22	111.7	111.6	113.1	112.7	111.9	110.8	111.3	111.0	110.3
23	142.1	142.0	141.0	140.6	140.7	139.8	140.4	140.1	142.7
28	78.0	78.2	19.5	19.2	18.8	19.5	19.0	18.3	78.0
29	19.7	20.0	94.6	94.2	93.5	94.2	94.1	102.9	18.8
30	15.3	15.8	14.7	14.4	15.5	14.2	22.8	22.8	20.7
Ac(*Me*)	20.9	21.3	21.8	21.4	20.7	20.8	21.6	21.4	21.1
	21.3				20.7				
					20.9				
Ac(*CO*)	170.2	170.9	169.7	169.8	168.9	166.6	170.1	169.9	170.2
	170.9				170.0				
					170.3				
COR	Tig		2-(Me)Bu	*iso*-Bu	*iso*-Bu	2-(Me)Bu	2-(Me)Bu	29-OMe	
1'	166.5		175.7	175.7	175.7	175.7	175.6	55.6	
2'	128.7		28.3	28.0	28.0	28.2	28.6		
2'-Me	11.9		16.8	18.6	18.7	16.4	16.8		
3'	138.0		26.9	18.9	18.7	22.8	26.8		
3'-Me	14.2		11.7			11.5	11.7		
COR'		Cin							Bz
1'		165.3							164.9
2'		117.1							130.5
3'		146.4							129.4
4'		133.9							128.5
5',9'		128.3							132.9
6',8'		129.0							128.5
7'		130.8							129.4
8'		129.0							
9'		128.3							

Table 1. ^{13}C NMR data of the limonoids from *M. toosendan* (continued)

C	36	37	38	40	42	45	46	47	49
1	71.2	71.7	71.5	71.5	71.9	70.8	70.8	71.1	72.2
2	29.3	27.6	27.8	27.2	27.7	30.5	28.0	28.0	28.4
3	72.5	71.8	71.8	72.8	72.0	75.1	70.9	70.3	71.8
4	42.4	42.4	42.4	42.6	42.7	47.1	42.3	42.7	43.0
5	39.2	40.6	40.6	40.0	40.5	39.5	35.0	35.1	39.4
6	72.6	71.8	70.8	71.8	72.0	69.1	71.1	71.1	74.9
7	74.6	75.6	73.9	75.2	75.3	85.3	83.5	83.8	67.3
8	45.2	45.1	45.0	47.4	47.3	47.5	51.5	51.2	60.3
9	38.2	37.0	37.3	38,7	38.9	35.9	47.8	47.9	35.9
10	41.0	40.1	40.8	40.7	40.9	41.9	49.9	49.7	39.3
11	31.1	32.5	32.7	32.0	32.0	25.0	106.7	107.0	34.0
12	92.4	171.2	171.2	173.6	173.2	172.5	170.1	170.1	76.6
13	142.2	138.4	138.6	133.5	133.5	135.7	94.9	94.9	81.6
14	142.7	147.9	146.8	148.5	148.7	146.1	93.1	93.3	96.7
15	77.8	83.9	85.4	82.0	82.2	87.6	81.2	81.1	80.7
16	38.2	37.7	37.6	36.7	36.7	41.2	29.8	29.7	32.6
17	46.8	47.0	47.0	47.5	47.4	49.6	50.8	50.8	45.2
18	16.4	16.0	16.0	16.9	17.0	17.0	26.4	25.9	20.7
19	16.2	15.4	15.5	16.0	16.4	16.7	70.4	70.7	16.9
20	128.2	126.5	126.5	127.8	127.9	126.9	86.3	86.2	123.9
21	139.0	139.2	143.5	143.2	143.2	143.0	109.3	109.3	142.7
22	110.3	110.0	110.0	109.8	109.9	110.6	108.0	107.9	111.4
23	142.9	143.4	139.2	139.5	139.5	138.9	145.7	145.8	139.9
28	77.9	78.0	78.0	78.0	77.8	204.3	76.4	76.5	79.1
29	18.8	19.2	18.9	19.7	20.1	14.4	18.3	18.0	20.8
30	20.7	20.1	20.5	20.1	20.2	13.0	17.7	17.8	42.6
Ac(*Me*)	21.1	20.1	20.8	20.7	20.7	20.5	21.0	21.0	21.3
		21.0		21.3	21.6	20.9			21.9
				21.6					
Ac(*CO*)	170.1	169.1	170.3	169.7	169.9	169.1	169.2	169.4	170.7
		169.6		170.0	171.0	170.1			170.7
				170.0					
COR	Tig	Tig	*iso*-Bu	*iso*-Bu	*iso*-Bu	Tig	11-OMe	Tig	Tig
1'	166.5	166.0	174.8	174.7	174.9	166.6	52.5	166.7	167.6
2'	128.8	128.6	34.7	33.5	33.6	128.9		128.4	129.3
2'-Me	12.2	12.1	19.5	17.6	17.6	12.0	CO_2Me	11.9	138.5
3'	136.7	137.2	19.5	19.9	29.8	137.7	53.3	138.2	12.5
3'-Me	14.5	14,5				14.1		14.4	15.0
COR'			Tig	CO_2Me	Tig		Cin		
1'			165.2	52.0	166.5	CO_2Me	165.6	11-OMe	
2'			129.0		129.4	51.6	117.3	52.3	
3'			12.2		12.0		145.8		
4'			137.6		136.4		133.9	$CO_2\mathit{Me}$	
5'			14.4		14.1		128.0	53.1	
6'							129.1		
7'							130.8		
8'							129.1		
9'							128.0		

3. INSECT ANTIFEEDANT ACTIVITY OF THE LIMONOIDS

Antifeedant activity of the limonoids from Meliaceae has been well studied.[1] Azadirachtin and related highly oxidized C-seco limonoids from *M. azadirachta indica* were known to be the most potent and their structure-activity relationships have been reported.[2] We also reported briefly antifeedant property of limonoids from Okinawan and Chinese *M. azedarach* and *M. toosendan.*[7]

The limonoids from *M. toosendan* and their effects on insect feeding are summarized in Table 2, which includes only naturally occurring limonoids. To develop a quantitative understanding of structure-activity relationships, the activity was tested by a conventional leaf disk method[47] against the third-instar larvae of voracious pest insects *Spodoptera eridania* and *S. littolalis* (Boisduval). The test was assessed by presenting each test compound on leaf disks to larvae and visually comparing the treated and untreated leaves eaten by the larvae. The feeding bioassay was terminated after the larvae had eaten approximately 50% of the control disk. To determine the minimum inhibitory concentration, this choice test was done at 50, 100, 150, 200, 300, 400, 500, and 1000 ppm, with 50 ppm corresponding to a concentration of *ca.* 1 μg/ leaf-cm^2. It is important to note that differences in the response of the test insects can mask any meaningful observations of structure-activity relations when compared with different test species. This is apparent from the data reported against different insects for compounds (12) and (44).

Some quantitative trends are apparent in the data in Table 2. The highly oxidized C-seco limonoids, meliacarpinins (46-48), are the most active of the limonoids from *M. toosendan* and much more potent antifeedants than the less oxidized class of C-seco limonoids exemplified by nimbolinins (34-36), ohchinolides (37 and 38), nimbolidins (39-43) and salannin (44). Aside from meliacarpinins, the most active compounds appear to be intact apo-euphol limonoids, amoorastatins (11 and 12), azedarachins (13-16), trichilins (19-25) and their 15-keto compounds (26-30), with a C-19/C-29 acetal bridged system (effective dose 150-500 ppm), in which 12-hydroxyamoorastatin (11) is the most active. In this class limonoids, some interesting structure-activity correlations are observed. First, activity is insensitive to substituent variation on ring A except for the nature of the C-29 bridged position: a hemiacetal bridge increases the activity in comparison to an acylated

Table 2. Antifeeding activity of limonoids from *M. toosendan*

Limonoid	Test insect	Effective conc. (ppm)	Refs	
			isolation	activity
Protolimonoid				
Butenolide (1)	*S. eridania*	not active	[15]	[37]
Meliacins				
Azadirone (2)	*S. eridania*	not active	[18]	[37]
Acetyltrichilenone (3)	*S. eridania*	not active	[19]	[37]
Trichilinins				
Trichilinin B (7)	*S. eridania*	1000	[22]	[22]
Trichilinin C (8)	*S. eridania*	1000	[22]	[22]
Trichilinin D (9)	*S. littoralis*	1000	[23]	[23]
Trichilinin E (10)	*S. littoralis*	1000	[23]	[23]
C-19/C-29 bridged acetals				
(14,15-Epoxide)				
12-Hydroxyamoorastatin (11)	*S. eridania*	150	[29]	[7]
Toosendanin (12)	*S. eridania*	300	[10,11]	[7]
	S. littoralis	300		[28]
	O. furnacalis	20		[48]
Azedarachin A (13)	*S. eridania*	200	[5]	[7]
12-*O*-Acetylazedarachin A (14)	*S. eridania*	400	[5]	[7]
	S. littoralis	400		[28]
Azedarachin B (15)	*S. littoralis*	200	[28]	[28]
12-*O*-Acetylazedarachin B (16)	*S. eridania*	400	[5]	[7]
Trichilin B (19)	*S. eridania*	200	[30]	[7]
Trichilin H (20)	*S. eridania*	400	[3]	[7]
Trichilin I (21)	*S. eridania*	400	[32]	[7]
Trichilin J (22)	*S. eridania*	400	[32]	[7]
Trichilin K (23)	*S. eridania*	400	[33]	[7]
Trichilin L (24)	*S. eridania*	400	[33]	[7]
1-*O*-Acetyltrichilin H (25)	*S. littoralis*	400	[34]	[34]
(15-Keto)				
12-hydroxyamoorastatone (26)	*S. eridania*	300	[29]	[34]
Iso-chuanliansu (27)	*S. littoralis*	400	[11]	[34]
Neoazedarachin A (28)	*S. littoralis*	400	[34]	[34]
Neoazedarachin B (29)	*S. littoralis*	400	[34]	[34]
Neoazedarachin D (30)	*S. littoralis*	400	[34]	[34]
Ring C-seco limonoids				
Nimbolinin A (34)	*S. littoralis*	1000	[23]	[23]
1-Deacetylnimbolinin A (35)	*S. littoralis*	1000	[23]	[23]
1-Deacetylnimbolinin B (36)	*S. littoralis*	1000	[38]	[23]
Ohchinolide B (37)	*S. eridania*	1000	[39]	[23]
Ohchinolide C (38)	*S. eridania*	1000	[37]	[38]

Table 2. Antifeeding activity of limonoids from *M. toosendan* (continued)

Limonoid	Test insect	Effective conc. (ppm)	Refs isolation	Refs activity
Nimbolidin B (39)	*S. eridania*	500	[39]	[42]
Nimbolidin C (40)	*S. eridania*	500	[42]	[42]
Nimbolidin D (41)	*S. eridania*	500	[42]	[42]
Nimbolidin E (42)	*S. eridania*	500	[42]	[42]
Nimbolidin F (43)	*S. eridania*	500	[37]	[38]
Salannin (44)	*S. eridania*	1000	[41]	[7]
	E. insulana	100		[49]
3-*O*-Acetylohchinolal (45)	*S. eridania*	1000	[37]	[37]
Highly oxidized C-seco limonoids				
Meliacarpinin A (46)	*S. eridania*	50	[4]	[6]
Meliacarpinin C (47)	*S. eridania*	50	[8]	[7]
Meliacarpinin D (48)	*S. eridania*	50	[8]	[7]
Spiro limonoid				
Spirosendan (49)	*S. littoralis*	1000	[44]	[44]

hemiacetal. The 12-OH group has also a pronounced effect and replacement of the 14,15-epoxide with a C-15 carbonyl results in reduced activity. Two meliacins (2 and 3) and four trichilinins (7-10) showed little or no activity. From these results, we believe that the antifeeding activity is due to a great extent to certain structural features contained within the 11/19 or 19/29 bridged acetal fragments inherent in all the foregoing active limonoids.

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