

Meliaceous Limonoids: Chemistry and Biological Activities

Qin-Gang Tan^{‡,§} and Xiao-Dong Luo^{*,‡}

[‡]State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650204, P.R.China

[§]Guilin Medical University, Guilin, 541004, P.R.China

CONTENTS

1. Background and Introduction	7437
2. Meliaceous Limonoids and Their Sources	7441
2.1. Ring Intact Limonoids	7441
2.1.1. Azadirone-Class	7441
2.1.2. Cedrelone-Class	7442
2.1.3. Havanensin-Class	7443
2.1.4. Trichilin-Class	7444
2.1.5. Vilasinin-Class	7444
2.1.6. Others	7445
2.2. Ring-seco Limonoids	7445
2.2.1. Demolition of a Single Ring	7445
2.2.2. Demolition of Two Rings	7449
2.2.3. Demolition of Three Rings (Rings A,B,D-seco Group)	7454
2.3. Rearranged Limonoids	7454
2.3.1. 1, <i>n</i> -Linkage Group	7454
2.3.2. 2,30-linkage Group	7456
2.3.3. 8,11-Linkage Limonoids (Trijugin-Class)	7463
2.3.4. 10,11-Linkage Limonoids (Cipadesin-Class)	7463
2.3.5. Other Linkages Group	7464
2.4. Limonoids Derivatives	7465
2.4.1. Pentanortriterpenoids, Hexanortriterpenoids, Heptanortriterpenoids, Octanortriterpenoids, and Enneanortriterpenoids Derivatives	7465
2.4.2. Simple Degraded Derivatives	7466
2.4.3. N-Containing Derivatives	7466
3. Chemotaxonomic Significance of Meliaceous Limonoids	7466
4. Synthesis of Meliaceous Limonoids	7468
5. Biological Activities of Meliaceous Limonoids	7484
5.1. Biological Activities in Agricultural Use	7485
5.1.1. Insects Antifeeding Activity	7485
5.1.2. Insects Growth Regulatory Activity	7491
5.1.3. Insecticidal Activity	7500
5.1.4. Antiphytopathogen Activity	7501
5.1.5. Others	7501
5.2. Biological Activities in Medicinal Use	7504
5.2.1. Antineoplastic Activity	7504

5.2.2. Antimicrobial Activity	7506
5.2.3. Antiprotozoal Activity	7506
5.2.4. Others	7507
Author Information	7508
Biographies	7508
Acknowledgment	7508
References	7509

1. BACKGROUND AND INTRODUCTION

The word "limonoids" originated from the bitterness of lemon or other citrus fruit. Structurally, limonoids are formed by loss of four terminal carbons of the side chain in the apotirucallane or apoeuphane skeleton and then cyclized to form the 17 β -furan ring, and thus limonoids are also known as tetranortriterpenoids. Limonoids in the plant kingdom occur mainly in the Meliaceae and Rutaceae families and less frequently in the Cneoraceae.¹ With 50 genera and more than 1400 species, Meliaceae are distributed in tropical and subtropical regions throughout the world.² As the characteristic natural products of the Meliaceae, limonoids have attracted considerable interest within the chemical and biological research communities. The neem tree (*Azadirachta indica*), one of the most famous limonoid producing plants in Meliaceae, has long been recognized as a source of environment-friendly biopesticide. Azadirachtin (292), a complex limonoid from neem seed kernel, is the main component responsible for the toxic effects on insects. The commercial application of the limonoids in the agricultural industry has enjoyed significant growth in recent decades. Commercial neem products (seed kernel extract of *A. indica*), such as Margosan-O, Azitin, Turplex, and Align were granted approval for pest control usage in the United States by the EPA.^{3–5} Furthermore, *A. indica* was also introduced and has been planted on a large scale in Yunnan province, P. R. China since the 2000s (Figure 1). Three commercial limonoids products (extracts of *A. indica*, *Melia toosendan*, and *M. azedarach*), known as biorational insecticides, were also granted approval in China for insect control on organic vegetable plantings. In a pharmaceutical application from China, a formulation with toosendanin, a limonoid from *M. toosendan* that displays dramatic antitubercular effects, was developed as a commercial product from TCM (Traditional Chinese Medicine), where it has been used as an anthelmintic vermifuge against ascarids for a long time.⁶

Some mini-reviews related to limonoids from Meliaceae have been presented since 1966. For example, the chemistry,^{7–13}

Received: December 14, 2009

Published: September 06, 2011

biosynthesis,^{1,13–15} and biological activities^{16–18} of meliaceous limonoids were summarized in different years. It is noteworthy that some reviews emphasize the well-known azadirachtin (**292**) and aspects of its chemistry,^{19–22} synthesis,^{23,24} and bioactivities including antifeedant activity,^{25–27} insecticidal activity,²⁵ and



Figure 1. *Azadirachta indica* at Yuanmou county, Yunnan Province, P. R. China. (A) Neem seedlings were bred on a large scale. (B) Neem trees were cultivated at both sides of the road. (C) Four-year-old neem trees produced plenty of fruit. Photographs courtesy of Dr. Yanping Zhang.

insect-growth-regulating activity,^{25,28,29} as well as its environmental behavior,¹⁹ and its physiological behavior properties.^{30,31} In addition, the toxicity characteristics of azadirachtin and the mechanisms of its insecticidal action^{32–35} were also reviewed. Reviews on the chemistry and biological activities of limonoids from *Azadirachta indica*,^{36–43} *Melia azedarach*, and *M. toosendan*^{37,44–47} have been presented. Moreover, some other reviews related to meliaceous limonoids have also been published, such as those on the chemistry of cedrelone (**81**),⁴⁸ the biological activity of gedunin (**416**),⁴⁹ and the occurrence, biosynthesis, biological activity, and NMR spectroscopy of D and B,D-ring seco-limonoids from Meliaceae.⁵⁰ However, none of them gave general insight into the chemistry and biological activities of meliaceous limonoids.

During our investigations on the biologically active constituents of Meliaceae, we noticed confusion and ambiguity about limonoids in the literature. (i) Some limonoids structures were

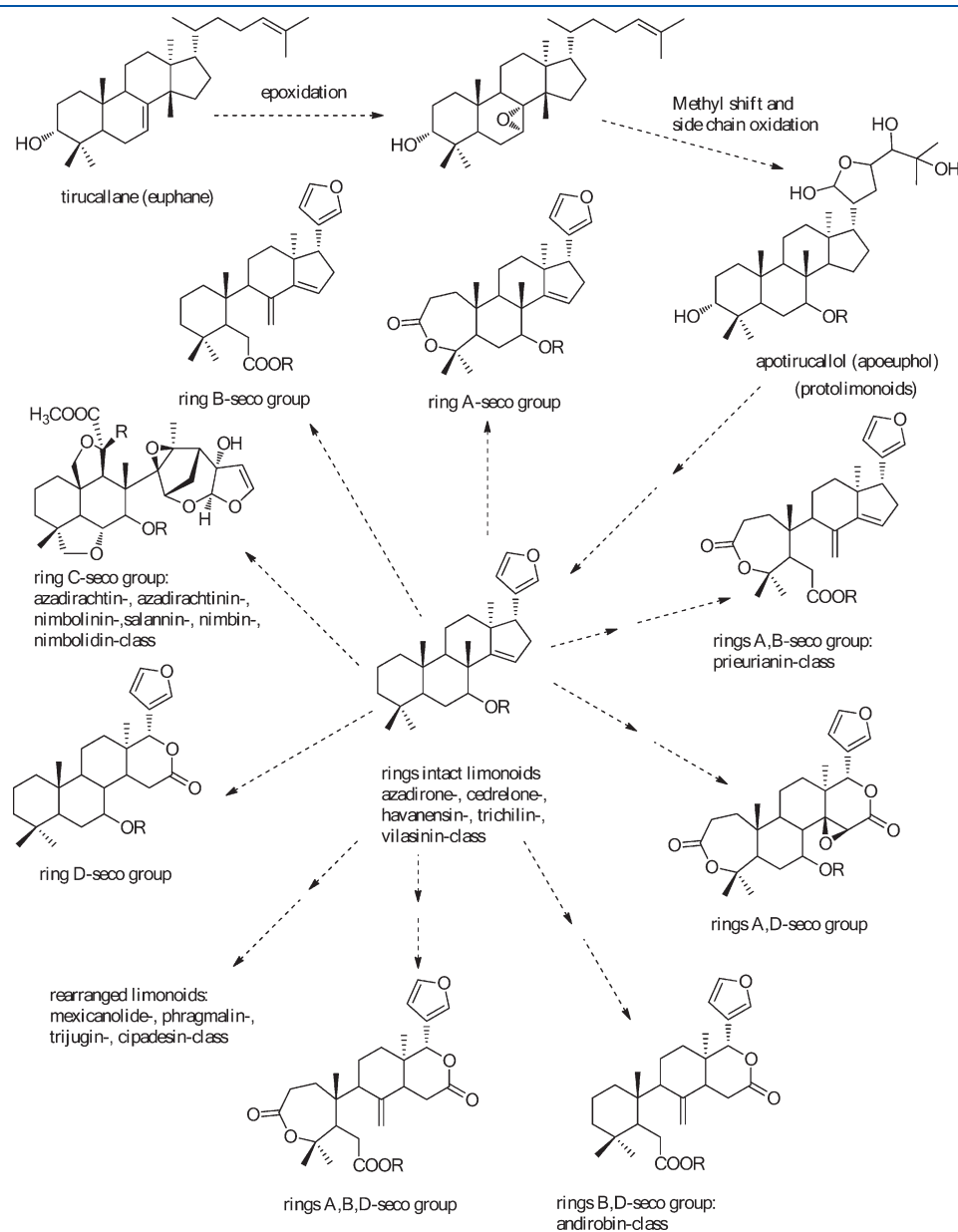


Figure 2. Proposed major biosynthesis routes and classification of meliaceous limonoids.

Table 1. Structures and Sources of Azadirone-Class Limonoids 1–80

no.	compounds	substitution groups and others	sources
1	azadirone	$R_1 = R_3 = R_4 = R_5 = H; R_2 = Ac$	<i>Azadirachta indica</i> ; ^{57–59,80–83} <i>Entandrophragma delevoyi</i> ; ⁷⁵ <i>Melia toosendan</i> ; ^{76,84,85} <i>Trichilia</i> <i>havanensis</i> ; ⁸⁶ <i>Turraea robusta</i> ; ⁸⁷ <i>Khaya anthotheca</i> ⁶⁰
2	7-deacetoxy-7-hydroxyazadirone	$R_1 = R_2 = R_3 = R_4 = R_5 = H$	<i>Walsura piscidia</i> ⁸⁸
3	11 α -acetoxyazadirone	$R_1 = R_4 = R_5 = H; R_2 = Ac,$ $R_3 = \alpha-OAc$	<i>Khaya anthotheca</i> ⁶⁰
4	11 β -acetoxyazadirone	$R_1 = R_4 = R_5 = H; R_2 = Ac,$ $R_3 = \beta-OAc$	<i>K. anthotheca</i> ^{60,89}
5	12 α -acetoxy-7-deacetylazadirone	$R_1 = R_2 = R_3 = R_5 = H; R_4 = OAc$	<i>Turraea cornucopia</i> ⁹⁰
6	chisosiamensin	$R_1 = R_3 = R_4 = R_5 = H;$ $R_2 = Ac; \Delta^{5,6}$	<i>Chisocheton siamensis</i> ⁹¹
7	nimonol (nimocinol)	$R_1 = \alpha-OH; R_2 = Ac; R_3 =$ $R_4 = R_5 = H$	<i>Azadirachta indica</i> ^{61,62,64,92}
8	6 α -O-acetyl-7-deacetylnimocinol	$R_1 = \alpha-OAc; R_2 = R_3 = R_4 =$ $R_5 = H$	<i>A. indica</i> ⁹³
9	6 α -acetoxyazadirone (paniculatin)	$R_1 = \alpha-OAc; R_2 = Ac; R_3 =$ $R_4 = R_5 = H$	<i>Chisocheton paniculatus</i> ; ^{69,94–96} <i>Entandrophragma delevoyi</i> ⁷⁵
10	nimocin	$R_1 = R_3 = R_4 = R_5 = H; R_2 = Bz$	<i>Azadirachta indica</i> ⁸⁰
11	dysobinin	$R_1 = \beta-OAc; R_2 = Ac; R_3 = R_4 =$ $R_5 = H$	<i>Dysoxylum binetiferum</i> ; ⁶⁶ <i>Chisocheton siamensis</i> ^{91,97}
12	azadiradione	$R_1 = R_3 = R_4 = H; R_2 = Ac; R_5 = O$	<i>C. siamensis</i> ; ^{91,97} <i>Cedrela odorata</i> ; ⁹⁸ <i>Quivisia papinae</i> ; ⁹⁹ <i>Lansium domesticum</i> ; ¹⁰⁰ <i>Azadirachta indica</i> ^{57,58,70,80–82,101–108}
13	nimbocinol (7-deacetylazadiradione)	$R_1 = R_2 = R_3 = R_4 = H; R_5 = O$	<i>A. indica</i> ^{101,109,110}
14	7-desacetyl-7-benzoylazadiradione (7-benzoylnimbocinol)	$R_1 = R_3 = R_4 = H; R_2 = Bz; R_5 = O$	<i>A. indica</i> ^{68,70}
15	7-deacetyl-7-angeloyl-6 α -hydroxyazadiradione	$R_1 = \alpha-OH; R_2 = Ang; R_3 =$ $R_4 = H; R_5 = O$	<i>Quivisia papinae</i> ⁹⁹
16	6 α -hydroxyazadiradione	$R_1 = \alpha-OH; R_2 = Ac; R_3 = R_4 = H;$ $R_5 = O$	<i>Q. papinae</i> ⁹⁹
17	6 α -acetoxy-16-oxoazadirone (mahonin)	$R_1 = \alpha-OAc; R_2 = Ac; R_3 = R_4 = H;$ $R_5 = O$	<i>Chisocheton paniculatus</i> ; ⁶⁹ <i>Swietenia mahagoni</i> ^{71,111,112}
18	17 β -hydroxyazadiradione	$R_1 = H; R_2 = Ac$	<i>Carapa guianensis</i> ; ¹¹³ <i>Azadirachta indica</i> ^{70,81,103,104,109,114–116}
19	7-deacetyl-17 β -hydroxyazadiradione	$R_1 = R_2 = H$	<i>A. indica</i> ^{101,107}
20	6 α -acetoxy-17 β -hydroxyazadiradione	$R_1 = OAc; R_2 = Ac$	<i>Chisocheton paniculatus</i> ^{94,117}
21	7-benzoyl-17-hydroxynimbocinol	$R_1 = H; R_2 = Bz$	<i>Azadirachta indica</i> ⁷⁰
22	15-hydroxyazadiradione		<i>A. indica</i> ⁷⁰
23	7-acetyl-16,17-dehydro-16-hydroxyneotrichilenone		<i>A. indica</i> ⁷⁰
24	isonimolide	$R_1 = OCH_3; R_2 = Ac; R_3 =$ $R_4 = R_5 = H; R_6 = OH; R_7 = O$	<i>A. indica</i> ¹¹⁸
25	isolimbolide	$R_1 = R_5 = H; R_2 = Ac; R_3 = OAc;$ $R_4 = R_6 = OH; R_7 = O$	<i>A. indica</i> ¹¹⁸
26	nimocinolide	$R_1 = R_7 = OH; R_2 = Ac; R_3 =$ $R_4 = R_5 = H; R_6 = O$	<i>A. indica</i> ⁸⁰
27	23-O-methylnimocinolide	$R_1 = OH; R_2 = Ac; R_3 = R_4 =$ $R_5 = H; R_6 = O; R_7 = OCH_3$	<i>A. indica</i> ¹¹⁹
28	7-O-deacetyl-23-O-methyl-7 α -O-senecioldimocinolide	$R_1 = OH; R_2 = Sen; R_3 = R_4 = R_5 = H;$ $R_6 = O; R_7 = OCH_3$	<i>A. indica</i> ^{119,120}
29	isonimocinolide	$R_1 = R_6 = OH; R_2 = Ac; R_3 = R_4 = R_5 = H;$ $R_7 = O$	<i>A. indica</i> ^{80,118}

Table 1. Continued

no.	compounds	substitution groups and others	sources
30	nimbocinolide	$R_1 = R_5 = H$; $R_2 = Ac$; $R_3 = OiBu(OH)$; $R_4 = R_7 = OH$; $R_6 = O$	<i>A. indica</i> ¹²¹
31	isonimbocinolide	$R_1 = R_5 = H$; $R_2 = Ac$; $R_3 = OiBu(OH)$; $R_4 = R_6 = OH$; $R_7 = O$	<i>A. indica</i> ¹²²
32	meliacinanhydride	$R_1 = OH$; $R_2 = Ac$; $R_3 = OCH_3$; $R_4 = OAc$; $R_5 = H$; $R_6 = R_7 = O$	<i>A. indica</i> ⁹²
33	22,23-dihydronimocinol	$R_1 = OH$; $R_2 = Ac$; $R_3 = R_4 = R_5 = R_6 =$ $R_7 = H$; 22,23-dihydro; $\Delta^{20,21}$	<i>A. indica</i> ¹²⁰
34	azadironolide	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = Ac$; $R_6 = O$; $R_7 = OH$	<i>A. indica</i> ¹²³
35	O-methylazadironolide	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = Ac$; $R_6 = O$; $R_7 = OCH_3$	<i>A. indica</i> ¹²⁴
36	12 α -acetoxyazadironolide	$R_1 = R_3 = R_5 = H$; $R_2 = Ac$; $R_4 = OAc$; $R_6 = O$; $R_7 = OH$	<i>Turraea parvifolia</i> ¹²⁵
37	23-deoxyazadironolide	$R_1 = R_3 = R_4 = R_5 = R_6 = H$; $R_2 = Ac$; $R_7 = O$	<i>Azadirachta indica</i> ⁷⁰
38	isoazadironolide	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = Ac$; $R_6 = OH$; $R_7 = O$	<i>A. indica</i> ; ¹²³ <i>Turraea pubescens</i> ¹²⁶
39	azadiradionolide	$R_1 = R_3 = R_4 = R_7 = H$; $R_2 = Ac$; $R_5 = R_6 = O$	<i>Azadirachta indica</i> ^{70,123,127}
40	salimuzzalin	$R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = R_7 = OAc$	<i>A. indica</i> ¹²⁸
41	turraparvin A	$R_1 = R_2 = R_3 = R_5 = H$; $R_4 = OAc$; $R_6 = O$; $R_7 = OH$	<i>Turraea parvifolia</i> ¹²⁵
42	turraparvin B	$R_1 = R_2 = R_3 = R_5 = H$; $R_4 = OAc$; $R_6 = OH$; $R_7 = O$	<i>T. parvifolia</i> ¹²⁵
43	turraparvin C	$R_1 = R_3 = R_5 = H$; $R_2 = Ac$; $R_4 = OAc$; $R_6 = OH$; $R_7 = O$	<i>T. parvifolia</i> ¹²⁵
44		$R_1 = OAc$; $R_2 = Ac$; $R_3 = R_4 = R_5 = H$; $R_6 = OH$; $R_7 = O$	<i>Chisocheton paniculatus</i> ¹¹⁷
45	7 α ,23-dihydroxy-3-oxo-24,25,26,27-tetranortirucall-1,14,20(22)-trien-21,23-olide	$R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = O$; $R_7 = OH$	<i>Trichilia estipulata</i> ¹²⁹
46	limocin A	$R_1 = R_4 = H$; $R_2 = Ac$; $R_3 = \alpha-OCH_3$	<i>Azadirachta indica</i> ⁷⁹
47	limocin B	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = OCH_3$	<i>A. indica</i> ⁷⁹
48	23-desmethyl limocin B	$R_1 = R_4 = H$; $R_2 = Ac$; $R_4 = OH$	<i>A. indica</i> ¹³⁰
49	limocin C	$R_1 = R_4 = H$; $R_2 = Ac$; $R_3 = OCH_2CH_3$	<i>A. indica</i> ¹²⁷
50	limocin D	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = OCH_2CH_3$	<i>A. indica</i> ¹²⁷
51	limocin E	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = \alpha-OCH_3$	<i>A. indica</i> ⁷⁰
52	23-epilimocin E	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = \beta-OCH_3$	<i>A. indica</i> ⁷⁰
53		$R_1 = R_2 = R_3 = H$; $R_4 = O$	<i>Chisocheton microcarpus</i> ¹³¹
54		$R_1 = OAc$; $R_2 = Ac$; $R_3 = H$; $R_4 = O$	<i>C. paniculatus</i> ¹¹⁷
55		$R_1 = OAc$; $R_2 = Ac$; $R_3 = H$; $R_4 = OH$	<i>C. paniculatus</i> ¹¹⁷
56	20,21,22,23-tetrahydro-23-oxoazadirone	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = O$	<i>C. microcarpus</i> ; ¹³¹ <i>Cedrela odorata</i> ; ⁹⁸ <i>C. fissilis</i> ; ¹³² <i>Azadirachta indica</i> ⁷⁰
57	meliatoosenin A	$R_1 = R_3 = H$; $R_2 = R_4 = O$	<i>Melia toosendan</i> ¹³³
58	meliatoosenin B	$R_1 = R_2 = R_3 = H$; $R_4 = O$; 1,2-dihydro	<i>M. toosendan</i> ¹³³
59	isonimolcinolide		<i>Azadirachta indica</i> ⁷²
60	nimbinin (epoxyazadiradione)	$R_1 = R_3 = R_4 = H$; $R_2 = Ac$; $R_5 = O$	<i>A. indica</i> ; ^{57,58,70,73,78,80–82,103–106,115,134–136} <i>Carapa guianensis</i> ; ¹³⁷ <i>Entandrophragma delevoyi</i> ; ⁷⁵ <i>Chisocheton siamensis</i> ⁹¹
61	7-desacetyl-7-benzoylpoxyazadiradione	$R_1 = R_3 = R_4 = H$; $R_2 = Bz$; $R_5 = O$	<i>Azadirachta indica</i> ^{68,70}
62	6 α -acetoxyepoxyazadiradione	$R_1 = OAc$; $R_2 = Ac$; $R_3 = R_4 = H$; $R_5 = O$	<i>Carapa guianensis</i> ; ¹³⁷ <i>Chisocheton siamensis</i> ^{91,138}
63	14,15-epoxynimonol	$R_1 = OH$; $R_2 = Ac$; $R_3 = R_4 = R_5 = H$	<i>Azadirachta indica</i> ¹³⁹

Table 1. Continued

no.	compounds	substitution groups and others	sources
64	trichilenone acetate (14 β ,15 β -epoxyazadirone; acetyltrichilenone)	R ₁ = R ₃ = R ₄ = R ₅ = H; R ₂ = Ac	<i>Melia toosendan</i> ; ^{76,84} <i>Azadirachta indica</i> ; ¹²⁴ <i>Trichilia havanensis</i> ; ⁷⁴ <i>Entandrophragma deleveyi</i> ⁷⁵
65	6 α -acetoxy-14 β ,15 β -epoxyazadirone	R ₁ = OAc; R ₂ = Ac; R ₃ = R ₄ = R ₅ = H	<i>E. deleveyi</i> ; ⁷⁵ <i>Toona ciliata</i> ; ¹⁴⁰ <i>Chisocheton paniculatus</i> ⁹⁴
66	heudelottin C	R ₁ = R ₅ = H; R ₂ = iVal(OH); R ₃ = OH; R ₄ = O-2-acetoxy-3-methylpentanoyl	<i>Trichilia heudelottii</i> ⁷⁷
67	heudelottin E	R ₁ = R ₅ = H; R ₂ = iVal(OH); R ₃ = OCHO; R ₄ = O-2-hydroxy-3-methylpentanoyl	<i>T. heudelottii</i> ; ^{77,141}
68	heudelottin F	R ₁ = R ₅ = H; R ₂ = iVal(OH); R ₃ = OCHO; R ₄ = O-2-acetoxy-3-methylpentanoyl	<i>T. heudelottii</i> ⁷⁷
69	6-acetoxy-7 α -hydroxy-3-oxo-14 β ,15 β - epoxymeliace-1,5-diene	R ₁ = OAc; R ₂ = R ₃ = R ₄ = R ₅ = H; Δ ^{5,6}	<i>Melia azedarach</i> ¹⁴²
70	7-acetoxyneotrichilenone	R ₁ = R ₃ = H; R ₂ = Ac	<i>Azadirachta indica</i> ⁶⁸
71	12 α -acetoxyneotrichilenone	R ₁ = R ₂ = H; R ₃ = OAc;	<i>Turraea floribunda</i> ¹⁴³
72	walsurin	R ₁ = O; R ₂ = R ₃ = H	<i>Walsura yunnanensis</i> ¹⁴⁴
73	toonaciliatone A	R ₁ = OH; R ₂ = R ₃ = H	<i>Toona ciliata</i> ¹⁴⁵
74	7-deacetyl-21-hydroxyneotrichilenonolide	R ₁ = OH; R ₂ = O	<i>Trichilia estipulata</i> ¹²⁹
75	7-deacetyl-23-hydroxyneotrichilenonolide	R ₁ = O; R ₂ = OH	<i>T. estipulata</i> ¹²⁹
76	17-epinimbocinol	R ₁ = R ₂ = H	<i>Azadirachta indica</i> ^{110,146}
77	17-epiazadiradione	R ₁ = Ac; R ₂ = H	<i>A. indica</i> ^{70,103,104,114}
78	17-epi-17-hydroxyazadiradione	R ₁ = Ac; R ₂ = OH	<i>A. indica</i> ^{70,107}
79	vepinin		<i>A. indica</i> ⁷⁸
80	limocinin		<i>A. indica</i> ⁷⁹

assigned incorrectly because of the lack of the advanced spectral methods, such as 2D-NMR, HRMS, in the early time. For example, even though azadirachtin (**292**) was found early in 1968,⁵¹ its structure was revised several times before the final unambiguous assignment was made in 1986.⁵² (ii) On one hand, some limonoids were given the same nomenclature but had different structures, such as cipadesin D being used for both compound **578**⁵³ and **1038**⁵⁴ even though they were ascribed to different classes. On the other hand, some limonoids have the same structure but different names. Taking compound **805** as an example, it was first reported as 8,30-epoxy swietenine acetate in 1983⁵⁵ and subsequently mistaken as swietemahonin F in 1990.⁵⁶

This review is an extensive coverage of all naturally occurring limonoids from Meliaceae discovered in the last six decades (from 1942 to June 30, 2010) along with their various bioactivities. The distribution, chemotaxonomy significance, synthesis, and biological activity of meliaceous limonoids are summarized. In the cases where sufficient information is available, the structure–activity relationship (SAR) and the mode of action of the active limonoids have been presented. Furthermore, we try to clarify the confusing trivial names in meliaceous limonoid investigations. However, limonoids whose names were not proposed by their discoverers (**44**, **53–55**, **119**, **125–127**, **231**, **457**, **511**, **563**, **602**, **607**, and **844**) were presented only with numbers in the tables.

2. MELIACEOUS LIMONIDS AND THEIR SOURCES

Limonoids are supposed to arise from Δ^7 -tirucallol (20S) or Δ^7 -euphol (20R). The Δ^7 -bond is epoxidized and is then opened inducing a Wagner–Meerwein shift of Me-14 to C-8, which leads to the formation of the OH-7 and the introduction of a double bond at C-14/15. This scheme account for both the ubiquitous presence of oxygen at C-7 and the correct stereochemistry of the C-30 methyl group. Subsequently the side chain is cyclized with

the loss of four carbons to form the 17 β -furan ring. That the latter step is accomplished after the formation of the 4,4,8-trimethyl-steroid skeleton is indicated by the occurrence of several protolimonoids. Followed formation of the basic limonoid skeleton, a variety of oxidations and skeletal rearrangements can occur and lead to various classes of limonoids (Figure 2),¹⁷ which will be discussed in detail in this review.

2.1. Ring Intact Limonoids

2.1.1. Azadirone-Class. Azadirone-type limonoids are characteristic of 3-oxo- $\Delta^{1,2}$ and C-7 oxygenation. In their ¹H NMR spectroscopy, the chemical shifts of H-1 and H-2 were δ 7.0–7.2 and 5.7–6.0, respectively, which showed the coupling constant of \sim 10 Hz. In their ¹³C NMR spectroscopy, the α,β -unsaturated ketone system exhibited signals of δ = 156–160 (C-1), 124–127 (C-2), and 202–205 (C-3), respectively. The signal of H-7 (δ 5.2–5.4) might shift by 0.1–0.2 ppm and the signal of C-7 (\sim δ 70–75) shifts to 75–83 ppm if C-6 is oxygenated.

Azadirone (**1**) was first isolated from oil of *Azadirachta indica* in 1967,⁵⁷ and its structure was later elucidated in 1971.⁵⁸ It was also obtained from a rare stem exudation of *A. indica*, together with nimbin (**391**) and gedunin (**416**).⁵⁹ The interrelationship between azadirone (**1**), azadiradione (**12**), and nimbinin (**60**) was analyzed in terms of a possible chemical degradation through a stepwise oxidation and transformation in nature.⁵⁸ The relative stereochemistry of 11 α - and 11 β -acetoxyazadirone (**3** and **4**) was assigned from the downfield shift of the angular methyl groups at C-8 and C-10, in which the shifts in the 11 β -isomer were more strongly influenced by the acetate function.⁶⁰

The structure corresponding to **7** was assigned to be nimonol^{61,62} and confirmed by crystal analysis⁶³ despite once having been mistaken to be nimocinol.⁶⁴ Photooxygenation of nimonol (**7**) yielded a novel product, 14,15,20,21-diepoxy-23-nimonolactone, and involved interesting Diels–Alder and ene

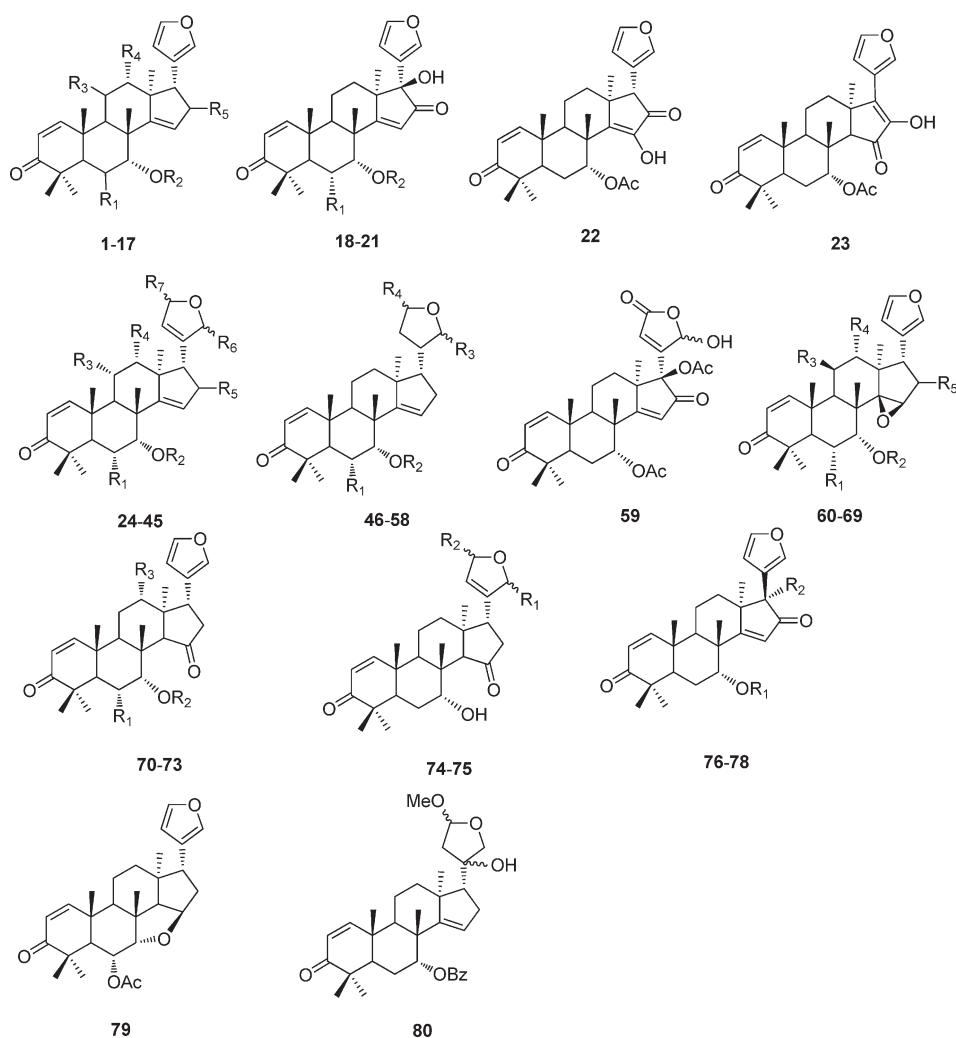


Figure 3. Structures of azadirone-class limonoids 1–80.

reactions. This was the first example of the photolysis of intact limonoids in the absence of a sensitizer and of the epoxidation of the D-ring with an α stereochemistry under photolysis.⁶⁵ The structure of dysobinin (**11**) was elucidated on the basis of chemical evidence⁶⁶ and then confirmed by X-ray diffraction.⁶⁷ 7-Desacetyl-7-benzoylazadiradione (**14**)⁶⁸ and 6 α -acetoxy-16-oxoazadirone (**17**)⁶⁹ were mistaken for 7-benzoylnimbocinol⁷⁰ and mahonin,⁷¹ respectively. Isonimolicinolide (**59**), the first limonoid with an acetoxy function at C-17, might be regarded as a possible intermediate in the biosyntheses of 17 β -hydroxyazadiradione (**18**) and nimolicinol (**451**).⁷² Compound **60** was obtained and named as epoxyazadiradione⁵⁷ and nimbinin⁷³ by two separate research groups in 1967. The structure corresponding to **64** was first named as trichilenone acetate early in 1973,⁷⁴ and mistaken for 14 β ,15 β -epoxyazadirone in 1994⁷⁵ and acetyl-trichilenone in 1995,⁷⁶ when it was isolated from different plants. Heudelottins E and F (**67** and **68**) were of interest because they were the simplest limonoids containing the 11 β -formyloxy-12 α -(2-hydroxy-3-methylvaleryloxy) system, which had been found very commonly in the complex A,B-seco limonoids of priurianin class.⁷⁷ Three 17-*epi* isomers **76–78** obtained from *A. indica* were rare in limonoids from Meliaceae. Vepinin (**79**)⁷⁸ and limocinin (**80**)⁷⁹ two unique compounds from *A. indica*,

were distinguished by the 7 α ,15 β -epoxy ring of the former and the –OH substitution at C-20 of the latter.

2.1.2. Cedrelone-Class. The cedrelone-class limonoids are characterized as the 5,6-enol-7-one derivatives. The ¹³C NMR spectra showed signals of δ = 132–135 (C-5), 140–143 (C-6), and 196–199 (C-7). The UV spectra showed the absorption at 277 nm (in EtOH) from the diosphenol chromophore.

The molecular formula of cedrelone (**81**), the principal constituent of *Cedrela toona*, was first assigned as C₂₅H₃₀O₅,¹⁴⁷ and later was revised to be C₂₆H₃₀O₅ based on chemical and mass spectroscopic work.^{148–151} Its structure was finally confirmed by X-ray diffraction.¹⁵² Furthermore, the X-ray study of cedrelone iodoacetate proved its biosynthetic relationship to limonin.^{148,153} On the basis of the HMBC and DEPT experiments, the signals for C-9, -11, -12, -17, -21, -23, and -28 of **81** were reassigned.¹⁵⁴ The chemistry of **81** was reviewed in some detail by Govindachari in 1968.⁴⁸ The structure of one of the photooxidation product of **81**, in particular the product with epoxy lactone, was established by NMR data and confirmed by X-ray crystallography.¹⁵⁵

In the course of model experiments with anthothecol (**84**) aimed at structural correlation with 11 β -acetoxyazadirone (**4**), a Zn–Cu couple was found in the meliacin series to be a

Table 2. Structures and Sources of Cedrelone-Class Limonoids 81–105

no.	compounds	substitution groups and others	sources
81	cedrelone	$R_1 = R_2 = H$	<i>Cedrela toona</i> ; ^{147,158–160} <i>Toona ciliata</i> ; ^{154,161} <i>T. australis</i> ; ¹⁶² <i>Khaya anthotheca</i> ; ^{163,164} <i>Trichilia catigua</i> ; ¹⁶⁵ <i>Walsura yunnanensis</i> ¹⁴⁴
82	11 β -hydroxycedrelone	$R_1 = \beta\text{-OH}$; $R_2 = H$	<i>W. yunnanensis</i> ¹⁴⁴
83	11 β ,12 α -diacetoxycedrelone	$R_1 = \beta\text{-OAc}$; $R_2 = \alpha\text{-OAc}$	<i>Turraea holstii</i> ¹⁴³
84	anthothecol	$R_1 = \alpha\text{-OAc}$; $R_2 = H$	<i>Khaya anthotheca</i> ^{60,89,163,164,166–168}
85	deacetylantothecol	$R_1 = \alpha\text{-OH}$; $R_2 = H$	<i>K. anthotheca</i> ^{89,163}
86	23-hydroxycedrelonolide (walsuranolide)	$R_1 = H$; $R_2 = O$; $R_3 = OH$	<i>Toona ciliata</i> ; ¹⁵⁴ <i>Walsura yunnanensis</i> ¹⁴⁴
87	11 β -acetoxywalsuranolide	$R_1 = OAc$; $R_2 = O$; $R_3 = OH$	<i>W. yunnanensis</i> ¹⁴⁴
88	20,22-dihydro-22,23-epoxywalsuranolide	$R_1 = H$; $R_2 = O$; 20,22-dihydro; 22,23-epoxy	<i>W. yunnanensis</i> ¹⁴⁴
89	21-hydroxycedrelonolide (isowalsuranolide)	$R_1 = H$; $R_2 = OH$; $R_3 = O$	<i>W. yunnanensis</i> ; ¹⁴⁴ <i>Toona ciliata</i> ¹⁵⁴
90	1,2-dihydrocedrelone	$R = H$	<i>Cedrela toona</i> ¹⁵⁸
91	11 β -hydroxydihydrocedrelone	$R = \beta\text{-OH}$	<i>Walsura yunnanensis</i> ¹⁴⁴
92	11 β -acetoxydihydrocedrelone	$R = \beta\text{-OAc}$	<i>W. yunnanensis</i> ¹⁴⁴
93	1 α ,11:14 β ,15 β -diepoxy-6-hydroxymeliaca-5,9,20,22-tetraene-3,7-dione		<i>Khaya anthotheca</i> ⁶⁰
94	hirtin	$R_1 = Ac$; $R_2 = \text{propanoyl}$	<i>Trichilia hirta</i> ; ^{169,170} <i>T. pallida</i> ¹⁷¹
95	deacetylhirtin	$R_1 = H$; $R_2 = \text{propanoyl}$	<i>T. hirta</i> ; ¹⁶⁹ <i>T. pallida</i> ¹⁷¹
96	methyl 6-hydroxy-11 β -acetox-12 α -(2-methylpropanoyloxy)-3,7-dioxo-14 β ,15 β -epoxy-1,5-meliacadien-29-oate	$R_1 = Ac$; $R_2 = iBu$	<i>T. pallida</i> ¹⁷¹
97	methyl 6,11 β -dihydroxy-12 α -(2-methylpropanoyloxy)-3,7-dioxo-14 β ,15 β -epoxy-1,5-meliacadien-29-oate	$R_1 = H$; $R_2 = iBu$	<i>T. pallida</i> ¹⁷¹
98	methyl 6-hydroxy-11 β -acetox-12 α -(2-methylbutanoyloxy)-3,7-dioxo-14 β ,15 β -epoxy-1,5-meliacadien-29-oate	$R_1 = Ac$; $R_2 = \text{Piv}$	<i>T. pallida</i> ¹⁷¹
99	methyl 11 β -acetox-6-hydroxy-12 α -(2-methylpropionyloxy)-3,7-dioxo-1,5,14,20,22-meliacapentaen-29-oate		<i>T. hirta</i> ¹⁷²
100	methyl 11 β -acetox-6,23-dihydroxy-12 α -(2-methylpropionyloxy)-3,7,21-trioxo-1,5,14,20,22-meliacatetraen-29-oate		<i>T. hirta</i> ¹⁷²
101	azecin 3	$R_1 = \alpha\text{-L-Rha-(1}\rightarrow\text{4)-}\beta\text{-D-Glc-(1}\rightarrow\text{6)-}\beta\text{-D-Glc}$; $R_2 = H$	<i>Melia azedarach</i> ¹⁷³
102	6,11-diacetox-7-oxo-14 β ,15 β -epoxymeliacin-1,5-diene-3- $O\text{-}\beta\text{-D-glucopyranoside}$	$R_1 = \beta\text{-D-Glc}$; $R_2 = OAc$	<i>M. azedarach</i> ¹⁷⁴
103	6-acetox-3 β -hydroxy-7-oxo-14 β ,15 β -epoxymeliac-1,5-diene-3- $O\text{-}\beta\text{-D-xylopyranoside}$	$R_1 = \beta\text{-D-Xyl}$; $R_2 = H$	<i>M. azedarach</i> ¹⁷⁵
104	6-acetox-11 α -hydroxy-7-oxo-14 β ,15 β -epoxymeliacin-1,5-diene-3- $O\text{-}\alpha\text{-L-rhamnopyranoside}$	$R_1 = \alpha\text{-L-Rha}$; $R_2 = OH$	<i>M. azedarach</i> ¹⁷⁶
105	6-acetox-3 β -hydroxy-7-oxo-14 β ,15 β -epoxymeliac-1,5-diene-3- $O\text{-}\beta\text{-D-glucuronopyranoside}$	$R_1 = \beta\text{-D-glucuronic acid}$; $R_2 = H$	<i>M. azedarach</i> ¹⁴²

convenient and superior reagent for the reduction of epoxides to olefins, α,β -unsaturated ketones to saturated ketones, and ketols and their acetates to ketones.⁸⁹ Burke et al. presented the chemical correlation of **84** with hirtin (**94**), which differ in oxidation status at C-29.¹⁵⁶ Walsuranolide and isowalsuranolide reported by Luo et al. in 2000¹⁴⁴ were actually 23-hydroxycedrelonolide (**86**) and 21-hydroxycedrelonolide (**89**) isolated in 1994,¹⁵⁴ respectively, whose structures were introduced incorrectly as 30-nor (C-8 Methyl) derivatives by Chemical Abstracts (CA, 1994). In the crystal structure which was established for 1,2-dihydrocedrelone (**90**), the rings A, B, C, and D adopted sofa, half-chair, twist and envelope conformations, respectively.¹⁵⁷ In 1 α ,11:14 β ,15 β -diepoxy-6-hydroxymeliaca-5,9,20,22-tetraene-3,7-dione (**93**), an unusual compound with a 1,11-ether and a

9,11-double bond, the enol ether group of was stable to both acid and base. This unreactivity was probably because of steric hindrance to attack on the enol system.⁶⁰

2.1.3. Havanensin-Class. The havanensin-class limonoids bear oxygenic substituent at C-1, C-3, and C-7, and the degree of oxidation at C-28 varies from methyl to carboxyl. Under mildly acid conditions, the first stage of the ring-opening of havanensin (**106**) gives a 15-hydroxy-14-carbonium ion, which then either undergoes Wagner–Meerwein rearrangement or loses a proton to give a 15-ketone enolate and involves participation of the oxygenated function at C-7.¹⁷⁷ Grandifolione (**112**) was the first natural representative of a stage regarded as intermediate in the in vivo transformation of apo-euphol (or apo-tirucallo) into the typical pentenolide system found in limonoids.¹⁷⁸

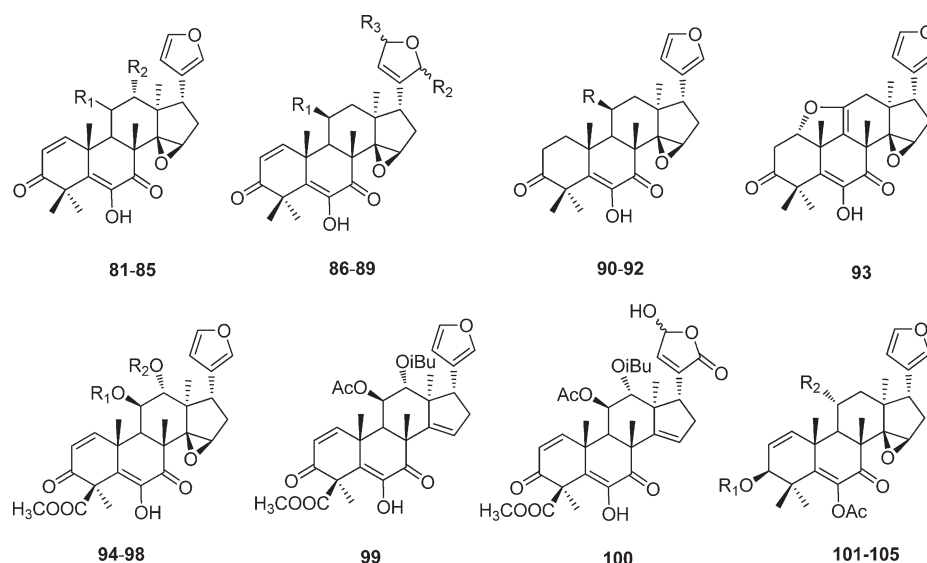


Figure 4. Structures of cedrelone-class limonoids 81–105.

14,15-Deoxyhavanensin 3,7-diacetate (**114**) and deoxyhavanensin triacetate (**115**) isolated from the unripened seeds of *Trichilia havanensis* revealed a lower degree of oxidation of the limonoid skeleton and could be viewed as the biosynthetic precursors of the limonoids isolated from the mature seeds.⁸⁶ Sendanal (**122**) was of biosynthetic interest from the viewpoint that it was closely related to a precursor of the 14,15-epoxy-12-hydroxy moiety, which could yield limonoids of the nimbin class through a Grob fragmentation followed by formation of an ether ring between the C-7 and C-15 hydroxyl groups via an S_N1 mechanism. The co-occurrence of **122** and ohchinal (**343**) in the same tree provided a piece of evidence for such pathway.¹⁷⁹ Unfortunately, limonoids **131**–**134** isolated by Torto et al. were named mistakenly as 28-nor-4 α -carbomethoxy derivatives of havanensin (**106**). However, C-28 of **131**–**134** was present and so numbered in the original paper, and **131** was confirmed by X-ray diffraction.¹⁸⁰

2.1.4. Trichilin-Class. The trichilin-class limonoids mostly originated from genera *Melia* and *Trichilia* (Table 4), and contained the C-19/29 lactol bridge and the 14,15-epoxide moieties except in compounds **172**–**185**. The ¹³C NMR spectral assignments for trichilin A (**135**) were revised based on 2D-NMR data in 1998.¹⁹² Treatment of **135** with zinc borohydride in 2-propanol led to acyl migration in ring A and gave its 1,2-diacetyl and 1,3-diacetyl isomers.¹⁹³ Trichilin D (**141**) from *Trichilia roka*, first assigned in 1981,¹⁹⁴ was subsequently obtained from *Melia azedarach* and mistaken for meliatoxin A₁ in 1983.¹⁹⁵ The structure of aphanastatin (**142**), along with amoorastatin (**165**) and 12 α -hydroxyamoorastatin (**166**) isolated from *Aphanamixis grandifolia*, has been determined from three-dimensional X-ray diffraction data.^{196,197} The absolute configuration of sendanin (**156**) was proposed based on CD data,¹⁹⁸ and the structure was confirmed by crystallographic means.¹⁹⁹ As concerns biosynthesis, it should be noted that all trichilins isolated from the root bark of *Trichilia roka* were oxidized at the C-2 position,^{194,200} while **156** obtained from the fruit of *T. roka* was not oxidized at C-2.¹⁹⁸ The structure of **156** could not be studied directly because it had been isolated from *Melia azedarach* only after acetylation of the crude limonoid fraction. Therefore the structure of its natural –OH precursor was studied and it was determined from the chemical and spectral data obtained that

156 derived from that precursor should be an epimer mixture of the hemiacetal.²⁰¹ The structure of 28-deacetylSENDANIN referred to in some literature^{202–204} should in fact be 29-deacetylSENDANIN (**157**),²⁰⁵ which was isolated as a 5:3 mixture of epimer with respect to C-29.²⁰⁶ In fact, the structure of compound 29-isobutylSENDANIN²⁰⁵ obtained from *Melia azedarach* in 1995 was the same as 12-O-acetylazedarachin B (**161**)²⁰⁷ found in 1994 in the same species. Meliartenin (**164**) was shown to be a mixture of two interchangeable isomers.²⁰⁸ Huang et al. mistook compound **166** as 12-deacetyltoosendanin²⁰⁹ when citing its origin, in which it was in fact named as 12 α -hydroxyamoorastatin.²¹⁰ The structure of toosendanin^{211,212} and 12 α -acetoxyamoorastatin^{213,214} was in fact proved to be identical with that of chuanliansu (**167**), which was first assigned in 1975²¹⁵ and subsequently corrected in 1980.²¹⁶ Based on the observation of a significant difference in the chemical shift between 3 α -deacetylamoarastatin (**168**, δ C-9: 39.5) and 9 β -amoarastatin (**169**, δ C-9: 48.2), Vardamides et al. proposed the stereochemistry of H-9 as β in **169**.²¹⁷ The biosynthetic formation of 7,14-epoxyazedarachin B (**183**) could presumably be explained by an intramolecular nucleophilic attack of the hydroxyl group on the C-14 position of the epoxide ring, and in contrast a preferable alternative route led to neoazedarachin B (**181**) with a 1,2-hydrogen shift.²¹⁸ As for the structure of toosendanin (**185**), it contained one more lactol bridge at C-1/29 in addition to the C-19/29 ether bridge.²¹¹

2.1.5. Vilasinin-Class. The vilasinin-class limonoids characterized by a 6 α ,28-ether bridge were proposed as biosynthetic precursor of ring C cleaved salannin-type limonoids,^{237,238} which were formed through a Grob type olefin-forming fragmentation of a 12-hydroxy-14,15-epoxyvilasinin-class compound and subsequent ether ring formation between C-7 and C-15 hydroxyl groups to yield nimbolidins and salannins.²³⁹ The occurrence of nimbolins A and B (**202** and **366**) in both *Melia azedarach* and *Azadirachta indica* further underlined the close relationship between the two species.²⁴⁰ Munronolide 21-O- β -D-glucopyranoside (**213**), from *Munronia henryi*, was the first limonoid with a D-glucose moiety attached to the C-21 position.²⁴¹ Malleastrones A–C (**227**–**229**) possessed a rare skeleton with an acetyl group at C-6 and the C-6/29 ether bridge. Of these, the structure of **227** was confirmed by X-ray diffraction.²⁴²

Table 3. Structures and Sources of Havanensin-Class Limonoids 106–134

no.	compounds	substitution groups and others	sources
106	havanensin	$R_1 = R_2 = R_3 = R_4 = H$	<i>Trichilia havanensis</i> ; ¹⁸¹ <i>Khaya anthotheca</i> ¹⁶³
107	3,7-di- <i>O</i> -acetylhavanensin	$R_1 = R_4 = H$; $R_2 = R_3 = Ac$	<i>K. anthotheca</i> ; ¹⁶³ <i>Trichilia havanensis</i> ^{74,181}
108	1,7-di- <i>O</i> -acetylhavanensin	$R_1 = R_3 = Ac$; $R_2 = R_4 = H$	<i>T. havanensis</i> ; ^{74,181} <i>Khaya anthotheca</i> ¹⁶³
109	havanensin triacetate	$R_1 = R_2 = R_3 = Ac$; $R_4 = H$	<i>K. anthotheca</i> ; ¹⁶³ <i>Trichilia havanensis</i> ^{74,86,181}
110	trifolin	$R_1 = Ac$; $R_2 = H$; $R_3 = iVal(OH)$; $R_4 = O$	<i>T. trifolia</i> ¹⁸²
111	khayanthone	$R_1 = R_2 = R_3 = Ac$; $R_4 = O$	<i>Khaya anthotheca</i> ; ^{163,164,183} <i>K. nyasica</i> ¹⁸⁴
112	grandifolione	$R_1 = R_2 = Ac$; $R_3 = H$; $R_4 = O$	<i>K. grandifolia</i> ^{164,178,185}
113	1 α -methoxy-1,2-dihydroepoxyazadiradione		<i>Azadirachta indica</i> ⁶⁸
114	14,15-deoxyhavanensin 3,7-diacetate	$R_1 = R_4 = R_5 = H$; $R_2 = R_3 = Ac$	<i>Khaya anthotheca</i> ; ¹⁶³ <i>Chisocheton paniculatus</i> ¹¹⁷
115	deoxyhavanensin triacetate	$R_1 = R_2 = R_3 = Ac$; $R_4 = R_5 = H$	<i>Trichilia havanensis</i> ⁸⁶
116	14,15-deoxyhavanensin 1,7-diacetate	$R_1 = R_3 = Ac$; $R_2 = R_4 = R_5 = H$	<i>T. havanensis</i> ; ⁸⁶ <i>Melia toosendan</i> ¹⁸⁶
117	1 α ,12 α -diacetoxo-7-deacetyl-1,2-dihydro-3 α -hydroxyazadirone	$R_1 = Ac$; $R_4 = OAc$; $R_2 = R_3 = R_5 = H$	<i>Turraea cornucopia</i> ⁹⁰
118	deoxykhayanthone	$R_1 = R_2 = R_3 = Ac$; $R_4 = H$; $R_5 = O$	<i>Khaya nyasica</i> ¹⁸⁴
119		$R_1 = R_2 = Ac$; $R_3 = OH$; 20,22-didehydro	<i>Trichilia havanensis</i> ⁸⁶
120	melianin C	$R_1 = Ac$; $R_2 = Bz$; $R_3 = H$	<i>Melia volkensii</i> ¹⁸⁷
121	toosendone		<i>M. toosendan</i> ¹⁸⁶
122	sendanal		<i>M. azedarach</i> ¹⁷⁹
123	1 α ,7 α ,11 β -triacetoxo-4 α -carbomethoxy-12 α -(2-methylpropanoyloxy)-14 β ,15 β -epoxyhavanensin	$R_1 = R_3 = Ac$; $R_2 = H$; $R_4 = iBu$	<i>Turraea floribunda</i> ¹⁸⁸
124	1 α ,7 α ,11 β -triacetoxo-4 α -carbomethoxy-12 α -(2-methylbutanoyloxy)-14 β ,15 β -epoxyhavanensin	$R_1 = R_3 = Ac$; $R_2 = H$; $R_4 = Piv$	<i>T. floribunda</i> ¹⁸⁸
125		$R_1 = R_4 = Ac$; $R_2 = R_3 = H$	<i>T. floribunda</i> ¹⁸⁹
126		$R_1 = R_4 = Ac$; $R_2 = H$; $R_3 = iBu$	<i>T. floribunda</i> ¹⁸⁹
127		$R_1 = H$; $R_2 = R_4 = Ac$; $R_3 = iBu$	<i>T. floribunda</i> ¹⁸⁹
128	11 β -acetoxo-3,7-diacetyl-4 α -carbomethoxy-12 α -isobutyryloxy-28-nor-1-tigloyl-havanensin	$R_1 = Tig$; $R_2 = R_3 = Ac$; $R_4 = iBu$	<i>T. floribunda</i> ¹⁹⁰
129	nilotin	$R_1 = R_2 = R_3 = Ac$; $R_4 = Tig$	<i>T. nilotica</i> ¹⁹¹
130	1 α ,11 β -diacetoxo-4 α -carbomethoxy-7 α -hydroxy-12 α -(2-methylpropanoyloxy)-15-oxohavanensin		<i>T. floribunda</i> ¹⁸⁸
131	28-nor-4 α -carbomethoxy-11 β -acetoxo-12 α -(2-methylbutanoyloxy)-14,15-deoxyhavanensin-1,7-diacetate	$R_1 = R_2 = Ac$	<i>T. floribunda</i> ¹⁸⁰
132	28-nor-4 α -carbomethoxy-11 β -hydroxy-12 α -(2-methylbutanoyloxy)-14,15-deoxyhavanensin-1-acetate	$R_1 = R_2 = H$	<i>T. floribunda</i> ¹⁸⁰
133	28-nor-4 α -carbomethoxy-11 β -acetoxo-12 α -(2-methylbutanoyloxy)-14,15-deoxyhavanensin-1-acetate	$R_1 = H$; $R_2 = Ac$	<i>T. floribunda</i> ¹⁸⁰
134	28-nor-4 α -carbomethoxy-7-deoxy-7-oxo-11 β -acetoxo-12 α -(2-methylbutanoyloxy)-14,15-deoxyhavanensin-1-acetate		<i>T. floribunda</i> ¹⁸⁰

2.1.6. Others. The characterization of the epoxides 1 α ,2 α -epoxy-17 β -hydroxyazadiradione (**248**) and 1 α ,2 α -epoxynimolicinol (**453**) in *Azadirachta indica* oil was of biosynthetic significance, as they might be considered as intermediates between A-ring 3-oxo- $\Delta^{1,2}$ and 1,3-diols among the *A. indica* limonoids.¹¹⁵

2.2. Ring-seco Limonoids

2.2.1. Demolition of a Single Ring. **2.2.1.1. Ring A-seco Group.** The cleavage of C-3/4 and then formation of a 3,4-lactone mostly occurred in the ring A-seco group, and usually led to either the $\Delta^{1,2}$ system or 1 α -acetyl substitution (Figure 9). Dregeanas 3–5 (**256**, **261**, and **260**) were considered as intermediates between the intact limonoids such as heudelottins C, E,

and F (**66–68**) and the complex compounds of the prieurianin-class.²⁷⁴ Kihadalactone A obtained from *Aphanamixis polystachya* in 1999²⁷⁵ was in fact identical with carapolide I (**257**) obtained from *Carapa grandiflora* in 1994.²⁷⁶ In addition, **257** was of interest because the complex rohitukin limonoids could arise from compounds of this relatively simple type by oxidation of ring B and the Δ^{14} -double bond.²⁷⁵

2.2.1.2. Ring B-seco Group. Up to now, the limonoids of ring B-seco (C-7/8) from Meliaceae were found only in the *Turraea* and *Toona* genera (Table 8). The substituents at C-11 in turraflorins A–C (**266**, **267**, and **283**), first isolated from *Turraea floribunda*,²⁸⁴ were revised to be β -oriented¹⁴³ and the complete assignment of the NMR spectra of **266** and **267** were presented.²⁸⁵ The structure of 6-acetoxytoonacilin (**269**), the first B-seco

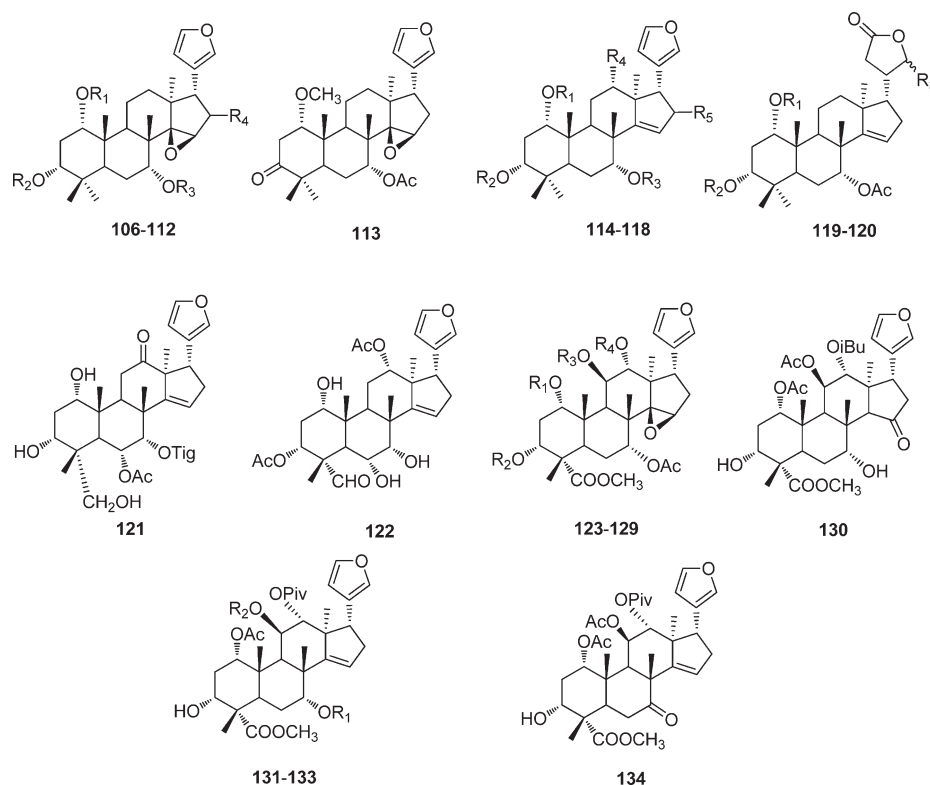


Figure 5. Structures of havanensin-class limonoids **106–134**.

limonoid with an intact A ring related to cedrelone (**81**), was confirmed by X-ray analysis.²⁸⁶ The absolute configurations of turrupubesins D–G (**275**–**278**) were established by correlating their CD spectra to that of turrupubesin B (**1153**),⁵⁹ a model compound whose absolute configuration was assigned by CD analysis of its dihydrogenated derivatives.²⁶⁶ Unlike the limonoids **266**–**286**, all of which have a $\Delta^{8,30}$ exocyclic double bond, turrupubesins A (**290**) and C (**291**) both have a $\Delta^{8,14}$ double bond, and the latter also has a 1,30-oxygen bridge. Wang et al. presented the first report on the determination of the absolute configuration of **290** by chlorine-based X-ray crystallography²⁸⁷ and proposed a plausible biosynthetic pathway to **291** starting from the precursor 11-*epitoonacilin* (**271**).¹²⁶

2.2.1.3. Ring C-seco Group. 2.2.1.3.1. Azadirachtin/Meliacarpin-Class. The ring C-seco limonoids originated mainly from the *Azadirachta* and *Melia* genera (Table 9). Deciphering the structure of the very potent biopesticide azadirachtin (**292**), first isolated from *Azadirachta indica* (syn. *Melia azadirachta*),⁵¹ also called azadirachtin A according to Rembold,³⁵ was a long journey. Butterworth et al. presented the correct formula of **292** as C₃₅H₄₄O₁₆²⁹³ and delineated important structural features.²⁹⁴ Based on the NMR study including the NOE experiments, the structure of **292** was proposed^{295,296} and subsequently revised.^{297,298} The final and unambiguous determination did not arrive until 1986 based on the X-ray crystallographic analysis of its derivatives,^{52,257} and thus reassignments of its NMR data have been proposed by several research groups.^{299–301} Crystalline **292** was obtained in 1994 and its crystal parameters were measured by X-ray diffraction.^{302,303} Then its absolute configuration was finally determined by high field NMR application of the Mosher method.³⁰⁴ To determine the properties of **292**, it was converted to the natural product 22,23-dihydro-23β-

methoxyazadirachtin (**303**) via selective bromomethoxylation of the C-22,23 enol ether double bond and tri-*n*-butyltin hydride reduction.³⁰⁵ A wonderful review of the chemistry of **292** was presented by Ley et al.,²¹ and a methodology of structure determination was also developed taking **292** as an example.³⁰⁶ The structure of 3-tigloylazadirachtol (**296**),³⁰⁷ once incorrectly assigned as deacetylazadirachtinol,³⁰⁸ was also called azadirachtin B.³⁰⁹ Azadirachtin F and 11-hydroxyazadirachtin B, both reported in 1996 by two different research groups, had the same structure as **300**.^{130,310} The spectral data of azadirachtin D (**309**), which was identical with 1-tigloyl-3-acetyl-11-hydroxy-4- β -methylmelicarpin isolated in 1992,³¹¹ were introduced by Govindachari in the same year.³¹² Unlike most azadirachtin/melicarpin-class limonoids, azadirachtin G (**305**) and 13,14-desepoxyazadirachtin A (**306**) had a double bond at C-13/14 instead of an epoxy moiety. 1,3-Diacetyl-11,19-deoxa-11-oxo-melicarpin (**311**) from *Azadirachta indica* was considered to be a possible intermediate in the biosynthesis of **292**.³¹³

2.2.1.3.2. *Azadirachtin/Meliacarpinin-Class.* It was thought that an intramolecular S_N2 nucleophilic reaction resulted in the formation of $7\alpha,13\beta$ -ether bridge moiety in azadirachtin/meliacarpin-class limonoids. 1-Cinnamoyl-3-acetyl-11-methoxymeliacarpinin (**327**) reported in 1994³³⁹ was cited as meliacarpinin A by Zhou et al. in 1997.²¹⁴ It was odd that Nakatani et al. reported 1-deoxy-3-tigloyl-11-methoxymeliacarpinin (**328**)³⁴⁰ in 1993 and 1-acetyl-3-tigloyl-11-methoxymeliacarpinin (**329**)²¹⁹ in 1994, but then presented these two compounds as meliacarpins B and C in 1995,³⁴¹ respectively. The structure **330** had been variously assigned to meliacarpinin D³⁴¹ and, in 1995, to 1-tigloyl-3-acetyl-11-methoxymeliacarpinin,²⁰⁵ while **331** was reported as meliacarpinin E³⁴² in 1996 and was in fact the 3-tigloyl-11-methoxymeliacarpinin reported in 1993.²⁰⁶

Table 4. Structures and Sources of Trichilin-Class Limonoids 135–185

no.	compounds	substitution groups and others	sources
135	trichilin A	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_6 = \beta-OH$; $R_7 = Piv$	<i>Trichilia emetica</i> ; ¹⁹² <i>T. roka</i> ¹⁹⁴
136	7-acetyltrichilin A	$R_1 = H$; $R_2 = OAc$; $R_3 = R_4 = Ac$; $R_5 = O$; $R_6 = \beta-OH$; $R_7 = Piv$	<i>T. roka</i> ²⁰⁰
137	trichilin B	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = Piv$	<i>T. roka</i> ; ¹⁹⁴ <i>Melia azedarach</i> ; ^{206,207,209,219,220} <i>M. toosendan</i> ^{85,214}
138	12-O-acetyltrichilin B	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = Piv$	<i>M. azedarach</i> ; ^{206,207,209,219,220} <i>M. toosendan</i> ²¹⁴
139	1,12-diacetyltrichilin B	$R_1 = R_3 = Ac$; $R_2 = OAc$; $R_4 = H$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = Piv$	<i>M. azedarach</i> ^{206,207,209,219–221}
140	trichilin C	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = OH$; $R_6 = O$; $R_7 = Piv$	<i>Trichilia roka</i> ¹⁹⁴
141	trichilin D (meliatoxin A ₁)	$R_1 = R_4 = R_6 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_7 = Piv$	<i>T. roka</i> ; ¹⁹⁴ <i>Melia azedarach</i> ^{195,206,207,209,219–222}
142	aphanastatin	$R_1 = R_3 = Ac$; $R_2 = OH$; $R_4 = H$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = Piv$	<i>M. azedarach</i> ; ^{209,219} <i>Aphanamixis grandiflora</i> ; ¹⁹⁶ <i>Trichilia roka</i> ¹⁹⁴
143	trichilin F	$R_1 = Ac$; $R_2 = OAc$; $R_3 = R_4 = H$; $R_5 = O$; $R_6 = \beta-OH$; $R_7 = Piv$	<i>T. roka</i> ^{194,223}
144	trichilin G	$R_1 = R_4 = H$; $R_2 = OH$; $R_3 = Ac$; $R_5 = O$; $R_6 = \beta-OH$; $R_7 = Piv$	<i>T. roka</i> ²²³
145	trichilin H	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>Melia azedarach</i> ; ^{206,207,209,219–221} <i>M. toosendan</i> ^{85,211,224}
146	1-acetyltrichilin H	$R_1 = R_3 = Ac$; $R_2 = OAc$; $R_4 = H$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>M. azedarach</i> ; ^{221,225} <i>M. toosendan</i> ⁸⁵
147	1-acetyl-2-deacetyltrichilin H	$R_1 = R_3 = Ac$; $R_2 = OH$; $R_4 = H$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>M. azedarach</i> ²²¹
148	3-deacetyltrichilin H	$R_1 = R_3 = R_4 = H$; $R_2 = OAc$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>M. azedarach</i> ²²¹
149	1-acetyl-3-deacetyltrichilin H	$R_1 = Ac$; $R_2 = OAc$; $R_3 = R_4 = H$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>M. azedarach</i> ²²¹
150	12-O-deacetyltrichilin H	$R_1 = R_4 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = iBu$	<i>M. azedarach</i> ²²⁶
151	trichilin I	$R_1 = R_4 = H$; $R_2 = OH$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = Piv$	<i>M. toosendan</i> ^{85,209,224,227}
152	12-deacetyltrichilin I	$R_1 = R_4 = H$; $R_2 = OH$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = Piv$	<i>M. azedarach</i> ²²¹
153	trichilin J	$R_1 = R_4 = R_6 = H$; $R_2 = OH$; $R_3 = Ac$; $R_5 = O$; $R_7 = Piv$	<i>M. toosendan</i> ^{85,209,224,227}
154	trichilin K	$R_1 = R_4 = R_6 = H$; $R_2 = OH$; $R_3 = Ac$; $R_5 = O$; $R_7 = iBu$	<i>M. toosendan</i> ^{85,224}
155	trichilin L	$R_1 = R_3 = R_4 = R_6 = H$; $R_2 = OAc$; $R_5 = O$; $R_7 = Piv$	<i>M. toosendan</i> ^{85,224}
156	sendanin	$R_1 = R_2 = R_4 = H$; $R_3 = R_7 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$;	<i>M. azedarach</i> ; ¹⁹⁹ <i>Trichilia roka</i> ¹⁹⁸
157	29-deacetylsendanin	$R_1 = R_2 = R_4 = R_7 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$;	<i>Melia azedarach</i> ; ²⁰⁵ <i>M. toosendan</i> ^{202–204}
158	azedarachin A	$R_1 = R_2 = R_4 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = Piv$	<i>M. azedarach</i> ; ^{206,207,209,219} <i>M. toosendan</i> ^{85,224}
159	12-O-acetylazedarachin A	$R_1 = R_2 = R_4 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = Piv$	<i>M. azedarach</i> ; ^{205,207,209,219} <i>M. toosendan</i> ^{85,133}
160	azedarachin B	$R_1 = R_2 = R_4 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$; $R_7 = iBu$	<i>M. azedarach</i> ; ^{205,206,218} <i>M. toosendan</i> ^{85,214}
161	12-O-acetylazedarachin B (29-isobutylsendanin)	$R_1 = R_2 = R_4 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$; $R_7 = iBu$	<i>M. azedarach</i> ; ^{207,209,219} <i>M. toosendan</i> ²²⁴

Table 4. Continued

no.	compounds	substitution groups and others	sources
162	azedarachin C	$R_1 = R_2 = R_4 = R_6 = H$; $R_3 = Ac$; $R_5 = O$; $R_7 = iBu$	<i>M. azedarach</i> ^{206,209,228}
163	meliatoxin A ₂	$R_1 = R_4 = R_6 = H$; $R_2 = OAc$; $R_3 = Ac$; $R_5 = O$; $R_7 = iBu$	<i>M. azedarach</i> ^{195,206,207,219,220,222}
164	meliartenin	$R_1 = R_2 = R_4 = R_7 = H$; $R_3 = Ac$; $R_5 = OH$; $R_6 = O$	<i>M. azedarach</i> ²⁰⁸
165	amoorastatin	$R_1 = R_2 = R_4 = R_6 = R_7 = H$; $R_3 = Ac$; $R_5 = O$	<i>Pterohraxis zenkeri</i> ²¹⁷ <i>Aphanamixis grandiflora</i> ²²⁹
166	12 α -hydroxyamoorastatin (12-deacetyltoosendanin)	$R_1 = R_2 = R_4 = R_7 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OH$	<i>A. grandiflora</i> ²¹⁰ <i>Melia toosendan</i> ^{85,133,214} <i>M. azedarach</i> ^{201,205,209,213,230}
167	chuanliansu (toosendanin; 12 α -acetoxyamoorastatin)	$R_1 = R_2 = R_4 = R_7 = H$; $R_3 = Ac$; $R_5 = O$; $R_6 = \alpha-OAc$	<i>M. toosendan</i> ^{85,133,211,212,214} <i>M. azedarach</i> ^{209,213,230}
168	3 α -deacetylamoostatatin	$R_1 = R_2 = R_3 = R_4 = R_6 =$ $R_7 = H$; $R_5 = O$	<i>Pterohraxis zenkeri</i> ²¹⁷
169	9 β -amoorastatin	$R_1 = R_2 = R_4 = R_6 = R_7 = H$; $R_3 = Ac$; $R_5 = O$; 9 β -H	<i>P. zenkeri</i> ²¹⁷
170	meliatoosenin D	$R_1 = R_2 = R_3 = R_4 = H$; $R_5 = O$ $R_6 = \alpha-OAc$; $R_7 = OH$	<i>Melia toosendan</i> ¹³³
171	meliatoosenin C		<i>M. toosendan</i> ¹³³
172	amoorastatone	$R_1 = \alpha-OH$; $R_2 = R_4 = R_5 = H$; $R_3 = \alpha-OAc$	<i>Aphanamixis grandiflora</i> ²¹⁰ <i>Melia azedarach</i> ²³⁰
173	12 α -hydroxyamoorastatone	$R_1 = \alpha-OH$; $R_2 = R_5 = H$; $R_3 = \alpha-OAc$; $R_4 = OH$	<i>M. azedarach</i> ^{213,230–232} <i>M. toosendan</i> ^{85,133,225}
174	29-[(2-methylbutanoyl)oxy]-2 α - hydroxyamoorastatone	$R_1 = \alpha-OH$; $R_2 = OH$; $R_3 = \alpha-OAc$; $R_4 = H$; $R_5 = Piv$	<i>M. toosendan</i> ²³³
175	1,3- <i>epi</i> -29-[(2-methylbutanoyl)oxy]-2 α - hydroxyamoorastatone	$R_1 = \beta-OH$; $R_2 = OH$; $R_3 = \beta-OAc$; $R_4 = H$; $R_5 = Piv$	<i>M. toosendan</i> ²³³
176	1,3- <i>epi</i> -29-[(2-methylpropanoyl)oxy]-2 α - hydroxyamoorastatone	$R_1 = \beta-OH$; $R_2 = OH$; $R_3 = \beta-OAc$; $R_4 = H$; $R_5 = iBu$	<i>M. toosendan</i> ²³³
177	meliatoxin B ₁	$R_1 = \alpha-OH$; $R_2 = OAc$; $R_3 = \alpha-OAc$; $R_4 = H$; $R_5 = Piv$	<i>M. azedarach</i> ^{195,211,221,222}
178	meliatoxin B ₂	$R_1 = \alpha-OH$; $R_2 = OAc$; $R_3 = \alpha-OAc$; $R_4 = H$; $R_5 = iBu$	<i>M. azedarach</i> ^{195,222}
179	isochuanliansu (isotoosendanin)	$R_1 = \alpha-OH$; $R_2 = R_5 = H$; $R_3 = \alpha-OAc$; $R_4 = OAc$	<i>M. azedarach</i> ^{230,234} <i>M. toosendan</i> ^{85,225,234,235}
180	neoazedarachin A	$R_1 = \alpha-OH$; $R_2 = H$; $R_3 = \alpha-OAc$; $R_4 = OH$; $R_5 = Piv$	<i>M. toosendan</i> ^{85,225}
181	neoazedarachin B	$R_1 = \alpha-OH$; $R_2 = H$; $R_3 = \alpha-OAc$; $R_4 = OH$; $R_5 = iBu$	<i>M. toosendan</i> ^{85,218,225}
182	neoazedarachin D	$R_1 = \alpha-OH$; $R_2 = H$; $R_3 = \alpha-OAc$; $R_4 = OH$; $R_5 = CH_3$	<i>M. toosendan</i> ²²⁵
183	7,14-epoxyazedarachin B		<i>M. azedarach</i> ²¹⁸
184	azadirachtanin		<i>Azadirachta indica</i> ²³⁶
185	toosendanal		<i>Melia toosendan</i> ²¹¹

2.2.1.3.3. *Salannin-Class*. The structures of salannin (332) and 3-deacetylsalannin (333), in which many of the conformations were similar to those of in azadirachtins, were confirmed by X-ray diffraction analysis.³⁴⁷ Photooxidation of 332 and nimbin (391) by UV light in the presence of oxygen led to more polar unstable intermediates that rearranged on silica gel to two final products in which the furan ring had been oxidized to isomeric hydroxybutenolides.³⁴⁸ The photooxidation products of 332, salanninolide (349), and its isomer isosalanninolide (348) were also isolated as natural products from *Azadirachta indica*.^{317,318}

The molecules of 2',3'-dehydrosalannol (338) were linked into chains by intermolecular O—H...O hydrogen bonds.³⁴⁹ The biosynthetic pathway to nimbolide (345) from [2-¹⁴C,₄(4R)-³H₁]-mevalonic acid lactone was confirmed by feeding experiments.^{350–354} The isomer of 345 was unexpectedly produced when it was treated with boron trifluoride etherate and tetrabutyl ammonium bromide.³⁵⁵ Salannolide³⁵⁶ and compositolide²⁵³ were both obtained in 1984 by two research groups, and had the same structure as 348. In addition, it was mistaken for isosalanninolide by Jarvis et al. in 1999.³¹⁷

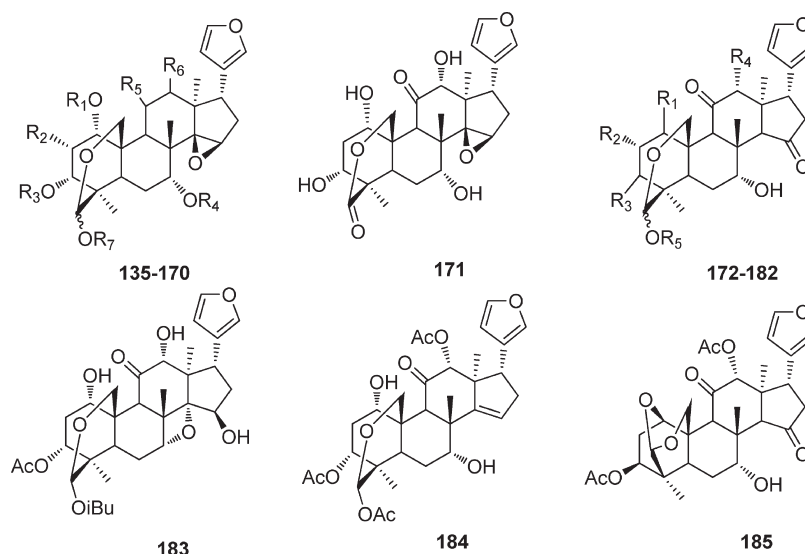


Figure 6. Structures of trichilin-class limonoids 135–185.

2.2.1.3.4. Nimbolin-Class. It seems that melianolide (389) was situated in a position to link ring C-*seco* limonoids such as nimbolin B (358) to azadirachtin-class limonoids.³⁶¹ The biosynthetic routes from ohchinolide A (371) to salannal (396) and further to salannin (332) involving Grob type olefin formation and subsequent ether ring formation were presented.³⁶¹ Zhang et al. proposed 12-ethoxynimbolinins A–D¹⁸⁶ for the structure of 357, 361, 385, and 388 based on comparison of the skeleton with the virtual compound nimbolin, which was a presumed intermediate in the biosynthetic pathway to more highly rearranged limonoids not yet isolated as a natural product. However, 12-ethoxynimbolinins A–D were not simple ethoxyl derivatives of nimbolin A–D (355, 358, 363, and 364), which might cause misunderstanding and confusion.²¹²

2.2.1.3.5. Nimbin-Class. The structure of nimbin (391), the major crystal bitter constituent of *Azadirachta indica*, was characterized by chemical means^{392–401} and spectroscopic analysis.⁴⁰² The assignment of the absolute configuration in 391 was determined by making certain biosynthetic assumptions⁴⁰³ and using information from the ORD study of pyronimbinic acid.⁴⁰⁴ The NMR spectral data of 391, 6-deacetylnimbin (392), nimbanal (393), and nimbolide (345) were subsequently partially reassigned in 1990.³⁷⁷ Ohchinolal (396), obtained from *Melia azedarach* early in 1983,³⁷⁰ was isolated from the same species and renamed as salannal by Nakatani et al. in 1995.³⁶⁰ 3-O-Acetylochinolal (399) was considered to be one of the biosynthetic precursors to the ring C-*seco* limonoids with C-6/28 and C-7/15 ether linkages, such as are found in salannin (332) and ohchinin (340).⁸⁴

2.2.1.3.6. Nimbolidin-Class. Walsogyne (414), with a C-11/14 ether bridge, might be derived through keto–enol isomerization of the aldehyde at C-9 followed by formation of a tetrahydrofuran-2-ol.⁴¹² 7 α -Acetyl-15 β -methoxy-29-methylene-7,15-deoxonimbolide (415) should be named as 7 α -acetyl-15 β -methoxy-28a-methylene-7,15-deoxonimbolide based on its skeleton numbering, and the source of C-28a was not biosynthetically available.⁴¹¹

2.2.1.4. Ring D-*seco* Group. Limonoids in this group with a δ -lactone in ring D derived from azadirone class via ring expansion by a Baeyer–Villiger type reaction.⁴¹³ Gedunin (416), the representative compound of this class, was obtained from various species (Table 15). For 416 the MS^{135,414} and NMR spectral

data⁴¹⁵ presented were used for its characterization, and its constitution and relative stereochemistry were deduced from the dihydrogedun-3 β -yl iodoacetate⁴¹⁶ derivative and confirmed by X-ray diffraction analysis.⁴¹⁷ Moreover, reactions of 416 were described and explained by a structure similar to that proved for limonin.⁴¹⁸ The crystal structure of 6 α -acetoxygedunin (418) was determined by X-ray analysis.⁴¹⁹ The ¹H NMR data of 7-deacetylgedunin (421) had not been completely assigned until 2006¹¹³ although it was isolated from *Azadirachta indica* in 1967.⁵⁷ Cespedes et al. presented the isolation of the epimeric mixture of photogedunin (433) and the formation and phyto-synthetic activities of its acetates.⁴²⁰ The chemical conversion of 416 and khivorin (434) to deacetoxy-7-oxoisogedunin confirmed the structure of 434.⁴²¹ The crystal packing of 3 α ,7 α -dideacetylkhivorin (440) was stabilized by both intra- and intermolecular hydrogen bonds, whose six-membered rings showed chair, boat and half-chair conformations while the furan ring was planar.⁴²² Biosynthetically, formation of mahmoodin (454), the first limonoid with a C-17 ethylene glycol side chain, might be considered as being from isonimolicinolide (59) through oxidation of ring D to a δ -lactone, as is observed in the case of the epoxyazadiradione-gedunin conversion, followed by transformation of the acetyl group to an ethylene glycol group.⁸¹

2.2.2. Demolition of Two Rings. 2.2.2.1. Rings A,B-*seco* Group. 2.2.2.1.1. Prieurianin-Class.

The complex prieurianin-class limonoids were depicted as arising from cleavages of C-3/4 and C-7/8 and the formation of 3(4)-lactone or 7(4)-lactone, with the substitution of a formyloxy or acetoxy group at C-11 (Figure 18 and Table 16). Prieurianin (458), first isolated from *Trichilia prieuriana*, is the representative compound of this class,¹⁶⁸ but the presence of multiple conformational isomers at room temperature caused its ¹H NMR peaks to be poorly resolved so that its structure remained obscure. However, the ¹H NMR spectrum was well resolved when the sample was heated to ~67 °C so that at that temperature it was possible to perform a detailed analysis and make proton assignments.⁴⁸¹ Similarly, its ¹³C NMR spectrum should be measured at 50 °C to avoid broad or missing peaks which occur in measurements made at 33 °C. Finally, the structure of 458 was unambiguously confirmed

Table 5. Structures and Sources of Vilasinin-Class Limonoids 186–229

no.	compounds	substitution groups and others	sources
186	vilasinin	$R_1 = R_2 = R_3 = R_4 = H$	<i>Azadirachta indica</i> ²³⁸
187	1 α -acetyl-3 α -propionylvilasinin	$R_1 = Ac$; $R_2 = \text{propanoyl}$; $R_3 = R_4 = H$	<i>Turraea wakefieldii</i> ; ¹⁸⁸ <i>T. parvifolia</i> ²⁴³
188	1 α ,3 α -diacetyl-7 α -tigloylvilasinin	$R_1 = R_2 = Ac$; $R_3 = Tig$; $R_4 = H$	<i>T. parvifolia</i> ²⁴³
189	1 α ,3 α -diacetylvilasinin	$R_1 = R_2 = Ac$; $R_3 = R_4 = H$	<i>T. parvifolia</i> ; ²⁴³ <i>T. holstii</i> ; ¹⁴³ <i>Chisocheton paniculatus</i> ; ¹¹⁷ <i>Malleastrum antsingyense</i> ; ²⁴⁴ <i>Melia volkensii</i> ; ¹⁸⁷ <i>Azadirachta indica</i> ²⁴⁵
190	1,3-diacetyl-7-tigloyl-12 α -hydroxyvilasinin	$R_1 = R_2 = Ac$; $R_3 = Tig$; $R_4 = OH$	<i>A. indica</i> ; ¹³⁰ <i>Malleastrum antsingyense</i> ²⁴⁴
191	trichilinin	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = OAc$	<i>Trichilia roka</i> ²³⁷
192	1-cinnamoyltrichilinin	$R_1 = Cin$; $R_2 = Ac$; $R_3 = H$; $R_4 = OAc$	<i>Melia volkensii</i> ; ²⁴⁶ <i>M. toosendan</i> ^{186,212}
193	1-tigloyltrichilinin	$R_1 = Tig$; $R_2 = Ac$; $R_3 = H$; $R_4 = OAc$	<i>M. volkensii</i> ²⁴⁶
194	1-acetyltrichilinin	$R_1 = R_2 = Ac$; $R_3 = H$; $R_4 = OAc$	<i>M. volkensii</i> ; ²⁴⁶ <i>M. toosendan</i> ¹⁸⁶
195	trichilinin B	$R_1 = Tig$; $R_2 = Ac$; $R_3 = H$; $R_4 = OAc$	<i>M. toosendan</i> ^{85,186,239}
196	trichilinin C	$R_1 = Ac$; $R_2 = Tig$; $R_3 = R_4 = H$	<i>M. toosendan</i> ^{85,239}
197	trichilinin D	$R_1 = Cin$; $R_2 = R_3 = H$; $R_4 = OAc$	<i>M. toosendan</i> ^{85,212,247}
198	trichilinin E	$R_1 = Bz$; $R_2 = R_3 = H$; $R_4 = OAc$	<i>M. toosendan</i> ^{85,212,247}
199	meliavolkinin	$R_1 = Bz$; $R_2 = Ac$; $R_3 = R_4 = H$	<i>M. volkensii</i> ¹⁸⁷
200	meliavolkin	$R_1 = Cin$; $R_2 = Ac$; $R_3 = R_4 = H$	<i>M. volkensii</i> ²⁴⁸
201	nimbadinin	$R_1 = R_2 = R_3 = H$; $R_4 = O$	<i>Azadirachta indica</i> ^{249,250}
202	nimbolin A	$R_1 = R_2 = Ac$; $R_3 = Cin$; $R_4 = H$	<i>A. indica</i> ; ²⁴⁰ <i>Melia azedarach</i> ; ^{240,251} <i>M. birmanica</i> ²⁵²
203	compositin	$R_1 = R_3 = Tig$; $R_2 = R_4 = H$	<i>M. dubia</i> ²⁵³
204	compositin acetate	$R_1 = R_3 = Tig$; $R_2 = OAc$; $R_4 = H$	<i>M. composita</i> ²⁵⁴
205	dysoxylin A	$R_1 = Ac$; $R_2 = R_5 = H$; $R_3 = Tig$; $R_4 = OAc$; $R_6 = O$; 20,22-dihydro	<i>Dysoxylum gaudichaudianum</i> ²⁵⁵
206	dysoxylin B	$R_1 = Ac$; $R_2 = R_5 = H$; $R_3 = Bz$; $R_4 = OAc$; $R_6 = O$; 20,22-dihydro	<i>D. gaudichaudianum</i> ²⁵⁵
207	dysoxylin C	$R_1 = Ac$; $R_2 = R_5 = H$; $R_3 = Piv$; $R_4 = OAc$; $R_6 = O$; 20,22-dihydro	<i>D. gaudichaudianum</i> ²⁵⁵
208	dysoxylin D	$R_1 = Ac$; $R_2 = R_5 = H$; $R_3 = 3,4\text{-dimethylpent-2-enoyl}$; $R_4 = OAc$; $R_6 = O$; 20,22-dihydro	<i>D. gaudichaudianum</i> ²⁵⁵
209	azadirachtolide	$R_1 = Sen$; $R_2 = Ac$; $R_3 = R_4 = R_5 = H$; $R_6 = O$	<i>Azadirachta indica</i> ²⁵⁶
210	deoxyazadirachtolide	$R_1 = Sen$; $R_2 = Ac$; $R_3 = R_4 = R_5 = R_6 = H$	<i>A. indica</i> ²⁵⁶
211	3-acetoxy-7-tigloylvilasinin lactone	$R_1 = R_4 = R_5 = H$; $R_2 = Ac$; $R_3 = Tig$; $R_6 = O$	<i>A. indica</i> ^{70,257}
212	munronolide	$R_1 = R_2 = Ac$; $R_3 = R_4 = H$; $R_5 = OH$; $R_6 = O$; $\Delta^{20,22}$	<i>Munronia henryi</i> ²⁴¹
213	munronolide 21-O- β -D-glucopyranoside	$R_1 = R_2 = Ac$; $R_3 = R_4 = H$; $R_5 = \beta\text{-D-glc}$; $R_6 = O$; $\Delta^{20,22}$	<i>M. henryi</i> ²⁴¹
214	neem A	$R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = O$	<i>Azadirachta indica</i> ²⁵⁸
215	neem B	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = H$	<i>A. indica</i> ²⁵⁸
216	munronin G		<i>Munronia delavayi</i> ²⁵⁹
217	limbocinin	$R_1 = R_2 = H$	<i>Azadirachta indica</i> ²⁶⁰
218	limbocidin	$R_1 = R_2 = OH$	<i>A. indica</i> ²⁶⁰
219	TS1	$R_1 = OH$; $R_2 = H$; 9 β ,11 β -epoxy; 14 β ,15 β -epoxy	<i>Trichilia rubescens</i> ²⁶¹
220	TS2	$R_1 = OCOC(CH_3)=CH_2$; $R_2 = H$; 9 β ,11 β -epoxy; 14 β ,15 β -epoxy	<i>T. rubescens</i> ²⁶¹
221	TS3	$R_1 = R_2 = H$; 9 β ,11 β -epoxy; 14 β ,15 β -epoxy; $\Delta^{6,7}$	<i>T. rubescens</i> ²⁶¹
222	ceramicine B	$R_1 = R_2 = H$; $\Delta^{14,15}$	<i>Chisocheton cermicus</i> ²⁶²
223	ceramicine C	$R_1 = H$; $R_2 = \text{methylacryl}$; $\Delta^{14,15}$	<i>C. cermicus</i> ²⁶²
224	ceramicine D	$R_1 = R_2 = H$	<i>C. cermicus</i> ²⁶²
225	trichirubine B	$R_1 = OBz$; $R_2 = OH$; 9 β ,11 β -epoxy	<i>Trichilia rubescens</i> ²⁶³
226	trichirubine A		<i>T. rubescens</i> ²⁶³
227	malleastrone A	$R_1 = H$; $R_2 = CH_3$; $\Delta^{1,2}$	<i>a Malleastrum sp.</i> ²⁴²
228	malleastrone B	$R_1 = H$; $R_2 = CH_2CH_3$; $\Delta^{1,2}$	<i>a Malleastrum sp.</i> ²⁴²
229	malleastrone C	$R_1 = OH$; $R_2 = CH_3$	<i>a Malleastrum sp.</i> ²⁴²

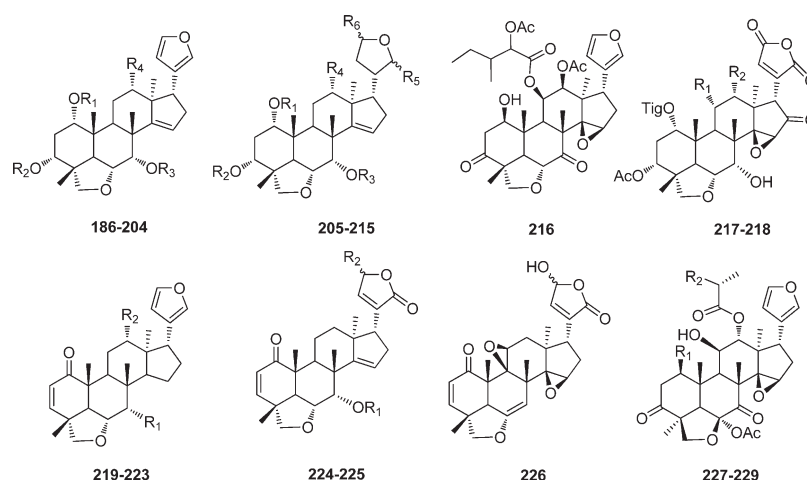


Figure 7. Structures of vilasinin-class limonoids 186–229.

Table 6. Other Structures and Sources of Rings Intact Limonoids 230–248

no.	compounds	substitution groups	sources
230	neeflone		<i>Azadirachta indica</i> ²⁶⁴
231			<i>Cedrela odorata</i> ²⁶⁵
232	11 β -acetoxy-7 α -acetyl-12 α -hydroxy-1,2-dihydroneotrichilenone	R ₁ = Ac, R ₂ = β -OAc; R ₃ = OH	<i>Turraea floribunda</i> ¹⁴³
233	12 α -acetoxy-7-acetyl-1,2-dihydroneotrichilenone	R ₁ = Ac, R ₂ = H; R ₃ = OAc	<i>T. floribunda</i> ¹⁴³
234	12 α -acetoxy-1,2-dihydroneotrichilenone	R ₁ = R ₂ = H; R ₃ = OAc	<i>T. floribunda</i> ¹⁴³
235	turranolide	R = H	<i>T. robusta</i> ⁸⁷
236	lenticellatumin	R = OH	<i>Dysoxylum lenticellatum</i> ²⁶⁶
237	1,2-dihydroazadirone	R ₁ = O; R ₂ = R ₄ = H; R ₃ = Ac	<i>Turraea robusta</i> ⁸⁷
238	12 α -acetoxy-1,2-dihydroazadirone	R ₁ = O; R ₂ = H; R ₃ = Ac; R ₄ = OAc	<i>T. parvifolia</i> ²⁴³
239	1,2-dihydro-6 α -acetoxyazadirone	R ₁ = O; R ₂ = OAc; R ₃ = Ac; R ₄ = H	<i>Chisocheton paniculatus</i> ²⁶⁷
240	mzikonone	R ₁ = O; R ₂ = R ₃ = H; R ₄ = OAc	<i>Turraea robusta</i> ; ^{87,268} <i>T. parvifolia</i> ; ²⁴³ <i>T. cornucopia</i> ⁹⁰
241	mzikonol	R ₁ = OH; R ₂ = R ₃ = H; R ₄ = OAc	<i>T. robusta</i> ⁸⁷
242	meldenindiol	R ₁ = O; R ₂ = OH; R ₃ = R ₄ = H	<i>Azadirachta indica</i> ²⁶⁹
243	meldenin	R ₁ = Ac; R ₂ = H	<i>A. indica</i> ; ^{134,270,271} <i>Melia azedarach</i> ¹⁷⁶
244	isomeldenin	R ₁ = H; R ₂ = Ac	<i>Azadirachta indica</i> ^{62,92,270,271}
245	meliatetraolone		<i>A. indica</i> ²⁷²
246	1 β ,2 β ;21,23-diepoxy-7 α -hydroxy-24,25,26,27-tetranor-apotirucalla-14,20,22-trien-3-one		<i>Trichilia havanensis</i> ²⁷³
247	1 β ,2 β -diepoxiazadiradione		<i>Azadirachta indica</i> ⁶⁸
248	1 α ,2 α -epoxy-17 β -hydroxiazadiradione		<i>A. indica</i> ¹¹⁵

by X-ray analysis of prieurianin 2'-p-bromobenzenesulphonate,^{481,482} and the stereochemical ambiguities remaining for C-1, C-4 and C-14 were resolved.⁴⁸¹ Just as for 458, spectral measurements of epoxyprieurianin (464),⁴⁵⁴ dysoxylumins A-C (465–467),⁴⁸³ and rohitukas 1, 2, 4, and 7–9 (490, 491, 459, 483, 469, and 484)⁴⁸⁴ were performed at 60 °C to obviate the difficulties caused by restricted rotation around the C-9/10 bond at lower temperatures. The isolation of these compounds was impeded, just as was previously experienced for rohitukas and prieurianin, by difficulties such as a mild alkaline hydrolysis causing opening of the ring A-lactone, followed by a variety of further changes, which produced a complex mixture of products difficult to resolve.⁴⁸⁴

Some complicated prieurianin-class structures were revised with the development of new structure determination techniques. The ¹³C NMR data of Tr-B (479) were analyzed¹⁹² and

subsequently reassigned for the formate, acetyl, methylene groups and for two quaternary carbons.⁴⁸⁵ X-ray crystallography showed that rohituka 7 (483) bore the 15 β -substituent,⁴⁸⁶ as opposed to the original assignment.⁴⁸⁴ The assigned structure of dregeanin with ring A as a seven-membered lactone⁴⁸⁷ was revised by comparison of the spectroscopy data with those of prieurianin derivatives to contain instead an eight-membered lactone ring as is shown in 488.⁴⁸⁸ Cipadessalide (489), the first prieurianin-class compound isolated from *Cipadessa* plants, was the first example of a limonoid with an oxygen bridge between C-1 and C-30. Moreover, a biosynthetic relationship between 489 and mombasol (471) was proposed.²⁸² MacLachlan et al. revised the seven membered 3(4)-lactone ring in rohitukas 1, 2 (490, 491)⁴⁸⁴ and D-5 (493)⁴⁸⁹ as five membered 7(4)-lactone rings and expressed doubt as to whether they were true natural products.⁴⁹⁰

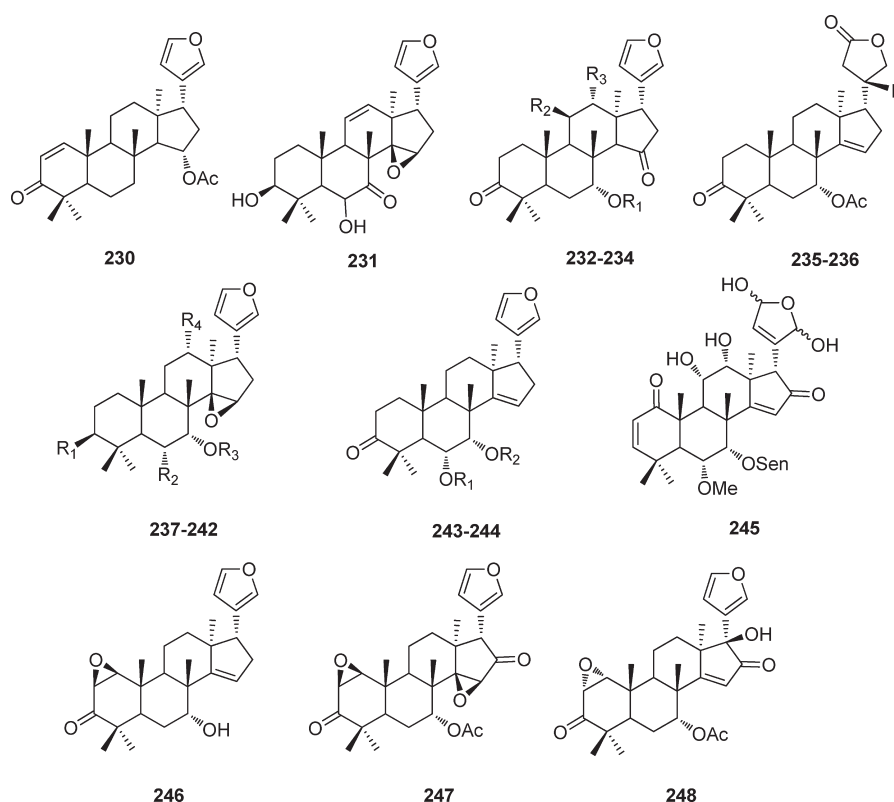


Figure 8. Other structures of rings intact limonoids 230–248.

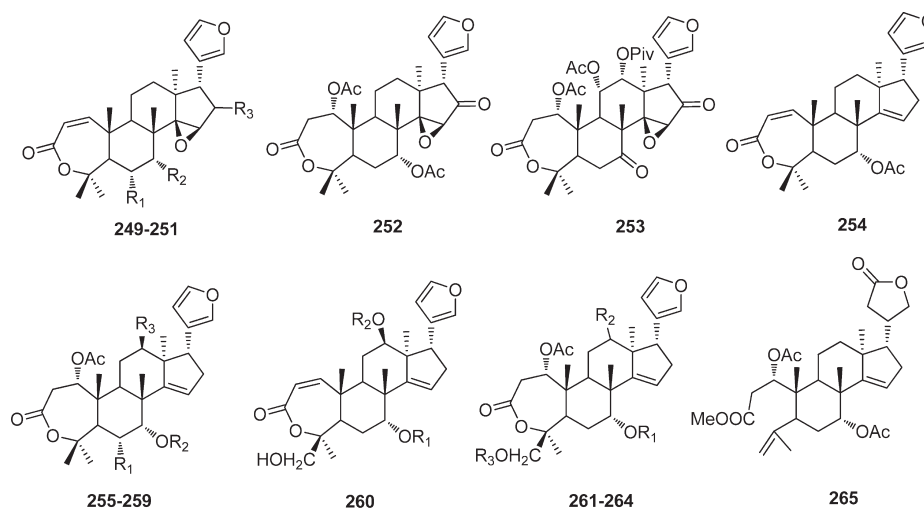


Figure 9. Structures of ring A-seco limonoids 249–265.

2.2.2.1.2. Others. All of 494–497 contain 3-oxo- $\Delta^{1,2}$ system and 3(4)-lactone groups, with toonaciliatin E and H (494 and 495) having an 8 α ,14 α -epoxide, while toonaciliatin I (496) and surenolactone (497) have a 14 β ,15 β -epoxide bridge. The co-occurrence of 494–496 in *Toona ciliata* suggested that 494 and 495 might derive from 496 through an acid-catalyzed intramolecular rearrangement followed by an oxidation and acetylation of 495 to produce 494.²⁹⁰ Zhang et al. demonstrated that the ¹³C NMR data previously reported for rohituka 3 (507)¹⁹² agreed instead with the structure for rohituka 15 (516).⁴⁸⁵ For rohituka 14 (510) a complete reassignment of

the previously reported assignment²⁷⁵ of the ester carbons (C-1', C-3) and quaternary carbons (C-10, C-14) was presented.⁴⁸⁵ Limonoids 514–517 are characterized by the 1 α ,14 β -ether linkage, $\Delta^{8,30}$ system and 15-oxo groups. Although previously reported differently,⁵⁰³ the C-1 substituent in polystachin (517) has been reassigned as α .²⁷⁵ Rubrins A-G (518–524), isolated from *Trichilia rubra* in 1994, possessed the C-3/29 cyclic hemi *ortho* ester structure, which alleviated the steric congestion of groups in the vicinity of the C-9, C-10 bond and thus eliminated the broadening of their ¹H NMR peaks.⁵⁰⁴ Among them, the structures of rubrins C and E (520 and 522) were identical to

Table 7. Structures and Sources of Ring A-seco Limonoids 249–265

no.	compounds	substitution groups and others	sources
249	evodulone	R ₁ = H, R ₂ = OAc; R ₃ = O	<i>Carapa procera</i> ; ²⁷⁷ <i>C. grandiflora</i> ²⁷⁶
250	surenin	R ₁ = R ₂ = OAc, R ₃ = H	<i>Toona sureni</i> ²⁷⁸
251	surenone	R ₁ = OH; R ₂ = O, R ₃ = H	<i>T. sureni</i> ²⁷⁸
252	carapolide H		<i>Carapa grandiflora</i> ²⁷⁶
253	amotsangin G		<i>Amoora tsangii</i> ²⁷⁹
254	proceranone		<i>Carapa procera</i> ²⁸⁰
255	rubralin C	R ₁ = H; R ₂ = Tig, R ₃ = OAc	<i>Trichilia rubra</i> ²⁸¹
256	dregeana 3	R ₁ = H; R ₂ = Ac, R ₃ = O-(2-acetoxy-3-methylpentanoxy)	<i>T. dregeana</i> ²⁷⁴
257	carapolide I (kihadalactone A)	R ₁ = R ₃ = H; R ₂ = Ac	<i>Carapa grandiflora</i> ; ²⁷⁶ <i>Aphanamixis ploystacha</i> ²⁷⁵
258	delevoyin B	R ₁ = OAc; R ₂ = Ac; R ₃ = H	<i>Entandrophragma delevoyi</i> ⁷⁵
259	quivisianthone	R ₁ = OH; R ₂ = Ang; R ₃ = H	<i>Quivisia papinae</i> ⁹⁹
260	dregeana 5	R ₁ = iVal(OH); R ₂ = 2-acetoxypivaloyl	<i>Trichilia dregeana</i> ²⁷⁴
261	dregeana 4	R ₁ = iBu(OH); R ₂ = β -O-(2-acetoxypivaloyl); R ₃ = H	<i>T. dregeana</i> ; ²⁷⁴ <i>T. emetica</i> ¹⁹²
262	rubralin A	R ₁ = R ₃ = 2-hydroxy-3-methylpentanoyl; R ₂ = α -OAc	<i>T. rubra</i> ²⁸¹
263	rubralin B	R ₁ = iVal(OH); R ₂ = α -OAc; R ₃ = 2-hydroxy-3-methylpentanoyl	<i>T. rubra</i> ²⁸¹
264	rubralin D	R ₁ = iVal(OH); R ₂ = α -OAc; R ₃ = 2,3-dihydroxy-3-methylvaleroyl	<i>Cipadessa baccifera</i> ²⁸²
265	nymania 2		<i>Nymania capensis</i> ²⁸³

Table 8. Structures and Sources of Ring B-seco Limonoids 266–291

no.	compounds	substitution groups and others	sources
266	turraflorin A	R = Ac	<i>Turraea floribunda</i> ^{284,285}
267	turraflorin B	R = H	<i>T. floribunda</i> ^{284,285}
268	toonacilin	R ₁ = H; R ₂ = α -OAc; R ₃ = OAc	<i>Toona ciliata</i> ^{140,161,286,288,289}
269	6-acetoxytoonacilin	R ₁ = R ₃ = OAc; R ₂ = α -OAc	<i>T. ciliata</i> ^{286,288,289}
270	12-deacetoxytoonacilin	R ₁ = R ₃ = H; R ₂ = α -OAc	<i>T. ciliata</i> ¹⁴⁰
271	11- <i>epi</i> -toonacilin	R ₁ = H; R ₂ = β -OAc; R ₃ = OAc	<i>Turraea floribunda</i> ¹⁴³
272	turraflorin D	R ₁ = Ac; R ₂ = O; R ₃ = OH	<i>T. floribunda</i> ²⁸⁵
273	turraflorin E	R ₁ = Ac; R ₂ = OH; R ₃ = O	<i>T. floribunda</i> ; ²⁸⁵ <i>T. pubescens</i> ¹²⁶
274	turraflorin F	R ₁ = R ₃ = H; R ₂ = O	<i>T. floribunda</i> ²⁸⁵
275	turrapubesin D	R ₁ = β -OAc; R ₂ = COCH ₂ Ph; R ₃ = O; R ₄ = OH	<i>T. pubescens</i> ¹²⁶
276	turrapubesin E	R ₁ = β -OAc; R ₂ = COCH ₂ Ph; R ₃ = OH; R ₄ = O	<i>T. pubescens</i> ¹²⁶
277	turrapubesin F	R ₁ = β -OAc; R ₂ = iBu; R ₃ = OH; R ₄ = O	<i>T. pubescens</i> ¹²⁶
278	turrapubesin G	R ₁ = β -OAc; R ₂ = Piv; R ₃ = OH; R ₄ = O	<i>T. pubescens</i> ¹²⁶
279	21-(<i>R,S</i>)-hydroxytoonacilide	R ₁ = α -OAc; R ₂ = Ac; R ₃ = OH; R ₄ = O	<i>Toona ciliata</i> ^{288,289}
280	23-(<i>R,S</i>)-hydroxytoonacilide	R ₁ = α -OAc; R ₂ = Ac; R ₃ = O; R ₄ = OH	<i>T. ciliata</i> ^{154,288,289}
281	11- <i>epi</i> -21-hydroxytoonacilide	R ₁ = β -OAc; R ₂ = Ac; R ₃ = OH; R ₄ = O	<i>Turraea parvifolia</i> ¹²⁵
282	11- <i>epi</i> -23-hydroxytoonacilide	R ₁ = β -OAc; R ₂ = Ac; R ₃ = O; R ₄ = OH	<i>T. parvifolia</i> ¹²⁵
283	turraflorin C	R ₁ = Ac; R ₂ = OAc	<i>T. floribunda</i> ²⁸⁴
284	turraflorin H	R ₁ = R ₂ = H	<i>T. floribunda</i> ²⁸⁵
285	turraflorin I		<i>T. floribunda</i> ²⁸⁵
286	turraflorin G		<i>T. floribunda</i> ²⁸⁵
287	toonaciliatin B		<i>Toona ciliata</i> ²⁹⁰
288	toonaciliatin C		<i>T. ciliata</i> ^{290,291}
289	toonafolin		<i>T. ciliata</i> ²⁹²
290	turrapubesin A		<i>Turraea pubescens</i> ²⁸⁷
291	turrapubesin C		<i>T. pubescens</i> ¹²⁶

those of hispidin A isolated from *T. hispida* in 1981⁵⁰¹ and nymania 1 isolated from *T. emetica* in 1998,¹⁹² respectively. Unlike the rohitukas 6, 3, 5, 13, 14 (505, 507–510), 511, dysoxylumolide A (512), and dysoxylumic acid (506), toonaciliatin D (513) was deduced on the basis of its NOESY spectrum to have 1/ β -substituent.²⁹⁰

2.2.2.2. Rings A,D-seco Group. Rings A,D-seco limonoids found in Meliaceae, most of which belong to the obacunol-class, were found only in the *Toona*, *Cedrela*, and *Dysoxylum* genera (Table 18). Except for dysoxylumolide C (554) and odorolide (555), they were characterized by a 3(4)-lactone with an epoxidized δ -lactonic D ring.⁵¹⁰ The biosynthesis of the

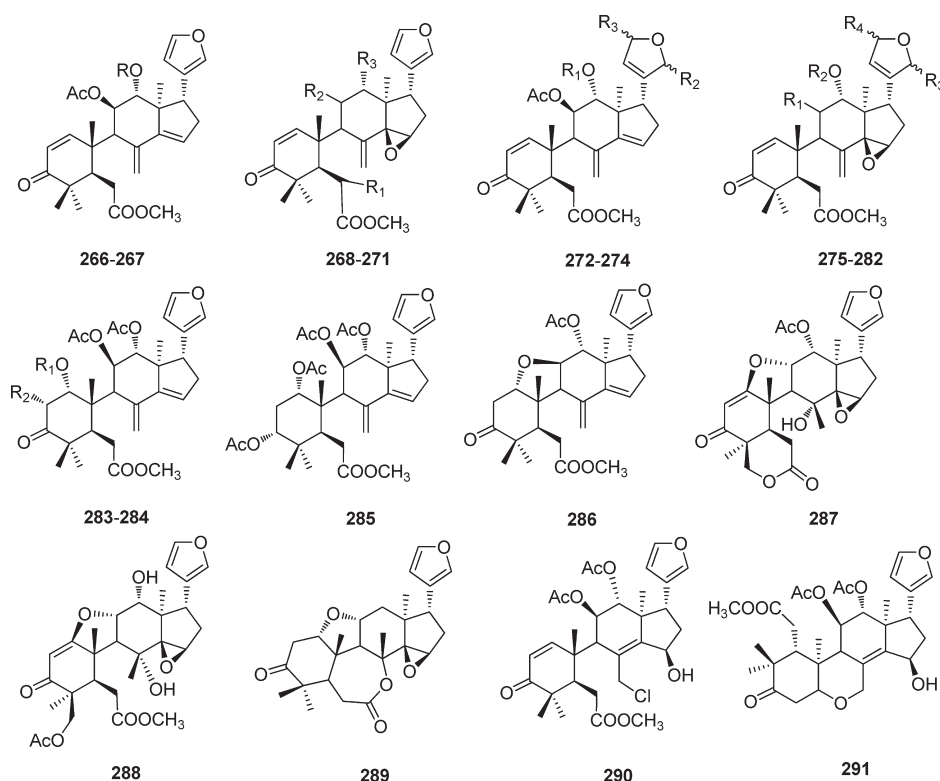


Figure 10. Structures of ring B-seco limonoids 266–291.

limonoids with an epoxy-lactone ring D proceeded through a 14,15-unsaturated meliacene, which was successively oxidized to a 14(15)-en-16-one, to a 14,15-epoxy-16-one, and finally to the lactone.⁷⁷ The structures of the three limonoids 11-oxo-7 α -obacunol (**532**), 11-oxo-7 α -obacunyl acetate (**533**), and 11-oxocneorin G (**548**), all of which contain the rare 11-ketone functionality, were confirmed by X-ray analysis.⁵¹¹ Of the seven kihadanin A and B derivatives obtained from *Trichilia elegans* ssp. *elegans*, the structure of 7-deoxo-7 α -acetoxykihadanin A (**539**) was confirmed by X-ray crystallographic analysis.⁵¹² 7-Deoxo-7 α -hydroxykihadanin A (**538**) and 7-deoxo-7 β -hydroxykihadanins A and B (**540** and **544**) were isolated after acetylation procedures as their mono- and/or diacetate derivatives.⁵¹² Moreover, limonoids **540** and **544**, together with 7-deoxo-7 β -acetoxykihadanins A and B (**541** and **545**), were the first reported natural occurrence of C-7 β -substituted limonoids without any oxygenated function at C-6.⁵¹² Ng et al. reported the crystal structure of 7 α -acetoxydihydronomilin (**546**)⁵¹³ and subsequently pointed out that it originated from *Xylocarpus granatum* rather than *Uncaria gambier*.⁵¹⁴

2.2.2.3. Rings B,D-seco Group. **2.2.2.3.1. Andirobin-Class.** Andirobin-class limonoids are characterized as the cleavages of C-7/8 and C-16/17 and the formation of $\Delta^{8,30}$ exocyclic double bond and δ -lactonic D ring. The chemical correlations of gedunin (**416**) with **556** and with methyl angolensate (**568**) supported the structures previously proposed for **556** and **568**.⁵²³ Methyl angolensate (**568**) was distributed widely, especially in the genus *Khaya* (Table 19). Its structure was proposed on the basis of chemical and spectroscopic evidence^{524–526} and confirmed by X-ray crystallographic analysis.⁵²⁷ The partial synthesis of **568** from 7-deacetoxy-7-oxokhivorin (**441**) has proved that the configuration of the etheroxygen attached to C-1 was α .^{528,529} Compound **568** might arise by a Bayer–Villiger type

peroxide oxidation of a 7-oxo compound or an earlier intermediate in the biosynthesis.⁵³⁰ The unusual chemical shift of the acetate methyl group (δ_{H} 1.55) in methyl 6,12 α -diacetoxyangolensate (**571**) was caused by the shielding effect of the furan ring.⁵³¹ Both sandoricin (**573**) and its 6-hydroxy derivative **574** were determined by NMR, mass spectra, and X-ray analysis.⁵³² It is worth noting that the two compounds **578**⁵³ and **1038**⁵⁴ were reported separately by two research groups in 2007, and both compounds were named as cipadesin D, but different skeletons were ascribed to them.

2.2.2.3.2. Others. Secomahoganin (**596**), in which ring C had a skew-boat conformation, was formed by oxidative cleavage of the C-6/7 bond in the normal tetranortriterpene nucleus and was an interesting compound from a biosynthetic viewpoint.⁷¹ Cedrelanolide I (**599**), for which the structure was established by spectroscopic methods and X-ray diffraction analysis, might be biosynthetically derived from a methyl angolensate type of precursor.⁵⁷⁰ However, Cespedes et al. cited it as cedrelanolide.⁵⁷¹ The structure of swiemahogin A (**600**), confirmed by single-crystal X-ray diffraction, incorporated a rare five-membered γ -lactone fused to the C-ring at C-8 and C-14, where the six-membered δ -lactone in the D-ring was destroyed.⁵⁷²

2.2.3. Demolition of Three Rings (Rings A,B,D-seco Group). Methyl ivorensate (**601**), the first A,B,D-seco limonoid obtained from plants of family Meliaceae, was structurally related to methyl angolensate (**568**) since treatment of **568** with perbenzoic acid produced a moderate yield of the corresponding lactone **601**.⁵⁷⁶ A detailed analysis of the NMR data of **601** was presented but some assignments were interchanged.⁴⁴⁶

2.3. Rearranged Limonoids

2.3.1. 1,n-Linkage Group. It is interesting that the carapollide-class compounds **607**–**613** were found only in genus

Table 9. Structures and Sources of Azadirachtin/Meliacarpin Limonoids 292–315

no.	compounds	substitution groups and others	sources
292	azadirachtin (azadirachtin A)	$R_1 = \text{Tig}; R_2 = \text{Ac}; R_3 = \text{OH}$	<i>Melia azedarach</i> ; ³¹⁴ <i>Azadirachta indica</i> ; ^{51,293,295,300,315–321} <i>A. excelsa</i> ³²²
293	3-deacetyl-11-desoxyazadirachtin	$R_1 = \text{Tig}; R_2 = R_3 = \text{H}$	<i>A. indica</i> ²⁵⁷
294	3-deacetyl-3-cinnamoylazadirachtin	$R_1 = \text{Tig}; R_2 = \text{Cin}; R_3 = \text{OH}$	<i>A. indica</i> ³⁰⁰
295	azadirachtol	$R_1 = R_2 = R_3 = \text{H}$	<i>A. indica</i> ; ³²³ <i>A. excelsa</i> ³²⁴
296	3-tigloylazadirachtol (azadirachtin B, deacetylazadirachtinol)	$R_1 = R_3 = \text{H}; R_2 = \text{Tig}$	<i>A. indica</i> ; ^{70,300,309,316,317,319,325,326} <i>A. excelsa</i> ³²⁴
297	1-tigloyl-3-acetylazadirachtol	$R_1 = \text{Tig}; R_2 = \text{Ac}; R_3 = \text{H}$	<i>A. excelsa</i> ; ³²² <i>A. siamensis</i> ³²⁷
298	3 α -acetoxy-1 α -hydroxyazadirachtol	$R_1 = R_3 = \text{H}; R_2 = \text{Ac}$	<i>A. indica</i> ³²⁸
299	azadirachtin E	$R_1 = \text{H}; R_2 = \text{Ac}; R_3 = \text{OH}$	<i>A. indica</i> ³⁵
300	azadirachtin F (11-hydroxyazadirachtin B)	$R_1 = \text{H}; R_2 = \text{Tig}; R_3 = \text{OH}$	<i>A. indica</i> ^{130,310}
301	azadirachtin O	$R_1 = \text{iVal}; R_2 = \text{Ac}; R_3 = \text{H}$	<i>A. excelsa</i> ³²⁴
302	azadirachtin Q	$R_1 = R_2 = \text{Ac}; R_3 = \text{H}$	<i>A. excelsa</i> ³²⁴
303	22,23-dihydro-23 β -methoxyazadirachtin (vepaol)	$R = \beta\text{-OCH}_3$	<i>A. indica</i> ^{70,298,300,325}
304	isovepaol(23- <i>epi</i> -vepaol)	$R = \alpha\text{-OCH}_3$	<i>A. indica</i> ^{70,325}
305	azadirachtin G		<i>A. indica</i> ³⁵
306	13,14-desepoxyazadirachtin A		<i>A. indica</i> ³²⁹
307	azadirachtin K		<i>A. indica</i> ¹⁰²
308	1-cinnamoylmelianolone		<i>Melia azedarach</i> ^{330–332}
309	azadirachtin D (1-tigloyl-3-acetyl-11-hydroxy-4 β -methylmeliacarpin)	$R_1 = \text{OH}; R_2 = \text{COOCH}_3$	<i>Azadirachta indica</i> ^{311,317,319,333,334}
310	11- <i>epi</i> -azadirachtin D	$R_1 = \text{COOCH}_3; R_2 = \text{OH}$	<i>A. indica</i> ^{70,335}
311	1,3-diacetyl-11,19-deoxa-11-oxomeliacarpin		<i>A. indica</i> ³¹³
312	1-cinnamoyl-3,11-dihydroxymeliacarpin	$R = \text{H}$	<i>Melia azedarach</i> ^{331,336,337}
313	1,3-dicinnamoyl-11-hydroxymeliacarpin	$R = \text{Cin}$	<i>M. azedarach</i> ³³⁸
314	1-cinnamoyl-3-acetyl-11-hydroxymeliacarpin	$R = \text{Ac}$	<i>M. azedarach</i> ³³⁸
315	1-cinnamoyl-3-methacrylyl-11-hydroxymeliacarpin	$R = \text{methacrylyl}$	<i>M. azedarach</i> ³³⁸

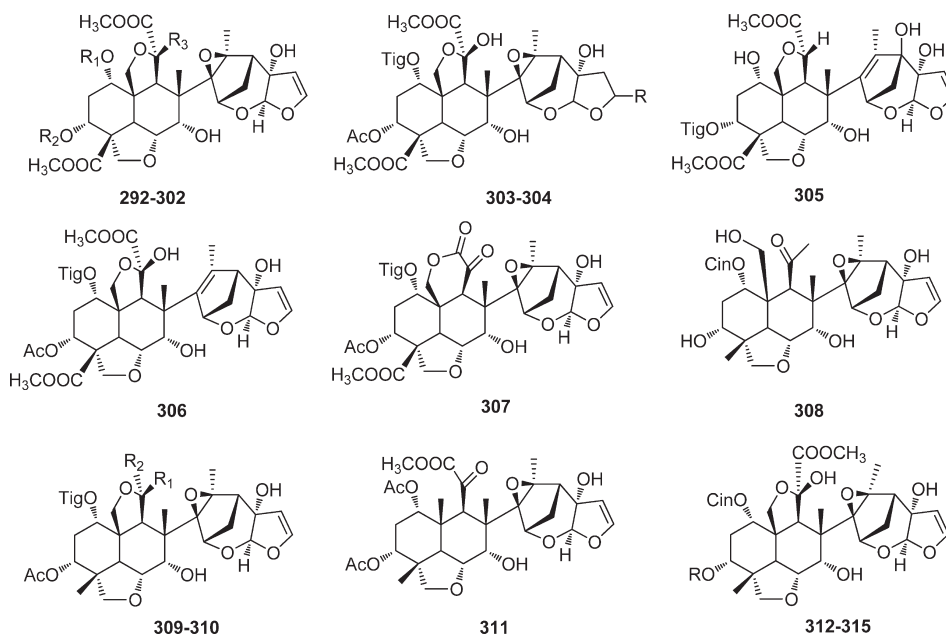


Figure 11. Structures of azadirachtin/meliacarpin-class limonoids 292–315.

carapa, the dukunolide-class limonoids **614–620** originated in genus *Lansium*, the neotecteanin-class compounds **621–625**

came from genus *Turraea* (Table 22). A possible biosynthetic pathway leading to the carapolides from carapolide G (**613**) as

Table 10. Structures and Sources of Azadirachtinin/Meliacarpinin Limonoids 316–331

no.	compounds	substitution groups and others	sources
316	3-tigloylazadirachtinin	R ₁ = R ₃ = H; R ₂ = Tig	<i>Azadirachta indica</i> ³²⁵
317	1-tigloyl-3-acetylazadirachtinin	R ₁ = Tig; R ₂ = Ac; R ₃ = H	<i>A. indica</i> ^{130,325}
318	1-tigloyl-3-acetyl-11-methoxyazadirachtinin	R ₁ = Tig; R ₂ = Ac; R ₃ = CH ₃	<i>A. indica</i> ^{70,300}
319	azadirachtin N		<i>A. indica</i> ³⁴³
320	3,20-diacetyl-11-methoxymeliacarpinin	R ₁ = H; R ₂ = R ₃ = Ac	<i>Melia azedarach</i> ³⁴⁴
321	1-tigloyl-3,20-diacetyl-11-methoxymeliacarpinin	R ₁ = OTig; R ₂ = R ₃ = Ac	<i>M. azedarach</i> ³⁴⁵ ; <i>M. toosendan</i> ¹³³
322	3-tigloyl-1,20-diacetyl-11-methoxymeliacarpinin	R ₁ = OAc; R ₂ = Tig; R ₃ = Ac	<i>M. azedarach</i> ³⁴⁵ ; <i>M. toosendan</i> ¹³³
323	1-cinnamoyl-3-hydroxy-11-methoxymeliacarpinin	R ₁ = OCin; R ₂ = R ₃ = H	<i>M. azedarach</i> ³⁴⁵
324	1-deoxy-3-methacrylyl-11-methoxymeliacarpinin	R ₁ = R ₃ = H; R ₂ = methacrylyl	<i>M. azedarach</i> ³⁴⁵
325	1-(2-methylpropanoyl)-3-acetyl-11-methoxymeliacarpinin	R ₁ = OiBu; R ₂ = Ac; R ₃ = H	<i>M. azedarach</i> ³⁴⁶
326	1-methacrylyl-3-acetyl-11-methoxymeliacarpinin	R ₁ = methacrylate; R ₂ = Ac; R ₃ = H	<i>M. azedarach</i> ³⁴⁶
327	1-cinnamoyl-3-acetyl-11-methoxymeliacarpinin (meliacarpinin A)	R ₁ = OCin; R ₂ = Ac; R ₃ = H	<i>M. azedarach</i> ^{206,209,339,345} ; <i>M. toosendan</i> ^{85,133,214}
328	1-deoxy-3-tigloyl-11-methoxymeliacarpinin (meliacarpinin B)	R ₁ = R ₃ = H; R ₂ = Tig	<i>M. azedarach</i> ^{209,219,340,341}
329	1-acetyl-3-tigloyl-11-methoxymeliacarpinin (meliacarpinin C)	R ₁ = OAc; R ₂ = Tig; R ₃ = H	<i>M. azedarach</i> ^{205,219,341} ; <i>M. toosendan</i> ^{85,214}
330	1-tigloyl-3-acetyl-11-methoxymeliacarpinin (meliacarpinin D)	R ₁ = OTig; R ₂ = Ac; R ₃ = H	<i>M. azedarach</i> ^{205,219,341,346} ; <i>M. toosendan</i> ^{85,214}
331	3-tigloyl-11-methoxymeliacarpinin (meliacarpinin E)	R ₁ = OH; R ₂ = Tig; R ₃ = H	<i>M. azedarach</i> ^{206,342}

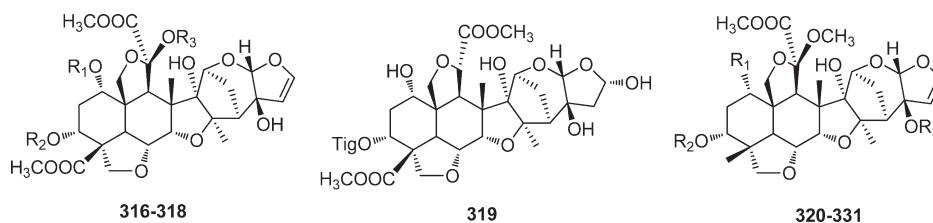


Figure 12. Structures of azadirachtinin/meliacarpinin-class limonoids 316–331.

the progenitor was proposed.²⁷⁶ The structures of dukunolides A–C (614–616) including their absolute configurations were established by X-ray analysis and chemical correlation.⁵⁷⁷ The biosynthesis of 614 was recognized by considering the intermediary mexicanolide or its analogs.⁵⁷⁸ Neotecleanins 621–625, the first natural occurrence of limonoids with a five-membered-ring A-seco structure, might serve as intermediates in the pathway to the formation of tecleanin and related compounds.⁵⁷⁹

2.3.2. 2,30-linkage Group. 2.3.2.1. Mexicanolide-Class. Mexicanolide (626), first isolated as the main constituent of *Carapa procera*,¹⁶⁷ was proved to be the “substance B” from *Cedrela odorata* by analysis of its spectral data.^{459,585} Its structure, including the absolute configuration, was assigned on the basis of its NMR spectral data,⁵⁸⁶ chemical reaction,⁵⁸⁷ and CD data,⁵⁸⁸ and was confirmed by its crystallographic analysis.⁵⁸⁹ The structure of 632 was assigned as 6-deoxyswietenolide early in 1968,⁵³³ but Sondengam et al. named it as proceranolide when they isolated it in 1980.⁵⁹⁰ As for 2′R- and 2′S-methylbutanoylproceranolide (633 and 634), the considerable steric interaction between the 2-methylbutanoyl group and the limonoid core made one stable conformation dominant in solution. Furthermore, a general rule for the determination of the absolute configurations of 2R- and 2S-methylbutanoyl at C-3 of a limonoid in a mixture was proposed based on the ¹H NMR conformational analysis.⁵⁹¹ The structure of swietenolide (638) was elucidated on the basis of evidence from chemical properties^{592–594} and spectroscopic data.⁵⁹⁴ The crystal structure analysis of diacetylswietenolide (647) was provided by Goh et al.⁵⁹⁵ One of the double bond of fissinolide (648) was first assigned as

C-8/14 in 1966⁵⁹⁶ and then was revised to be angustinolide, in which the double bond was assigned as C-8/9,^{597,598} to better fit its origin, but finally the original structure based on the spectroscopic and chemical properties was preferred.^{599,600} Subsequently, the ¹³C NMR signals of fissinolide were reassigned in 1998,⁶⁰¹ and the structures of the “grandifoliolin” isolated in 1967⁶⁰² and the “3β-acetoxymexicanolide” obtained in 1999 were shown to be 648.⁶⁰³ Gan et al. mistakenly cited khayasin (652) as 3β-isobutyryloxymexicanolide.⁵⁹¹ In terms of biosynthetic pathway, xylocensin N (669) was a possible intermediate on the route to xylocensin M (771), and they were once isolated from the same plant simultaneously as a pair of isomers of mexicanolides.^{604,605} The structure of swietenine (677) was elucidated on the basis of chemical^{606,607} and spectroscopic evidence,^{608,609} and confirmed by X-ray analysis of the *p*-iodobenzoate of detigloylswietenine^{610,611} and swietenine itself.⁶¹² The structure of the 3β-hydroxymexicanolide (Δ^{8,30} instead of Δ^{8,14}) reported by Govindachari et al. in 1997⁴⁶⁸ was in fact identical with 6-deoxydetigloylswietenine (684), which was reported in 1967.⁴⁶⁴ 2-Hydroxy-6-deoxyswietenine (690) was obtained early in 1988,⁶¹³ and was mistakenly reported as methyl 3β-tigloyloxy-2-hydroxy-1-oxo-meliac-8(30)-enate ten years later.⁶¹⁴ The structure of febrigugin (694), first obtained from *Soymida febrifuga*⁶¹⁵ and identical with 6-deoxyswietenine from *Swietenia mahagoni*,⁶¹⁶ was incorrectly assigned,²⁹⁰ and its spectroscopic data were revised.⁶¹⁷ The absolute configurations of 694 and cipadesin (703) were determined by spectroscopic and X-ray methods.⁶¹⁸ The mixture of methyl 2-hydroxy-3β-isobutyroxymeliac-8(30)-enate (699) and its 3β-tiglate derivative,

Table 11. Structures and Sources of Salannin-Class Limonoids 332–352

no.	compounds	substitution groups and others	sources
332	salannin	$R_1 = \text{Tig}; R_2 = \text{OAc}; R_3 = \text{CH}_3$	<i>Azadirachta indica</i> ^{102,104,106,107,295,316,317,357} <i>Melia dubia</i> ³⁵⁸ <i>M. azedarach</i> ^{142,176,219,342,359–361} <i>M. volkensii</i> ³⁶² <i>M. toosendan</i> ^{84,239,363}
333	3-deacetylsalannin	$R_1 = \text{Tig}; R_2 = \text{OH}; R_3 = \text{CH}_3$	<i>M. azedarach</i> ^{342,361,364} <i>Azadirachta indica</i> ^{103,104,245,316,317}
334	1-detigloyl-1-isobutylsalannin	$R_1 = \text{iBu}; R_2 = \text{OAc}; R_3 = \text{CH}_3$	<i>Melia volkensii</i> ³⁶⁵
335	2',3'-dihydrosalannin	$R_1 = \text{dihydrotigloyl}; R_2 = \text{OAc}; R_3 = \text{CH}_3$	<i>M. volkensii</i> ³⁶⁵
336	salannol	$R_1 = \text{iVal}; R_2 = \text{OH}; R_3 = \text{CH}_3$	<i>Azadirachta indica</i> ^{245,366}
337	salannol acetate	$R_1 = \text{iVal}; R_2 = \text{OAc}; R_3 = \text{CH}_3$	<i>A. indica</i> ^{366,367}
338	2',3'-dehydrosalannol	$R_1 = \text{Sen}; R_2 = \text{OH}; R_3 = \text{CH}_3$	<i>A. indica</i> ³⁶⁸
339	3-deoxymethylnimbide	$R_1 = R_2 = \text{H}; R_3 = \text{CH}_3$	<i>A. excelsa</i> ³⁶⁹
340	ohchinin	$R_1 = \text{Cin}; R_2 = \text{OH}; R_3 = \text{CH}_3$	<i>Melia azedarach</i> ³⁷⁰
341	ohchinin acetate (ohchinin-3-acetate)	$R_1 = \text{Cin}; R_2 = \text{OAc}; R_3 = \text{CH}_3$	<i>M. azedarach</i> ³⁶⁴ <i>M. volkensii</i> ²⁴⁶
342	nimbic acid	$R_1 = R_3 = \text{H}; R_2 = \text{OH}$	<i>Azadirachta indica</i> ^{249,250}
343	ohchinal	$R = \text{Bz}$	<i>Melia azedarach</i> ³⁶⁴
344	1-O-tigloyl-1-O-debenzoylohchinal	$R = \text{Tig}$	<i>M. toosendan</i> ^{235,371}
345	nimbolide	$R = \text{O}; \Delta^{2,3}$	<i>Azadirachta indica</i> ^{102,355,372–376} <i>A. excelsa</i> ³⁶⁹
346	28-deoxonimbolide	$R = \text{H}; \Delta^{2,3}$	<i>A. indica</i> ^{373,374,377} <i>A. excelsa</i> ³⁶⁹ <i>Owenia cepiodora</i> ³⁷⁸
347	2,3-dihydronimbolide	$R = \text{O}$	<i>Azadirachta excelsa</i> ³⁶⁹
348	salannolide (compositolide, isosalanninolide)	$R_1 = \text{OTig}; R_2 = \text{OAc}; R_3 = \text{O}; R_4 = \text{OH}$	<i>A. indica</i> ^{317,325,356} <i>Melia dubia</i> ²⁵³
349	salanninolide	$R_1 = \text{OTig}; R_2 = \text{OAc}; R_3 = \text{OH}; R_4 = \text{O}$	<i>Azadirachta indica</i> ^{317,318}
350	isoazadirolide	$R_1 = \text{OSen}; R_2 = R_3 = \text{OH}; R_4 = \text{O}$	<i>A. indica</i> ³⁷⁹
351	margosinolide	$R_1 = \text{H}; R_2 = R_3 = \text{O}; R_4 = \text{OH}; \Delta^{1,2}$	<i>A. indica</i> ³⁸⁰
352	isomargosinolide	$R_1 = \text{H}; R_2 = R_4 = \text{O}; R_3 = \text{OH}; \Delta^{1,2}$	<i>A. indica</i> ³⁸⁰

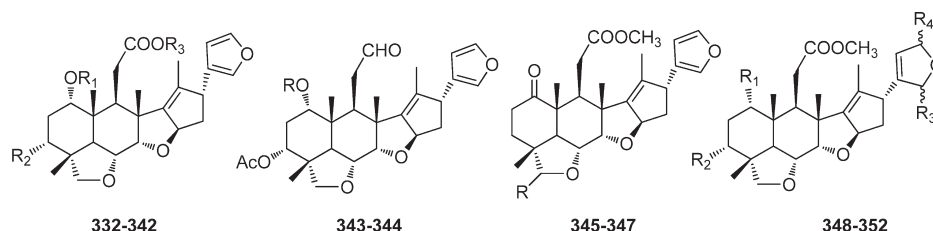


Figure 13. Structures of salannin-class limonoids 332–352.

which showed a mass peak at 556 with a less intense companion at 568, was very difficult to separate.⁶¹⁹ The $\Delta^{8,9}$ double bond in angustidienolide⁵⁹⁷ was revised to be $\Delta^{8,30}$ on the basis of chemical and spectroscopic evidence,^{162,600} and then 2 α -hydroxyangustidienolide was correspondingly shown as **722**. Unfortunately, methyl 3 β -acetoxo-6-hydroxy-1-oxomeliac-14-enoate (**743**) reported in 1998⁶⁰¹ was wrongly cited as 3 β -acetoxo-3-deoxo-6R-hydroxycarapin by Tchimine et al. in 2005.⁵⁵² The structures of utilins B (**749**) and C (**755**) from the barks of *Entandrophragma utile*, were assigned on the basis of extensive NMR experiments and then confirmed by single crystal X-ray measurements.^{620,621} The discovery of khayalenoids A–D (**751–754**) provided examples of limonoids containing the 8-oxa-tricyclo[4.3.2.0^{2,7}]undecane motif.^{622,623} The mixture having xylocensins X (**758**) and Y (**759**) with interchangeable substitutions of isobutyl and isopropyl group between the C-3 and C-30 positions was unequivocally assigned through the HMBC spectrum.⁶²⁴ The spectroscopic properties of xylocensin F (**768**) assigned by Connolly et al.⁶²⁵ were revised on the basis of extensive NMR analysis.⁶²⁶ Although the structure of

xylocensin K (**788**) was elucidated by X-ray crystallography, its NMR data corroborated and later clarified its structure as featuring a tetrahydrofuran subunit with oxygen bridging from C-3 to C-8.^{113,627,628} Unfortunately, the structure of **793** was first named as humilinolide A in 1993⁶²⁹ and was mistakenly documented as methyl 3 β -isobutyryloxy-2,6-dihydroxy-8 α ,30 α -epoxy-1-oxo-meliacate by Kojima et al. in 1998,⁶¹⁴ however, methyl 3 β -tigloyloxy-2-hydroxy-8 α ,30 α -epoxy-1-oxo-meliacate (**797**) reported by him in 1998⁶¹⁴ was renamed as 2-hydroxyswietenmahonolide in 2004 by another research group.⁶³⁰ In addition, the same incidents occurred to **805**, which was first named as 8,30-epoxy swietenine acetate in 1983⁵⁵ and subsequently reported mistakenly as swietenmahonin F in 1990 by Kadota et al.⁵⁶ It was noteworthy to point out that two compounds, **815**⁶¹⁷ and **1051**,⁶³¹ were isolated in 2005 by two research groups independently, and they were both named as cipadesin A though different skeletons were ascribed to them. Granaxylcarpin B and xylocarpin H, both of which were isolated from *Xylocarpus granatum* by two research groups in 2007, had the same structure as **822**.^{632,633} Xylocarponoid A (**825**),

Table 12. Structures and Sources of Nimbolinin-Class Limonoids 353–390

no.	compounds	substitution groups and others	sources
353	1 α -tigloyloxy-3 α -acetoxyl-7 α -hydroxyl-12 α -ethoxyl nimbolinin	R ₁ = Tig; R ₂ = H; R ₃ = OCH ₂ CH ₃	<i>Melia toosendan</i> ³⁸¹
354	1 α -benzoyloxy-3 α -acetoxyl-7 α -hydroxyl-12 α -ethoxyl nimbolinin	R ₁ = Bz; R ₂ = H; R ₃ = OCH ₂ CH ₃	<i>M. toosendan</i> ³⁸¹
355	nimbolinin A	R ₁ = Ac; R ₂ = Bz; R ₃ = OH	<i>M. toosendan</i> ^{85,212}
356	1-deacetylnimbolinin A	R ₁ = H; R ₂ = Bz; R ₃ = OH	<i>M. azedarach</i> ; ³⁸² <i>M. toosendan</i> ^{85,247}
357	12-ethoxynimbolinin A	R ₁ = 2'-methylacryl; R ₂ = H; R ₃ = OCH ₂ CH ₃	<i>M. toosendan</i> ¹⁸⁶
358	nimbolinin B	R ₁ = Ac; R ₂ = Tig; R ₃ = OH	<i>M. toosendan</i> ; ^{212,247} <i>M. azedarach</i> ; ^{342,360,361,382} <i>Turraea robusta</i> ⁸⁷
359	1-deacetylnimbolinin B	R ₁ = H; R ₂ = Tig; R ₃ = OH	<i>Melia toosendan</i> ^{85,247}
360	12-O-methylnimbolinin B	R ₁ = H; R ₂ = Tig; R ₃ = OCH ₃	<i>M. toosendan</i> ; ¹⁸⁶ <i>Turraea holstii</i> ¹⁴³
361	12-ethoxynimbolinin B	R ₁ = Cin; R ₂ = H; R ₃ = OCH ₂ CH ₃	<i>Melia toosendan</i> ¹⁸⁶
362	12-O-ethyl-1-deacetylnimbolinin B	R ₁ = H; R ₂ = Tig; R ₃ = OCH ₂ CH ₃	<i>M. toosendan</i> ³⁷¹
363	nimbolinin C	R ₁ = Cin; R ₂ = H; R ₃ = OCH ₃	<i>M. toosendan</i> ²¹²
364	nimbolinin D	R ₁ = H; R ₂ = Bz; R ₃ = OCH ₃	<i>M. toosendan</i> ²¹²
365	nimbolicin	R ₁ = methylacryl; R ₂ = Cin; R ₃ = OH	<i>Azadirachta indica</i> ³⁸³
366	nimbolin B	R ₁ = Ac; R ₂ = Cin; R ₃ = OH	<i>A. indica</i> ; ^{240,383} <i>Melia azedarach</i> ; ²⁴⁰ <i>M. volkensii</i> ³⁸⁴
367	nimbilin	R ₁ = Ang; R ₂ = Cin; R ₃ = OH	<i>Azadirachta indica</i> ³⁸⁵
368	heudebolin	R ₁ = R ₂ = Ac; R ₃ = OH	<i>Trichilia heudelotii</i> ³⁸⁶
369	volkensin	R ₁ = Tig; R ₂ = H; R ₃ = OH	<i>Melia volensii</i> ³⁶²
370	12-O-methylvolkensin	R ₁ = Tig; R ₂ = H; R ₃ = OCH ₃	<i>M. toosendan</i> ²¹¹
371	ohchinolide A	R ₁ = Ac; R ₂ = Bz; R ₃ = O	<i>M. azedarach</i> ; ^{382,387–389}
372	1-O-deacetyl-ohchinolide A	R ₁ = H; R ₂ = Bz; R ₃ = O	<i>M. azedarach</i> ³⁸⁷
373	1-O-deacetyl-1-O-tigloylochinolide A	R ₁ = Tig; R ₂ = Bz; R ₃ = O	<i>M. azedarach</i> ³⁸⁷
374	ohchinolide B	R ₁ = Ac; R ₂ = Tig; R ₃ = O	<i>M. azedarach</i> ; ^{382,387,389} <i>M. toosendan</i> ; ⁸⁵ <i>Azadirachta indica</i> ¹⁰²
375	1-O-deacetyl-ohchinolide B	R ₁ = H; R ₂ = Tig; R ₃ = O	<i>Melia azedarach</i> ³⁸⁷
376	1-O-deacetyl-1-O-tigloylochinolide B	R ₁ = R ₂ = Tig; R ₃ = O	<i>M. azedarach</i> ³⁸⁷
377	1-O-deacetyl-1-O-benzoylochinolide B	R ₁ = Bz; R ₂ = Tig; R ₃ = O	<i>M. azedarach</i> ³⁸⁷
378	chisonimbolinin A	R ₁ = R ₂ = Ac; R ₃ = OCH ₃	<i>Chisocheton paniculatus</i> ³⁹⁰
379	chisonimbolinin B	R ₁ = H; R ₂ = Ac; R ₃ = OCH ₃	<i>C. paniculatus</i> ³⁹⁰
380	chisonimbolinin C	R ₁ = H; R ₂ = Tig; R ₃ = OCH ₃	<i>C. paniculatus</i> ³⁹⁰
381	chisonimbolinin D	R ₁ = H; R ₂ = Ac; R ₃ = OH	<i>C. paniculatus</i> ³⁹⁰
382	chisonimbolinin E	R ₁ = H; R ₂ = Ac; R ₃ = OCH ₂ CH ₃	<i>C. paniculatus</i> ³⁹⁰
383	chisonimbolinin F	R ₁ = R ₃ = H; R ₂ = Ac	<i>C. paniculatus</i> ³⁹⁰
384	chisonimbolinin G	R ₁ = R ₂ = Ac; R ₃ = H	<i>C. paniculatus</i> ³⁹⁰
385	12-ethoxynimbolinin C		<i>Melia toosendan</i> ¹⁸⁶
386	ohchinolide C	R = iBu	<i>M. toosendan</i> ^{84,85}
387	azecin 2	R = H	<i>M. azedarach</i> ¹⁷³
388	12-ethoxynimbolinin D		<i>M. toosendan</i> ¹⁸⁶
389	melianolide		<i>M. azedarach</i> ³⁶¹
390	17- <i>epi</i> -12-dehydroxyheudebolin		<i>Turreanthus africanus</i> ³⁹¹

containing a C₂₈ limonoid skeleton, may originate from xylogranatin C (**823**) by an aldol condensation followed by intramolecular hemiacetal formation.⁶³⁴ In addition, its ring cleavage isomer (xylocarponoid B) was formed gradually in CDCl₃ during the NMR experiments and finally reached equilibrium at an A: B ratio of 4:1.⁶³⁴ Compound **829**, possessing a highly oxidized heptacyclic A,B,D-seco limonoid with an 8 α ,30 α -epoxy ring and 1,29-oxygen bridge, was patented as xylo lactone⁶³⁵ and then was named xylocensin L⁶³⁶ in *Tetrahedron Letters* in 2004 by Wu et al. The structure of xylogranatin A (**832**), featuring a 1,9-oxygen bridge, was confirmed by X-ray diffraction analysis.⁶³⁷ The hypothetical biosynthetic route and chemical correlations of

832 and xylogranatin D (**833**) were postulated in 2006,⁶³⁷ and **833**, the sole limonoid with a C-9/30 linkage, was apparently considered to be an artifact.⁶³⁸ Unfortunately, the trivial names “xylogranatin A–D” were also proposed for the compounds **737** and **762–764** isolated in 2006.⁶³⁹ Xylogranatins I–Q (**834–842**) all contained a central furan core, and they were derived from the key biosynthetic intermediates xylogranatins C and R (**823** and **843**).⁶³⁸ The possible biosynthetic pathway of grandifotane A (**845**) was postulated, in which an intermediate was formed from a mexicanolide-type limonoid by an enzymatic Baeyer–Villiger oxidation. Then, the intermediate might undergo serials of reactions to keep the required stereochemistry for **845**.⁶⁴⁰

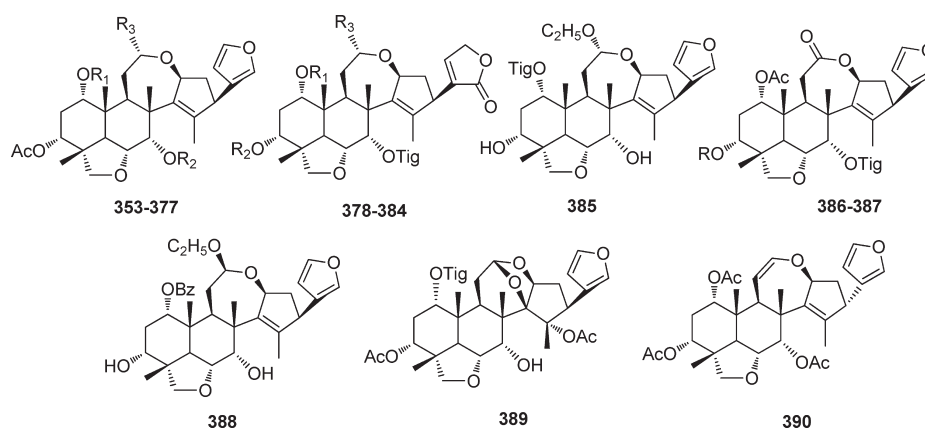


Figure 14. Structures of nimbolinin-class limonoids 353–390.

Table 13. Structures and Sources of Nimbin-Class Limonoids 391–404

no.	compounds	substitution groups and others	sources
391	nimbin	R ₁ = COOCH ₃ ; R ₂ = Ac	<i>Azadirachta indica</i> ^{59,70,81,102–106,115,136,317,325,357,405–407}
392	6-deacetylnimbin	R ₁ = COOCH ₃ ; R ₂ = H	<i>A. indica</i> ^{70,81,102–104,106,317,325,407,408}
393	nimbanal	R ₁ = CHO; R ₂ = Ac	<i>A. indica</i> ³⁶⁷
394	6-deacetylnimbanal	R ₁ = CHO; R ₂ = H	<i>A. indica</i> ³⁷⁷
395	nimbinol	R ₁ = CH ₂ OH; R ₂ = Ac	<i>A. indica</i> ³⁷⁷
396	ohchinolal (salannal)	R ₁ = Tig; R ₂ = H	<i>Melia azedarach</i> ^{342,360,370,387}
397	1- <i>O</i> -detigloyl-1- <i>O</i> -benzoylochinolal	R ₁ = Bz; R ₂ = H	<i>M. azedarach</i> ³⁸⁷
398	1- <i>O</i> -detigloyl-1- <i>O</i> -cinnamoylochinolal	R ₁ = Cin; R ₂ = H	<i>M. azedarach</i> ³⁸⁷
399	3- <i>O</i> -acetylochinolal	R ₁ = Tig; R ₂ = Ac	<i>M. toosendan</i> ^{84,85}
400	desacetylnimbinolide	R ₁ = H; R ₂ = O; R ₃ = OH	<i>Azadirachta indica</i> ⁴⁰⁸
401	isonimbinolide	R ₁ = Ac; R ₂ = OH; R ₃ = O	<i>A. indica</i> ⁴⁰⁹
402	desacetylnimbinolide	R ₁ = H; R ₂ = OH; R ₃ = O	<i>A. indica</i> ⁴⁰⁸
403	4- <i>epi</i> -nimbin		<i>A. indica</i> ⁴¹⁰
404	7 α -hydroxy-15 β -hydroxy-7,15-deoxo nimbin		<i>A. indica</i> ⁴¹¹

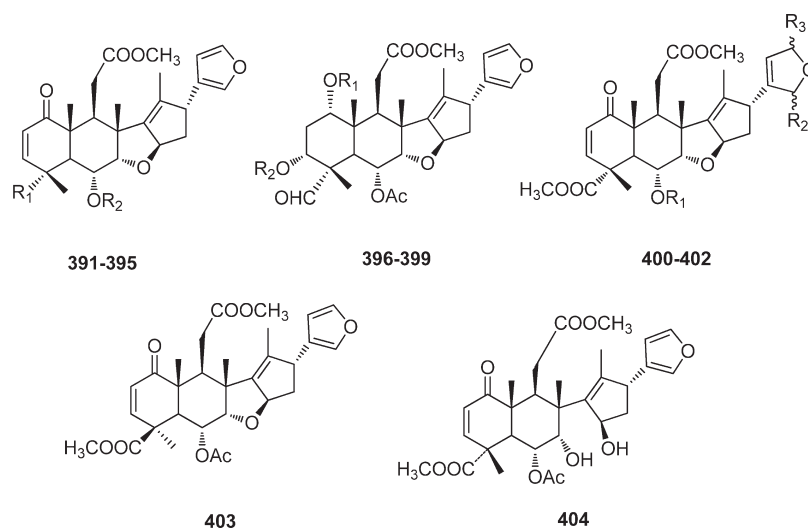


Figure 15. Structures of nimbin-class limonoids 391–404.

2.3.2.2. Phragmalin-Class. **2.3.2.2.1. Phragmalin-ortho Esters.** Phragmalin-class limonoids possessed characteristic rings of A and B tricyclo[3.3.1^{2,10}.1^{1,4}]decane or tricyclo[4.2.1^{10,30}.1^{1,4}]-

decane, and most of them also bore an ortho ester group. Up to now, four subtypes of phragmalin orthoesters have been reported, which were classified into 1,8,9- (–910), 8,9,11- (911–916),

Table 14. Structures and Sources of Nimbolidin-class 405–415

no.	compounds	substitution groups and others	sources
405	nimbolidin A	$R_1 = R_3 = \text{Ac}; R_2 = \text{Bz}$	<i>Melia azedarach</i> ³⁸²
406	15-O-deacetyl-15-O-methylnimbolidin A	$R_1 = \text{Ac}; R_2 = \text{Bz}; R_3 = \text{CH}_3$	<i>M. azedarach</i> ²²⁶
407	nimbolidin B	$R_1 = R_3 = \text{Ac}; R_2 = \text{Tig}$	<i>M. azedarach</i> ^{342,361,382} <i>M. toosendan</i> ^{209,363}
408	15-O-deacetylnimbolidin B	$R_1 = \text{Ac}; R_2 = \text{Tig}; R_3 = \text{H}$	<i>M. azedarach</i> ²²⁶
409	15-O-deacetyl-15-O-methylnimbolidin B	$R_1 = \text{Ac}; R_2 = \text{Tig}; R_3 = \text{CH}_3$	<i>M. azedarach</i> ²²⁶
410	nimbolidin C	$R_1 = R_3 = \text{Ac}; R_2 = \text{iBu}$	<i>M. toosendan</i> ^{85,363}
411	nimbolidin D	$R_1 = R_2 = \text{Tig}; R_3 = \text{Ac}$	<i>M. toosendan</i> ^{85,363}
412	nimbolidin E	$R_1 = \text{Tig}; R_2 = \text{iBu}; R_3 = \text{Ac}$	<i>M. toosendan</i> ^{85,363}
413	nimbolidin F	$R_1 = \text{Piv}; R_2 = \text{Tig}; R_3 = \text{Ac}$	<i>M. toosendan</i> ^{84,85}
414	walsogyne A		<i>Walsura chrysogyne</i> ⁴¹²
415	7 α -acetyl-15 β -methoxy-29-methylene-7,15-deoxonimbolide		<i>Azadirachta indica</i> ⁴¹¹

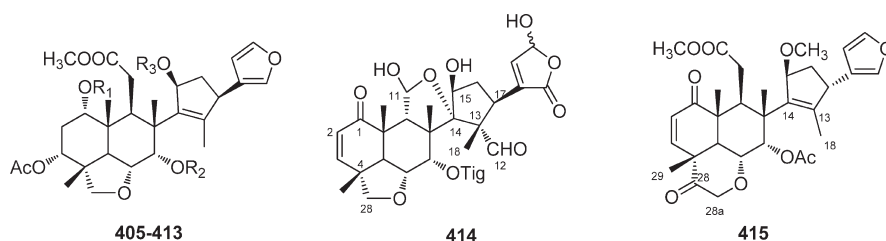


Figure 16. Structures of nimbolidin-class 405–415.

8,9,14- (917–930), and 8,9,30-phragmalin orthoesters (931–962) according to the position of the *ortho*-acetate group. The structure of phragmalin (846) was proposed on the basis of chemical and spectroscopic evidence⁶⁸⁹ and then determined by means of an X-ray study of its iodacetate.⁶⁹⁰ The distribution of phragmalins and mexicanolides in the stem barks, fruits, and seeds of the Chinese mangrove plant *Xylocarpus granatum* was discussed, and the conclusion was reached that the high concentration of phragmalin orthoesters in the stem barks of *Xylocarpus* plants might serve as an important chemical defense against invasion by pests or microorganisms.⁶³³ A biosynthetic route to 846 which could explain why 1,29-cycloswietenan derivatives were hydroxylated at C-8 and C-9 was presented.⁶⁸³ The structure of 850 was assigned as xylocensin E early in 1976,⁶²⁵ and was obtained and then reported as phragmalin 2,3,30-triacetate in 1992.¹⁶² The substance 'bussein' obtained from *Entandrophraga bussei*,^{424,530} was shown to be a mixture of busseins A (865) and B (866), whose structures were first assigned on the basis of spectroscopic properties and chemical reactions⁶⁹¹ and then were subsequently modified.^{692,693} The ¹H NMR-based conformational analysis on the epimeric compounds swietenitins A and B (897 and 898) provided a general approach to determining the absolute configuration of the 2,3-epoxy-2-methylbutyryloxy unit borne at C-3 by a large group of the phragmalin-orthoester limonoids.⁴⁵⁶ The structure of pseudrelone B (903) from *Pseudocedrela kotschyii*⁶⁹⁴ was revised to have C-11/19 instead of C-11/18 ether bridge based on the X-ray analysis of its triacetate.⁶⁹⁵ It was suggested on the basis of a plausible proposed biosynthetic origin that chukvelutildes A-F (904–909), which have a C-16/30 lactone ring, also have a three- or four-carbon enolized acyl substituent at C-15.⁶⁹⁶ Chuktabrin B (910) had a polycyclic skeleton containing a 4,5,6,7-tetrahydrobenzofuran formed via a cyclization reaction between C-15 and C-21, a δ -lactone furnished between C-16 and C-30, and a biosynthetically extended C2 unit at C-15.⁶⁹⁷ The structure

of utilin (920), possessing the 1,29-cycloswietenan skeleton, was confirmed by X-ray analysis, and its absolute configuration was established by chemical methods.⁶⁹⁸ The structure of xylocensin O (948), the first example of an 8,9,30-phragmalin orthoester limonoid, was confirmed by X-ray crystallographic analysis, and a biosynthetic pathway to it from mexicanolide was proposed.⁶⁹⁹ The structures of some xylocensins from *Xylocarpus granatum* were not in accord with the nomenclatures used by different research groups, which led to great confusion. On one hand, the structures of xylocensins Q (950), R (951), and V (955) obtained by Wu et al.^{639,659,700} were identical to xylocensins R, Q, and T reported by Cui et al.,⁷⁰¹ respectively. On the other hand, both 954^{659,700} and 987⁷⁰¹ were named xylocensin U.

2.3.2.2.2. Polyoxyphragmalins. Unfortunately, in 2010, two separate groups selected the trivial names moluccensins H–J to apply to six compounds (963–968) with the same skeleton but different substitutions, which caused each trivial name to correspond to two different structures (Figure 27 and Table 25). In fact, the structures of xylocarpins A (981) and D (984) obtained from *Xylocarpus granatum* and elucidated in 2007,⁶³³ were the same as granaxylocarpins E and D, respectively, obtained from the same species in the same year.⁶³² The structure of xylocensin U, isolated from *X. granatum*,⁷⁰¹ was revised to be 987 by analysis of its HMBC data and analogous comparison.^{632,633} From a biosynthetic perspective, atomasins such as atomasins A and B (974 and 975) from *Entandrophragma candollei*⁷¹⁹ and 8,9-dihydroxy phragmalins, such as tabulalides A and B (995 and 996) from *Chukrasia tabularis*,⁷⁰⁶ were the precursor of the phragmalin orthoesters. The extensive spectroscopic analyses including MS, NMR, and single crystal X-ray diffraction experiments suggested that methyl 1 α -acetoxy-6,8 α ,14 β ,30 β -tetrahydroxy-3-oxo-[3.3.1^{10,2,1}^{1,4}]-tricyclomeliac-7-oate (992)⁷²⁰ and methyl 1 α ,6,8 α ,14 β ,30 β -pentahydroxy-3-oxo-[3.3.1^{10,2,1}^{1,4}]-tricyclomeliac-7-oate (991)⁷²¹ were, in fact, khayanolide E (1007)

Table 15. Structures and Sources of Ring D-seco Limonoids 416–457

no.	compounds	substitution groups and others	sources
416	gedunin	$R_1 = R_3 = H; R_2 = OAc$	<i>Entandrophragma angolense</i> ; ⁴²³ <i>E. delevoyi</i> ; ^{424,425} <i>Xylocarpus granatum</i> ; ^{49,424,426,427} <i>X. obovatus</i> ; ⁴²⁸ <i>Azadirachta indica</i> ; ^{57–59,70,80–82,103,104,107,115,240,429} <i>Trichilia trifolia</i> ; ¹⁸² <i>Cabralea eichleriana</i> ; ⁴³⁰ <i>Melia azedarach</i> ; ^{240,251} <i>Cedrela fissilis</i> ; ^{113,132} <i>C. odorata</i> ; ^{98,431,432} <i>C. sinensis</i> ; ⁴³³ <i>Guarea grandiflora</i> ; ^{434,435} <i>Khaya grandifoliola</i> ; ⁴³⁶ <i>Chisocheton paniculatus</i> ; ¹¹⁷ <i>Carapa guianensis</i> ; ^{113,437}
417	6 α -hydroxygedunin	$R_1 = \alpha-OH; R_2 = OAc; R_3 = H$	<i>C. guianensis</i> ; ¹³⁷
418	6 α -acetoxygedunin	$R_1 = \alpha-OAc; R_2 = OAc; R_3 = H$	<i>C. guianensis</i> ; ^{113,137,437,438} <i>Cedrela fissilis</i> ; ¹¹³ <i>Chisocheton paniculatus</i> ; ^{94,117} <i>Swietenia mahagoni</i> ; ¹¹² <i>Guarea grandiflora</i> ; ⁴³⁴ <i>Aglaia elaeagnoides</i> ; ⁴¹⁹
419	6 α ,11 β -diacetoxygedunin	$R_1 = \alpha-OAc; R_2 = OAc; R_3 = \beta-OAc$	<i>A. elaeagnoides</i> ; ⁴³⁹ <i>Carapa guianensis</i> ; ^{438,440} <i>C. granatum</i> ; ⁴⁴¹
420	6 β -hydroxygedunin	$R_1 = \beta-OH; R_2 = OAc; R_3 = H$	<i>Azadirachta indica</i> ; ⁴⁴²
421	7-deacetylgedunin	$R_1 = R_3 = H; R_2 = OH$	<i>A. indica</i> ; ^{57,70,103,104} <i>Cedrela fissilis</i> ; ¹¹³ <i>C. odorata</i> ; ⁹⁸ <i>C. sinensis</i> ; ⁴³³ <i>Pseudocedrela kotschy</i> ; ^{443,444} <i>Trichilia trifolia</i> ; ¹⁸² <i>Swietenia aubrevilleana</i> ; ⁴⁴⁵ <i>Khaya ivorensis</i> ; ^{446,447} <i>K. grandifoliola</i> ; ¹⁶⁴ <i>Cabralea eichleriana</i> ; ⁴³⁰ <i>Carapa guianensis</i> ; ⁴³⁷ <i>Xylocarpus granatum</i> ; ⁴⁴⁸
422	7-desacetyl-7-benzoylgedunin	$R_1 = R_3 = H; R_2 = Bz$	<i>Azadirachta indica</i> ; ^{68,70}
423	7-deacetoxy-7-oxogedunin	$R_1 = R_3 = H; R_2 = O$	<i>Carapa guianensis</i> ; ^{113,137,437,449,450} <i>Pseudocedrela kotschy</i> ; ^{443,444} <i>Khaya senegalensis</i> ; ^{164,451} <i>K. ivorensis</i> ; ^{446,447} <i>Melia azedarach</i> ; ^{251,452} <i>Trichilia schomburgkii</i> ; ⁴⁵³ <i>Guarea grandiflora</i> ; ^{434,435} <i>G. guidona</i> ; ⁴⁵⁴ <i>Cabralea eichleriana</i> ; ⁴³⁰ <i>Xylocarpus granatum</i> ; ^{448,455} <i>X. moluccensis</i> ; ¹⁶² <i>Swietenia macrophylla</i> ; ^{445,456} <i>S. mahagoni</i> ; ^{112,457,458} <i>Cedrela fissilis</i> ; ^{113,132} <i>C. odorata</i> ; ^{98,167,459}
424	7-deacetoxy-7 α ,11 β -dihydroxygedunin	$R_1 = H; R_2 = OH; R_3 = \beta-OH$	<i>C. sinensis</i> ; ⁴³³
425	7-deacetoxy-7 α ,11 α -dihydroxygedunin	$R_1 = H; R_2 = OH; R_3 = \alpha-OH$	<i>C. sinensis</i> ; ⁴³³
426	11 α -hydroxygedunin	$R_1 = H; R_2 = OAc; R_3 = \alpha-OH$	<i>C. sinensis</i> ; ⁴³³
427	11 β -hydroxygedunin	$R_1 = H; R_2 = OAc; R_3 = \beta-OH$	<i>C. sinensis</i> ; ⁴³³
428	11 β -acetoxygedunin	$R_1 = H; R_2 = OAc; R_3 = \beta-OAc$	<i>Carapa guianensis</i> ; ⁴⁴⁰ <i>Entandrophragma delevoyi</i> ; ⁴²⁵
429	11-oxogedunin	$R_1 = H; R_2 = OAc; R_3 = O$	<i>Cedrela sinensis</i> ; ⁴³³
430	7 α -acetoxy-14 β ,15 β -epoxygedunin-1-ene-3-O- β -D-glucopyranoside	$R = \beta-D-Glc$	<i>Melia azedarach</i> ; ⁴⁶⁰
431	azecin 4	$R = \beta-D-Ara$	<i>M. azedarach</i> ; ¹⁷³
432	7-deacetoxy-7-hydroxyphotogedunin	$R = H$	<i>Cabralea eichleriana</i> ; ⁴³⁰
433	photogedunin	$R = Ac$	<i>Cedrela fissilis</i> ; ¹¹³ <i>C. salvadorensis</i> ; ^{413,420} <i>C. dugessi</i> ; ⁴¹³ <i>C. odorata</i> ; ⁴⁶¹ <i>C. ciliolata</i> ; ⁴⁶² <i>Xylocarpus granatum</i> ; ⁴²⁷
434	khivorin	$R_1 = R_2 = R_3 = OAc; R_4 = H$	<i>Khaya ivorensis</i> ; ^{446,463} <i>K. anthotheca</i> ; ^{163,183} <i>K. grandifolia</i> ; ^{164,167} <i>K. senegalensis</i> ; ^{451,464–466} <i>K. nyasica</i> ; ¹⁸⁴ <i>Swietenia mahagoni</i> ; ⁴⁵⁸
435	1-deacetylkhivorin	$R_1 = OH; R_2 = R_3 = OAc; R_4 = H$	<i>S. mahagoni</i> ; ⁴⁵⁸ <i>Khaya grandifoliola</i> ; ⁴³⁶
436	3-deacetylkhivorin	$R_1 = R_3 = OAc; R_2 = OH; R_4 = H$	<i>K. senegalensis</i> ; ^{464–468} <i>K. anthotheca</i> ; ^{163,183} <i>K. nyasica</i> ; ¹⁸⁴ <i>K. madagascariensis</i> ; ^{164,469} <i>K. ivorensis</i> ; ⁴⁴⁷ <i>Swietenia mahagoni</i> ; ⁴⁵⁸
437	7-deacetylkhivorin	$R_1 = R_2 = OAc; R_3 = OH; R_4 = H$	<i>S. mahagoni</i> ; ⁴⁵⁸ <i>Khaya grandifoliola</i> ; ⁴³⁶

Table 15. Continued

no.	compounds	substitution groups and others	sources
438	1,3,7-trideacetylkhivorin	$R_1 = R_2 = R_3 = \text{OH}; R_4 = \text{H}$	<i>K. ivorensis</i> ; ⁴⁴⁷ <i>K. senegalensis</i> ; ^{470,471} <i>Swietenia mahagoni</i> ⁴⁵⁸
439	3-deacetyl-7-oxokhivorin	$R_1 = \text{OAc}; R_2 = \text{OH}; R_3 = \text{O}; R_4 = \text{H}$	<i>Khaya senegalensis</i> ; ^{465,466,468,472}
440	3 α ,7 α -dideacetylkhivorin	$R_1 = \text{OAc}; R_2 = R_3 = \text{OH}; R_4 = \text{H}$	<i>K. senegalensis</i> ; ^{164,422,467,468,470,473} <i>K. ivorensis</i> ; ⁴⁴⁷ <i>Swietenia mahagoni</i> ⁴⁵⁸
441	7-deacetoxy-7-oxokhivorin	$R_1 = R_2 = \text{OAc}; R_3 = \text{O}; R_4 = \text{H}$	<i>Khaya senegalensis</i> ; ^{164,167,451,464,465}
442	11 β -acetoxykhivorin	$R_1 = R_2 = R_3 = R_4 = \text{OAc}$	<i>K. madagascariensis</i> ; ^{469,474} <i>K. nyasica</i> ^{164,184}
443	dihydrogedunin	$R_1 = R_4 = \text{H}; R_2 = \text{O}; R_3 = \text{OAc}$	<i>Guarea thompsonii</i> ; ^{167,475}
444	7-oxodeacetoxydihydro- α -gedunol	$R_1 = R_4 = \text{H}; R_2 = \text{OH}; R_3 = \text{O}$	<i>G. thompsonii</i> ; ⁴⁷⁵
445	1 α -hydroxy-1,2-dihydrogedunin	$R_1 = \text{OH}; R_2 = \text{O}; R_3 = \text{OAc}; R_4 = \text{H}$	<i>Xylocarpus granatum</i> ⁴⁹
446	1 α -methoxy-1,2-dihydrogedunin	$R_1 = \text{OCH}_3; R_2 = \text{O}; R_3 = \text{OAc}; R_4 = \text{H}$	<i>Cedrela odorata</i> ⁹⁸
447	nyasin	$R_1 = R_2 = R_3 = \text{OAc}; R_4 = \text{OH}$	<i>Khaya nyasica</i> ^{184,476,477}
448	1,2-dihydro-3 β -hydroxy-7-deacetoxy-7-oxogedunin		<i>Cedrela fissilis</i> ; ¹¹³ <i>C. guianensis</i> ¹¹³
449	azadirinin		<i>Azadirachta indica</i> ⁴⁷⁸
450	3,7-dideacetyl-6 α -hydroxykhivorin		<i>Khaya senegalensis</i> ⁴⁶⁶
451	nimolicinol	$R = \text{Ac}; \Delta^{1,2}$	<i>Azadirachta indica</i> ^{70,115,479}
452	7-deacetynimolicinol	$R = \text{H}; \Delta^{1,2}$	<i>A. indica</i> ¹¹⁵
453	1 α ,2 α -epoxynimolicinol	$R = \text{Ac}; 1,2\text{-epoxy}$	<i>A. indica</i> ¹¹⁵
454	mahmoodin		<i>A. indica</i> ⁸¹
455	piscidofuran		<i>Walsura piscidia</i> ⁸⁸
456	meliacinol		<i>Azadirachta indica</i> ⁹³
457			<i>Melia azedarach</i> ⁴⁸⁰

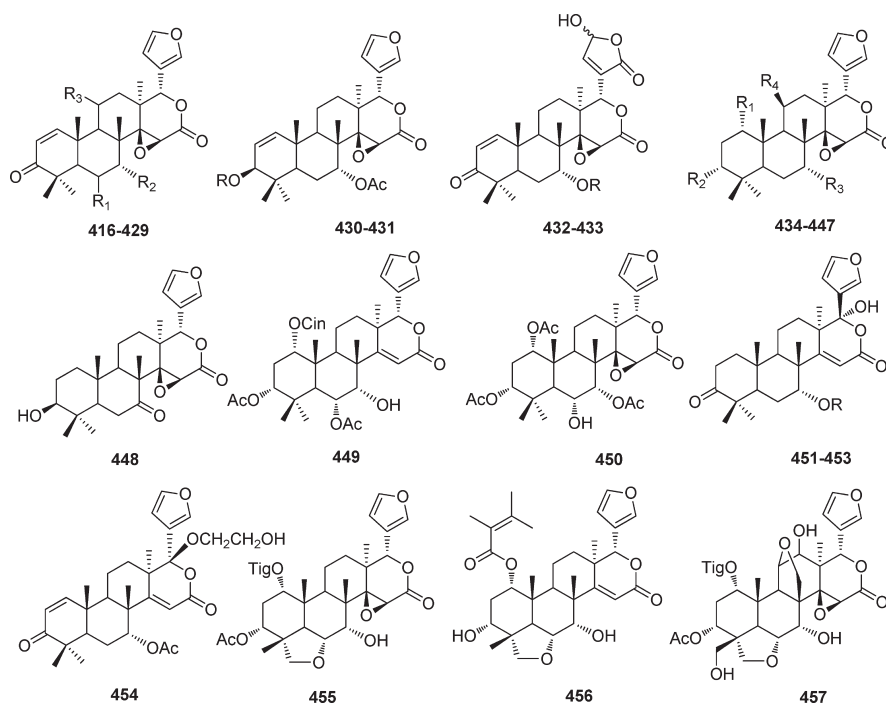


Figure 17. Structures of ring D-seco limonoids 416–457.

and 1-*O*-deacetylkhayanolide E (**1008**) respectively.⁷²² Swiema-hogin B (**993**) was an example of incorporating a rare five-membered γ -lactone fused to the C-ring at C-8 and C-14 and in which the six-membered δ -lactone in the D-ring was

destroyed.⁵⁷² The biosynthesis of trichiliton A (**997**), bearing a bicyclo[5.2.1]^{4,10}decane motif, involved an alternative new route from mexicanolide to phragmalin.⁶⁵¹ Khayalactone (**998**) could arise from a 1,2,3,8-tetrahydroxylated precursor by cleavage of the

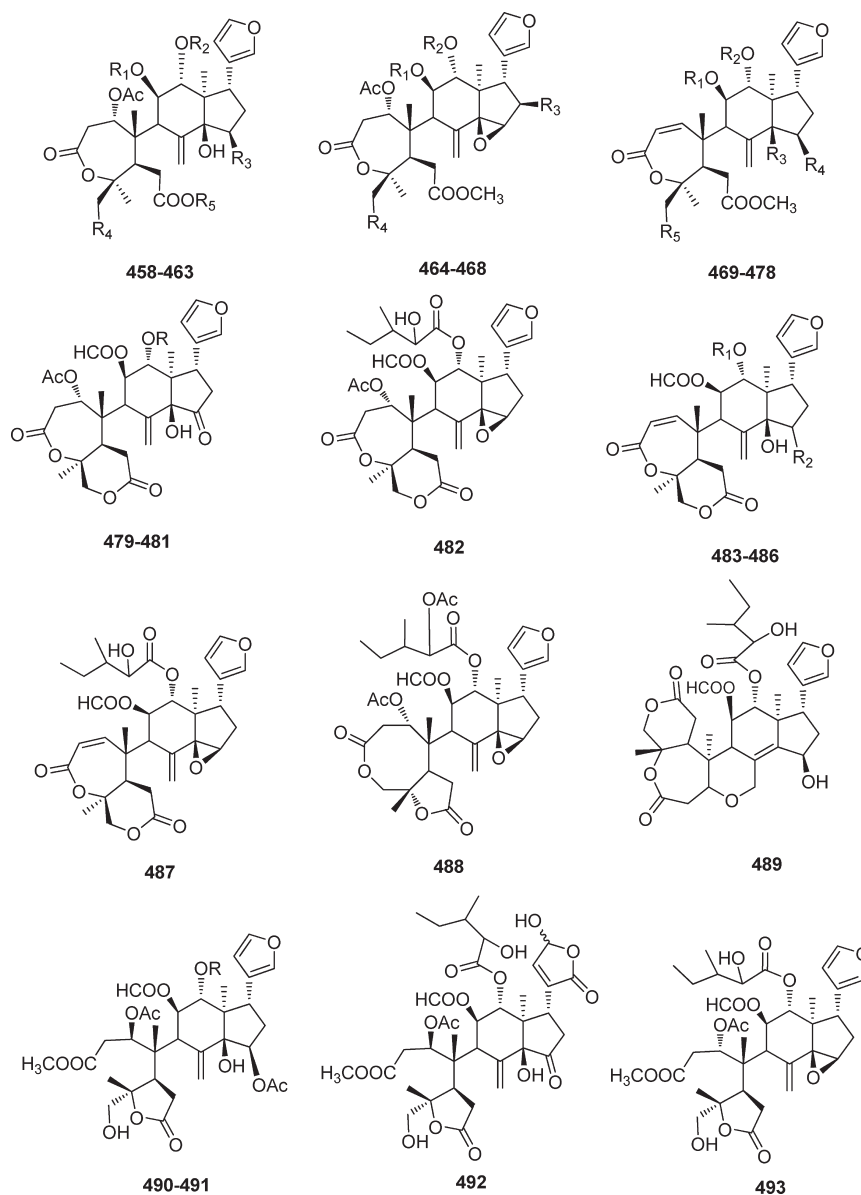


Figure 18. Structures of prieurianin-class limonoids 458–493.

1,2-diol followed by formation of the hemiketal by addition of the 8-hydroxyl group to the newly formed 1-carbonyl group.^{553,680} The absolute configuration of khayanolide A (**1002**) was established by X-ray analysis and a CD study.^{548,549} In biosynthetic terms, a pinacol–pinacolone rearrangement of a 2,3,30-trihydroxy-1,29-cyclomeliacate precursor is possible, resulting in a 2-oxo-tricyclo-[4,2,1^{10,30}.1^{1,4}]-decane, and subsequently reduction or addition of an hydroxyl group at C-14 to the ketone and O-2-methylation may then led to the limonoids **1013** and **1015**, respectively,⁷²⁰ which gives a further enlargement of the biosynthetic mexicanolide pathways.⁷²¹ In addition, a possible biosynthetic pathway leading to the formation of khayanolides from mexicanolide was proposed.⁵⁴⁹ On the basis the extensive spectroscopic analyses including MS, NMR, and single crystal X-ray diffraction experiments, Zhang et al. proposed that methyl 1 α ,2 β ,3 α ,6,8 α ,14 β -hexahydroxy-[4.2.1^{10,30}.1^{1,4}]-tricyclomeliac-7-oate (**1014**) and methyl 1 α -acetoxo-2 β ,3 α ,6,8 α ,14 β -pentahydroxy-[4.2.1^{10,30}.1^{1,4}]-tricyclomeliac-7-oate (**1015**)⁷²¹

were, in fact, khayanolide B (**1004**) and 1-O-acetylkhayanolide B (**1005**),⁷²² respectively.

2.3.3. 8,11-Linkage Limonoids (Trijugin-Class). Trijugin-class limonoids with contracted ring C were postulated to be produced biosynthetically via a pinacol–pinacolone rearrangement of a methyl 9, 11-dihydroxyangolensate.^{563,565,729} Capen-solactones 2 and 3 (**1034** and **1022**) were isolated as a mixture with their ester moieties interchanged at C-2 α and C-3 α .⁷³⁰ Trichilin B (**1043**), featuring a 9,17-oxygen bridge and a highly rearranged ring system, along with the biosynthetically correlated trichilin A (**1036**), was isolated from *Trichilia conmaroides*.⁷³¹ Unfortunately, the two trivial names were previously assigned to intact limonoids **137** and **135**, respectively.^{194,732}

2.3.4. 10,11-Linkage Limonoids (Cipadesin-Class). The rings A and C of cipadesin-class limonoids were joined via C-10/11, and among these limonoids the structure of cipadesin C (**1044**) was confirmed by X-ray crystallographic analysis.⁶³¹ Two compounds found in *Cipadesa cinerascens*, **1039**^{54,563} and **1045**,⁵³

Table 16. Structures and Sources of Prieurianin-Class Limonoids 458–493

no.	compounds	substitution groups and others	sources
458	prieurianin	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ = O; R ₄ = OAc; R ₅ = CH ₃	<i>Trichilia prieuriana</i> ¹⁶⁸ <i>Guarea guidona</i> ⁴⁵⁴ <i>Nymanian capensis</i> ²⁸³ <i>Turraea obtusifolia</i> ¹⁸⁹ <i>Entandrophragma candolei</i> ⁴⁹¹
459	rohituka 4	R ₁ = formacyl; R ₂ = iVal; R ₃ = O; R ₄ = OAc; R ₅ = CH ₃	<i>Aphanamixis polystacha</i> ⁴⁸⁴
460	dregeana 2	R ₁ = R ₂ = Ac; R ₃ = O; R ₄ = H; R ₅ = CH ₃	<i>Trichilia dregeana</i> ²⁷⁴
461	trichavensin	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ = OAc; R ₄ = pivalyloxy; R ₅ = CH ₃	<i>T. havanensis</i> ⁴⁹²
462	Tr-A	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ = OAc; R ₄ = OH; R ₅ = CH ₂ CH ₃	<i>T. roka</i> ⁴⁹³
463	Tr-C	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ = OAc; R ₄ = OH; R ₅ = CH ₃	<i>T. roka</i> ⁴⁹³
464	expoxyprieurianin	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ = H; R ₄ = OAc	<i>Guarea guidona</i> ⁴⁵⁴ <i>Entandrophragma candolei</i> ⁴⁹⁴
465	dysoxylum A	R ₁ = formacyl; R ₂ = iVal(OH); R ₃ = OPiv; R ₄ = OAc	<i>Dysoxylum hainanense</i> ⁴⁸³
466	dysoxylum B	R ₁ = formacyl; R ₂ = iVal(OH); R ₃ = iVal(OAc); R ₄ = OAc	<i>D. hainanense</i> ⁴⁸³
467	dysoxylum C	R ₁ = formacyl; R ₂ = iVal(OH); R ₃ = OiVal(OH); R ₄ = OAc	<i>D. hainanense</i> ⁴⁸³ <i>D. lenticellatum</i> ²⁶⁶
468	nymania 4	R ₁ = R ₂ = Ac; R ₃ = R ₄ = H	<i>Nymanian capensis</i> ²⁸³
469	rohituka 8	R ₁ = formacyl; R ₂ = iVal; R ₃ = OH; R ₄ = OAc; R ₅ = OAc	<i>Aphanamixis polystacha</i> ⁴⁸⁴
470	mombasone	R ₁ = formacyl; R ₂ = 2-oxo-3-methylpentanoyl; R ₃ R ₄ = O; R ₅ = OAc	<i>Turraea mombasana</i> ⁴⁹⁵
471	mombasol	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ R ₄ = O; R ₅ = OAc	<i>T. mombasana</i> ⁴⁹⁵ <i>Guarea guidona</i> ⁴⁹⁶
472	amotsangin A	R ₁ = Ac; R ₂ = Piv; R ₃ R ₄ = O; R ₅ = H	<i>Amoora tsangii</i> ²⁷⁹
473	amotsangin B	R ₁ = Ac; R ₂ = iBu; R ₃ R ₄ = O; R ₅ = H	<i>A. tsangii</i> ²⁷⁹
474	amotsangin C	R ₁ = Ac; R ₂ = 2-hydroxy-3-methylpentanoyl; R ₃ R ₄ = O; R ₅ = H	<i>A. tsangii</i> ²⁷⁹
475	amotsangin D	R ₁ = Ac; R ₂ = propanoyl; R ₃ R ₄ = O; R ₅ = H	<i>A. tsangii</i> ²⁷⁹
476	amotsangin E	R ₁ = Ac; R ₂ = Bz; R ₃ R ₄ = O; R ₅ = H	<i>A. tsangii</i> ²⁷⁹
477	amotsangin F	R ₁ = formacyl; R ₂ = Bz; R ₃ R ₄ = O; R ₅ = H	<i>A. tsangii</i> ²⁷⁹
478	nymania 3	R ₁ = R ₂ = Ac; R ₃ R ₄ = O; R ₅ = H	<i>Dysoxylum malabaricum</i> ⁴⁹⁷ <i>Nymanian capensis</i> ²⁸³
479	Tr-B	R = 2-hydroxy-3-methylpentanoyl	<i>Trichilia roka</i> ⁴⁹³ <i>T. emetica</i> ¹⁹² <i>Apanamixis ploystacha</i> ⁴⁸⁵
480	rohitukin	R = iVal	<i>A. ploystacha</i> ^{484,487} <i>Turraea obtusifolia</i> ⁴⁹⁸
481	2'-hydroxyrohitukin	R = iVal(OH)	<i>Guarea cedrata</i> ⁴⁹⁹
482	guarea B		<i>G. multiflora</i> ⁵⁰⁰ <i>G. thompsonii</i> ⁴⁸⁹
483	rohituka 7	R ₁ = 2-hydroxy-3-methylpentanoyl; R ₂ = β -OAc	<i>Aphanamixis polystacha</i> ^{275,484,485}
484	rohituka 9	R ₁ = iVal; R ₂ = β -OAc	<i>A. polystacha</i> ^{275,484}
485	hispidin B	R ₁ = 2-hydroxy-3-methylpentanoyl; R ₂ = α -OTig	<i>Trichilia hispida</i> ⁵⁰¹
486	hispidin C	R ₁ = 2-hydroxy-3-methylpentanoyl; R ₂ = α -OAc	<i>T. hispida</i> ⁵⁰¹
487	D-4		<i>T. prieuriana</i> ⁴⁸⁹
488	dregeanin		<i>T. dregeana</i> ⁴⁸⁷ <i>T. heudelottii</i> ⁷⁷
489	cipadessalide		<i>Cipadessa baccifera</i> ²⁸²
490	rohituka 1	R = iVal	<i>Aphanamixis polystacha</i> ⁴⁸⁴
491	rohituka 2	R = 2-hydroxy-3-methylpentanoyl	<i>A. polystacha</i> ⁴⁸⁴
492	gaudichaudysolin A		<i>Dysoxylum gaudichaudianum</i> ⁵⁰²
493	D-5		<i>Trichilia prieuriana</i> ⁴⁸⁹

had both been given the trivial name cipadesin E. Fang et al. postulated that cipadonoids C–G (**1046**–**1050**) might be biosynthetically derived from the methyl angolensate-class limonoid via a pinacol rearrangement, which was confirmed by a computational study at the DFT level with a B3LYP/6-31G basis set as well as by chemical transformation. In addition, the presence of a $\Delta^{8,30}$ double bond in the methyl angolensate precursor led to trijugin-class limonoids while its absence led to cipadesin-class limonoid.⁵⁴⁴

2.3.5. Other Linkages Group. The structure of walsuronoid A (**1054**), featuring a 3,4-peroxide bridge A-seco skeleton and a C-3/19 linkage bridge, was confirmed by single-crystal X-ray diffraction.⁷³⁹ The hypothetical biosynthesis route from 11 β -hydroxycedrelone (**82**) to walsuronoids B (**1058**) and C (**1059**), which have the 18 (13 \rightarrow 14) abeo limonoid skeletons, and the chemical correlations between them were proposed.⁷³⁹ The structure of delevoyn C (**1060**), possessing a cyclobutanyl ring incorporating C-19 and a cycloheptanyl ring C including C-30,

Table 17. Other Structures and Sources of Rings A,B-seco Limonoids 494–524

no.	compounds	substitution groups and others	sources
494	toonaciliatin E	R = OAc	<i>Toona ciliata</i> ²⁹⁰
495	toonaciliatin H	R = H	<i>T. ciliata</i> ²⁹⁰
496	toonaciliatin I		<i>T. ciliata</i> ²⁹⁰
497	surenolactone		<i>T. sureni</i> ⁵⁰⁵
498	munronin A	R ₁ = O; R ₂ = OH	<i>Munronia henryi</i> ⁵⁰⁶
499	munronin B	R ₁ = OH; R ₂ = O	<i>M. henryi</i> ⁵⁰⁶
500	munronin C	R ₁ = O; R ₂ = H	<i>M. henryi</i> ⁵⁰⁶
501	dysoxylumolide B	R = 2-hydroxy-3-methylpentanoyl	<i>Dysoxylum hainanense</i> ⁵⁰⁷
502	dysoxylumic acid D	R = 2-hydroxy-3-methylpentanoyl	<i>D. hainanense</i> ⁵⁰⁷
503	dysoxylumic acid A		<i>D. hainanense</i> ⁵⁰⁷
504	dysoxylumic acid B		<i>D. hainanense</i> ⁵⁰⁷
505	rohituka 6		<i>Aphanamixis polystacha</i> ⁴⁸⁴
506	dysoxylumic acid C		<i>Dysoxylum hainanense</i> ⁵⁰⁷
507	rohituka 3	R ₁ = 2-hydroxy-3-methylpentanoyl; R ₂ = OH; R ₃ = O; R ₄ = H	<i>Trichilia emetica</i> ; ¹⁹² <i>Aphanamixis polystacha</i> ^{484,485}
508	rohituka 5	R ₁ = 2-hydroxy-3-methylpentanoyl; R ₂ = OH; R ₃ = OAc; R ₄ = H	<i>A. polystacha</i> ^{484,485}
509	rohituka 13	R ₁ = iVal; R ₂ = OH; R ₃ = OAc; R ₄ = H	<i>A. polystacha</i> ²⁷⁵
510	rohituka 14	R ₁ = iVal; R ₂ = OH; R ₃ = O; R ₄ = H	<i>A. polystacha</i> ^{275,485}
511		R ₁ = formacyl; R ₂ R ₃ = O; R ₄ = H	<i>Trichilia prieuriana</i> ⁴⁸⁹
512	dysoxylumolide A	R ₁ = iVal(OH); R ₂ R ₃ = O; R ₄ = OiVal(OH)	<i>Dysoxylum hainanense</i> ⁵⁰⁷
513	toonaciliatin D		<i>Toona ciliata</i> ²⁹⁰
514	dregeana 1	R ₁ = formacyl; R ₂ = 2-hydroxy-3-methylpentanoyl	<i>Trichilia dregeana</i> ; ²⁷⁴ <i>Aphanamixis polystachya</i> ^{485,508}
515	rohituka 12	R ₁ = H; R ₂ = iVal	<i>A. polystacha</i> ²⁷⁵
516	rohituka 15	R ₁ = H; R ₂ = 2-hydroxy-3-methylpentanoyl	<i>A. polystacha</i> ^{485,508}
517	polystachin	R ₁ = formacyl; R ₂ = iVal	<i>A. polystacha</i> ^{275,503}
518	rubrin A	R ₁ = OH; R ₂ = OPiv	<i>Trichilia rubra</i> ⁵⁰⁴
519	rubrin B	R ₁ = OH; R ₂ = OiBu	<i>T. rubra</i> ⁵⁰⁴
520	hispidin A (rubrin C)	R ₁ = OH; R ₂ = OTig	<i>T. hispida</i> ; ⁵⁰¹ <i>T. rubra</i> ⁵⁰⁴
521	rubrin D	R ₁ = OH; R ₂ = propanoyle	<i>T. rubra</i> ⁵⁰⁴
522	rubrin E (nymania 1)	R ₁ = OH; R ₂ = O	<i>T. rubra</i> ; ⁵⁰⁴ <i>T. emetica</i> ; ¹⁹² <i>T. obtusifolia</i> ⁵⁰⁹
523	rubrin F	R ₁ = O; R ₂ = OAc	<i>T. rubra</i> ⁵⁰⁴
524	rubrin G	R ₁ = OH; R ₂ = OAc	<i>T. rubra</i> ⁵⁰⁴

was suggested by the LSD (Logic for Structure Determination) program.⁴²⁵ The absolute configurations of cipadonoid A (1061), which featured a tetrahydropyranyl ring B and characterized by a C-30 exomethylene group inserted between C-8 and C-10,⁷⁴⁰ was revised to be 1S,3R,5S,8S,10R,13S,14R,17R.⁷⁴¹

2.4. Limonoids Derivatives

2.4.1. Pentanortriterpenoids, Hexanortriterpenoids, Heptanortriterpenoids, Octanortriterpenoids, and Eneanortriterpenoids Derivatives. A possible degradation pathway for 2-oxo-deacetyl salannin (1063), the sole C-2 degraded limonoid, was not proposed or hypothesized.⁴¹¹ Azadirachtin L, obtained by Kanokmedhakul et al. in 2005,³²⁴ was in fact reported as marrangin (1067) early in 1993.⁷⁴⁶ The structure of 1068 was assigned as 11 α -hydroxy-12-norazadirachtin⁷⁴⁷ in 1994, but Ramji et al. isolated and mistook it as 11-*epiazadirachtin* H⁷⁴⁸ in 1996, and Kanokmedhakul et al. isolated and named it as 11 α -azadirachtin H in 2005.³²⁴ 11-*epiazadirachtin* I (1070) was characterized by both NMR and X-ray crystallography techniques.⁷⁴⁹ Chuktabularins A–D (1074, 1096, 1078, and 1089) are four 16-norphragmalin-class limonoids with a biosynthetically extended C2 or C3 unit at C-15 forming a unique 2,7-dioxabicycl[2.2.1]heptane moiety. Moreover, a plausible biosynthetic origin of chuktabularins A–D was also

postulated.⁷⁵⁰ The structure of chuktabrin A (1097), featuring motifs of a 1,3-dioxolan-2-one and a 3,4-dihydro-2H-pyran formed *via* an ether bond between C-30 and C-1 in the biosynthetically extended C3 unit at C-15, was confirmed by X-ray diffraction.⁶⁹⁷ The co-occurrence of limonoids and norlimonoids in *Toona ciliata* together with the possible mechanisms of conversion suggested a biosynthetic map that encompassed the pathways for all limonoids started from the common precursor 14,15-deoxyhavanensin.²⁹⁰

In biosynthetic terms, carapolide A (1115) could be derived from a spiro-precursor through pathway involving a retro-prins reaction, cleavage and protonation.⁵⁸¹ A limonoid belonging to the 1,8,9-orthoesters phragmalin-class might biosynthetically undergo insertion of an isobutyryl group from C-30 to C-15 through a Claisen reaction, cleavage of the C-16/17 δ -lactone, and then decarboxylation and de-*ortho*-acetylation to form another intermediate, which, after a series of ketal formations and esterifications, gives chukvelutins A–C (1086–1088).⁷⁵¹ Similarly, chuktabularins E–T (1090–1095, 1075, 1079–1085, 1076, 1077) possessed a biosynthetically extended propionyl or acetyl group at C-15 and a characteristic ketal moiety between the limonoid skeleton and the acyl substituent at C-15.⁷⁵² Ceramicine A (1118) could be transformed from limonoids skeleton via oxidation at C-28 and C-29 followed

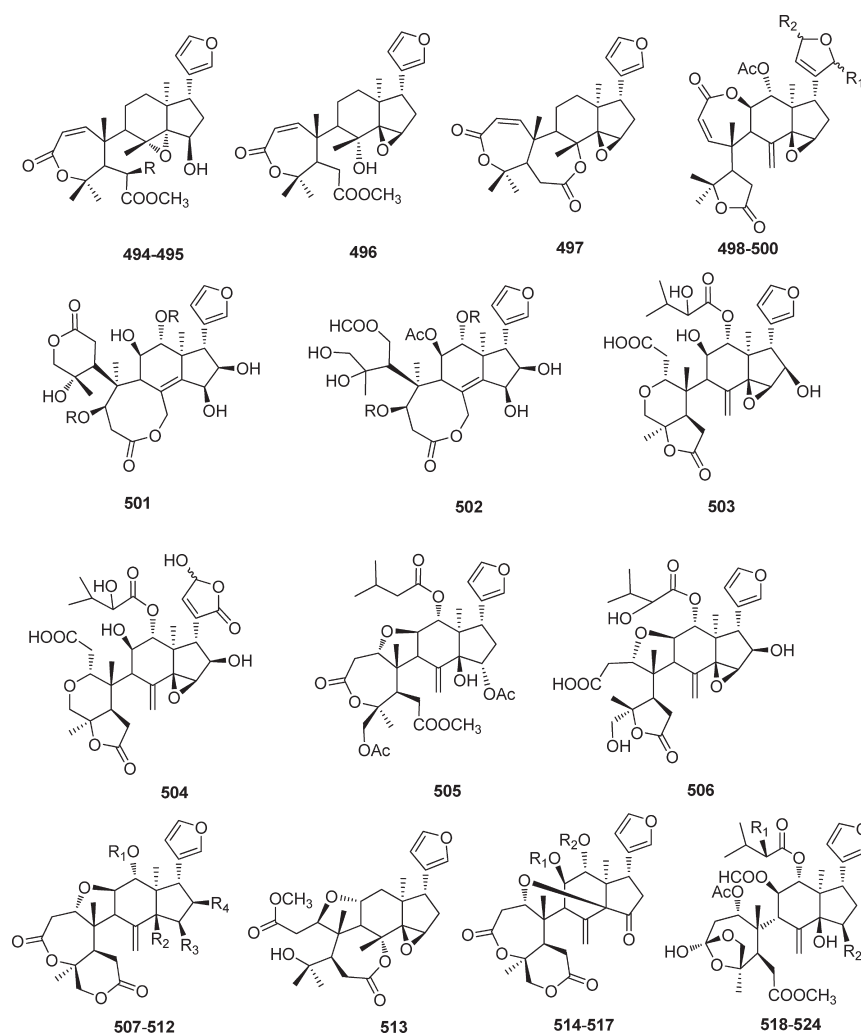


Figure 19. Other structures of rings A,B-seco limonoids 494–524.

by decarboxylation.⁴¹² Two degraded limonoids, assigned as 7 α -acetoxy-4,4,8-trimethyl-5 α -(13 α Me)-17-oxa-androsta-1,14-dien-3,16-dione (**1130**) and 7 α -acetoxy-4,4,8-trimethyl-5 α -17-oxa-androsta-1,14-dien-3,16-dione (**1131**) in 1992,⁷⁵³ were isolated and reported as 13 α -nimolactone and 13 β -nimolactone in 1994,¹⁰⁷ respectively.

2.4.2. Simple Degraded Derivatives. Trichiconnarins A and B (**1139** and **1140**) are degraded limonoids with a contracted five-membered ring-C. Of these, **1139** is likely to be the degradation products of trijugin C (**1111**) by cleavage of the C-2 and C-8 bonds, and **1140** is then derived from reaction of **1139** with acetone through an aldol reaction followed by dehydration.⁵⁷³ X-ray analysis of 9 β -bromofraxinellone has defined the absolute stereochemistry of fraxinellone (**1142**).⁷⁶³

2.4.3. N-Containing Derivatives. Microbes, such as endophytic fungi, may contribute to the biosynthesis of turrapubesin B (**1153**), which contains a maleimide ring.²⁸⁷ Wu et al. proposed a new biosynthetic pathway with xylogranatin R (**843**) as a key intermediate to reach the limonoids xylogranatins F–H (**1156**–**1158**), which bear a novel skeleton with a pyridine ring.⁶³⁸ Cui et al. suggested that granatoine (**1159**) could be biosynthetically derived from the precursor 9,10-seco-mexicanolide xylogranatin C (**823**) via a pathway in which the pyridine ring would be formed through ring condensation and dehydroxy-

lation while the γ -lactone would be formed by esterification between C-7 and C-10.⁷²⁶

3. CHEMOTAXONOMIC SIGNIFICANCE OF MELIACEOUS LIMONIDS

As one of many types of natural products in plants, the limonoids were significant chemotaxonomic markers of Meliaceae, Rutaceae, and Simarubaceae. A wonderful review presented in 1983 treated the chemotaxonomic significance of limonoids in Meliaceae and discussed the biosynthesis, distribution, and systematic significance of limonoids in the Meliaceae, Cneoraceae, and allied taxa.¹⁵ Up until the present, the chemotaxonomy significances of limonoids for Meliaceae focused mainly on the subfamily Swietenioideae and Melioideae.

Different research groups have proposed the chemotaxonomic significance of genera *Khaya*, *Soymida*, *Neobeguea*, *Swietenia*, *Toona*, and *Cedrela* of subfamily Swietenioideae. The western and eastern forms of *Khaya anthotheca* were different chemically in that the western variety gave no ring D-expanded meliacins, in contrast to the other species.¹⁶⁴ The timber of *Soymida febrifuga* contained no detectable level of limonoids and the bark contained ~0.1% methyl angolensate (**568**). These results showed that *Soymida* was closely related to the African genus *Khaya*.⁷⁶⁷

Table 18. Structures and Sources of Rings A,D-seco Limonoids 525–555

no.	compounds	substitution groups and others	sources
525	obacunol	R ₁ = R ₂ = R ₃ = R ₄ = H	<i>Lovoa trichilioides</i> ; ⁵¹⁵ <i>Trichilia trifolia</i> ¹⁸²
526	6 α -acetoxyobacunol acetate	R ₁ = α -OAc; R ₂ = Ac; R ₃ = R ₄ = H	<i>Dysoxylum spectabile</i> ; ⁵¹⁶ <i>D. richii</i> ; ⁵¹⁷ <i>D. muelleri</i> ; ⁵¹⁸ <i>Cedrela sinensis</i> ⁵¹⁹
527	11 β -acetoxyobacunyl acetate	R ₁ = R ₄ = H; R ₂ = Ac; R ₃ = β -OAc	<i>C. odorata</i> ⁵¹⁰
528	11 β -acetoxyobacunol	R ₁ = R ₂ = R ₄ = H; R ₃ = β -OAc	<i>C. odorata</i> ⁵¹⁰
529	6 β -acetoxyobacunol	R ₁ = β -OAc; R ₂ = R ₃ = R ₄ = H	<i>Trichilia trifolia</i> ¹⁸²
530	dysoxylone	R ₁ = O; R ₂ = iVal(OH); R ₃ = R ₄ = H	<i>Dysoxylum richii</i> ⁵¹⁷
531	11 β -hydroxy-7 α -obacunyl acetate	R ₁ = R ₄ = H; R ₂ = Ac; R ₃ = β -OH	<i>Cedrela sinensis</i> ⁵¹¹
532	11-oxo-7 α -obacunol	R ₁ = R ₂ = R ₄ = H; R ₃ = O	<i>C. sinensis</i> ⁵¹¹
533	11-oxo-7 α -obacunyl acetate	R ₁ = R ₄ = H; R ₂ = Ac; R ₃ = O	<i>C. sinensis</i> ⁵¹¹
534	7 α -obacunyl acetate	R ₁ = R ₃ = R ₄ = H; R ₂ = Ac	<i>C. sinensis</i> ⁵¹⁹
535	perforin A	R ₁ = R ₃ = α -OAc; R ₂ = Ac; R ₄ = β -OAc	<i>Toona ciliata</i> ¹⁴⁵
536	11 β -acetoxyobacunone		<i>Trichilia elegans</i> ¹⁶⁵
537	kihadanin A	R ₁ = R ₃ = O; R ₂ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰
538	7-deoxo-7 α -hydroxykihadanin A	R ₁ = α -OH; R ₂ = OH; R ₃ = O	<i>T. elegans</i> ssp. <i>elegans</i> ⁵¹²
539	7-deoxo-7 α -acetoxykihadanin A	R ₁ = α -OAc; R ₂ = OH; R ₃ = O	<i>T. elegans</i> ssp. <i>elegans</i> ^{512,520}
540	7-deoxo-7 β -hydroxykihadanin A	R ₁ = β -OH; R ₂ = OH; R ₃ = O	<i>T. elegans</i> ssp. <i>elegans</i> ⁵¹²
541	7-deoxo-7 β -acetoxykihadanin A	R ₁ = β -OAc; R ₂ = OH; R ₃ = O	<i>T. elegans</i> ssp. <i>elegans</i> ⁵¹²
542	kihadanin B	R ₁ = R ₂ = O; R ₃ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰
543	7-deoxo-7 α -acetoxykihadanin B	R ₁ = α -OAc; R ₂ = O; R ₃ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰
544	7-deoxo-7 β -hydroxykihadanin B	R ₁ = β -OH; R ₂ = O; R ₃ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵¹²
545	7-deoxo-7 β -acetoxykihadanin B	R ₁ = β -OAc; R ₂ = O; R ₃ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵¹²
546	7 α -acetoxydihydronomilin	R = H	<i>Xylocarpus granatum</i> ; ^{513,514} <i>Cedrela sinensis</i> ; ⁵¹⁹ <i>C. odorata</i> ⁵¹⁰
547	11 β -hydroxyceorin G	R = OH	<i>C. sinensis</i> ⁵¹¹
548	11-oxocneorin G	R = O	<i>C. sinensis</i> ⁵¹¹
549	7 α ,11 β -diacetoxydihydronomilin	R = OAc	<i>C. mexicana</i> ; ⁵²¹ <i>C. odorata</i> ⁵¹⁰
550	cedrellin		<i>C. sinensis</i> ⁵¹⁹
551	11 β ,19-diacetoxy-1-deacetyl-1-epidihydronomilin		<i>C. odorata</i> ⁵¹⁰
552	dysoxylin	R = H	<i>Dysoxylum richii</i> ^{517,522}
553	tigloydysoxylin	R = Tig	<i>D. richii</i> ⁵¹⁷
554	dysoxylumolide C		<i>D. hainanense</i> ⁵⁰⁷
555	odoramide		<i>Cedrela odorata</i> ⁵¹⁰

Zhang et al. concluded that the configuration at C-6 of mexicanolides, phragmalins, and khayanolides from *Khaya senegalensis* had a 6S configuration while those from *Swietenia* species had a 6R configuration, and then pointed out this difference implies a significant chemotaxonomy difference between the African mahogany genus *Khaya* and the genuine mahogany genus *Swietenia*.⁷²² Six phragmalin-class limonoids from *Swietenia macrophylla* showed significant chemotaxonomic evidence in favor of linking this species with *S. mahagoni*.⁷¹⁶ Furthermore, Wu et al. described the distribution of kinds of phragmalin orthoesters in *Xylocarpeae* and *Swietenieae* and pointed out that the two tribes were closely related subfamilies in *Meliaceae*.⁶⁵⁹ The chemotaxonomic significances of limonoids in *Toona* and *Cedrela* were hot topics for years. Agostinho et al. objected to the affiliation of *Toona* to *Swietenioideae* by the occurrence of the meliacin butenolides in both *Toona* and *Trichilia*.¹⁵⁴ In addition, Neto and da Silva et al. pointed out that *Toona* differed notably from other genera of *Swietenioideae* by the absence of the mexicanolide-class limonoids and the presence of limonoids rather typical of *Melioidae*, and thus showed a less pronounced relationship to the *Swietenioideae*.^{161,768} Neto et al. pointed out that the ring B-seco limonoids of *Toona* could be considered the biosynthetic

precursors of the mexicanolide-class limonoids which were common in *Cedrela*, suggesting a direct derivation of *Cedrela* from *Toona*-like ancestors.¹⁴⁰ Yet Liao et al. supported *Toona* as a separate subfamily because of the biosynthetic relationship between the limonoids from *Toona ciliata* and the occurrence of mexicanolide-class limonoids in this species.²⁹⁰

The chemotaxonomic significance of limonoids for genera *Ekebergia*, *Nymania*, *Trichilia*, *Turraea*, *Astrotrichilia*, *Dysoxylum*, *Malleastrum*, and *Cipadessa* ascribed to subfamily *Melioidae* were also investigated extensively. The limonoids of *Ekebergia* were not far removed from the general pattern found in *Trichileae*, in which highly oxidized ring B fissioned limonoids appeared to be the most common terpenoid constituents.⁵⁶⁷ Since trijugin-class limonoids were obtained both from *Heynea trijuga* and *Ekebergia terophylla*, the possible relationship between *Ekebergia* and *Heynea* was proposed.⁵⁶⁵ Because of the structural relation between astrotrichilin (566) and ekebergin (588), Mulholland et al. proposed a relationship between *Astrotrichilia* and *Ekebergia*,⁵⁴³ which disagreed with Pennington's viewpoint.⁷⁶⁹ Chemically, *Ekebergia* itself was rather distinct and not closely related to *Trichilia* so that it seemed possible that both *Quivisianthe* and *Ekebergia* occupy positions on the fringes

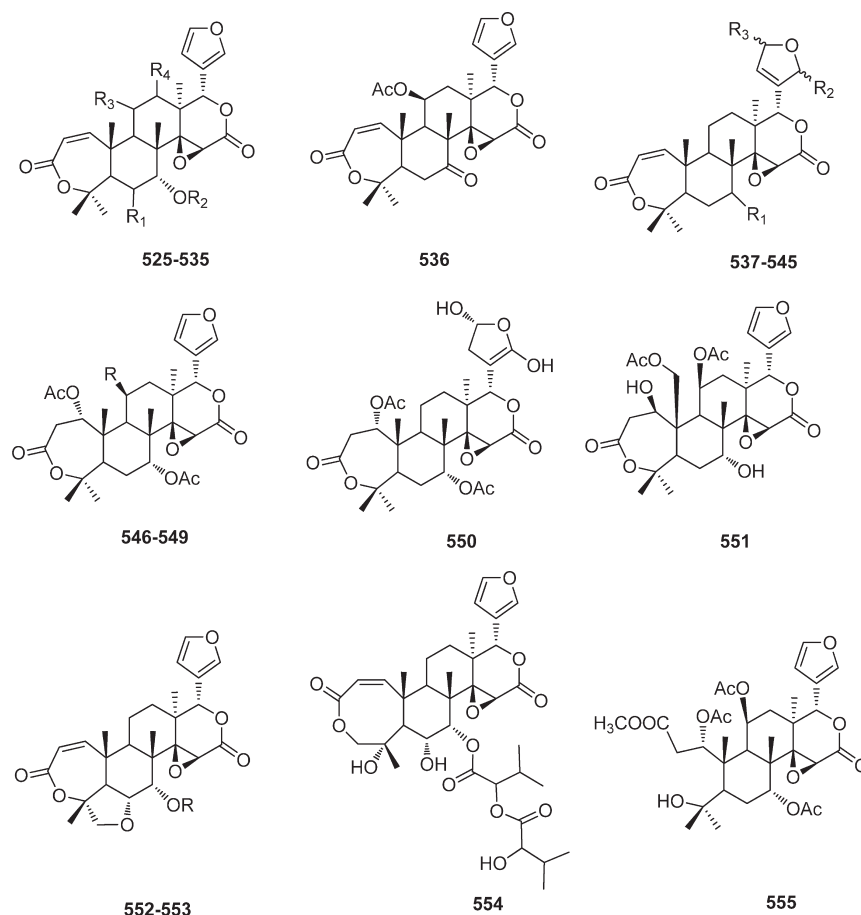


Figure 20. Structures of rings A,D-seco limonoids **525**–**555**.

of the main groups of the Meliaceae, perhaps without especially close relation to any other genera.⁶¹³ The limonoids from *Nymanian* were typical of those from species of the genera *Guarea*, *Trichilia*, and *Aphanamixis*, which strongly supported the placing of *Nymanian* in the subfamily Melioideae.²⁸³ The chemotaxonomic link between the genera *Nymanian* and *Turraea* was established based on the occurrence of nymanian-1 (**522**) in both *Nymanian capensis* and *Turraea obtusifolia*.⁵⁰⁹ Three limonoids from *Turraea obtusifolia* are structurally similar to hirtin (**94**) and havanensin (**106**) and thus represent intermediates or byways on the route to the more characteristic prieurianin group, and they are consistent with the close taxonomic relationship of *Turraea* and *Nymanian*.¹⁸⁹ In contrast to the other species of *Trichilia*, *T. connaroides* contains the andirobin, mexicanolide and trijugin class limonoids, which could be used as a chemical marker to differentiate this species from the other species in the same genus.⁵⁷³ Mzikonone (**240**), the principal limonoid of *Turraea robusta*, was much less oxidized than the havanensin-class limonoids from *T. obtusifolia* and the prieurianin-class from *T. floribunda*,¹⁸⁹ which suggested that caution needed to be exercised in defining the oxidation pattern of limonoids as taxonomic markers for the genus *Turraea*.²⁶⁸ The limonoids from *Turraea parvifolia* of the Turraeae tribe were typical of those from the genera *Melia* and *Azadirachta* of the Melioideae which suggests their close chemotaxonomic relationship.²⁴³ Dysodensiols A-C (**1135**–**1137**) from *Dysoxylum densiflorum*, which are likely biotransformed products from a common

precursor of a B-seco-limonoid, supported the proposition that it would be preferred to include the genus *Dysoxylum* in the subfamily Melioideae.⁷⁶⁴ The distribution of methyl ivorensate-like limonoids with A,B-seco and D carbocyclic rings **601**–**606** indicated the chemosystematic relevance between the genera *Khaya*,^{446,576} and *Soymida*⁵³⁸ of the subfamily Swietenioideae and the genera *Dysoxylum*,⁵¹⁶ and *Trichilia*⁵²⁰ of the Melioideae. The isolation of 1 α ,3 α -diacetylvilasinin (**189**) and 1,3-diacetyl-7-tigloyl-12 α -hydroxyvilasinin (**190**) from *Malleastrum antsingyense* supported the placement of *Malleastrum* in the subfamily Melioideae although no prieurianin or evodulone-class limonoids were found.²⁴⁴ The mexicanolide-class limonoids found in *Cipadessa fruticosa*⁶¹⁷ along with the andirobin- and trijugin-class limonoids from *C. cinerascens*^{563,647} provided firm support for including *Cipadessa* in Trichilieae, which is in agreement with Pennington's viewpoint.⁷⁶⁹

4. SYNTHESIS OF MELIACEOUS LIMONOIDS

Because of the important biological activities and the high structural complexity, the limonoids of Meliaceae have attracted considerable attention from the organic synthesis community, which has focused particularly on the total synthesis of the well-known azadirachtin (**292**).

The potent antifeedant activity of **292** against various insect coupled with its remarkable selectivity and nontoxicity toward mammalian organisms made it an attractive candidate as a natural pesticide. Enormous efforts directed toward the total synthesis of

Table 19. Structures and Sources of Andirobin-Class Limonoids 556–594

no.	compounds	substitution groups and others	sources
556	andirobin	R = O	<i>Carapa guianensis</i> ; ^{137,437,449,450} <i>Cedrela odorata</i> ; ⁵³³ <i>Swietenia macrophylla</i> ⁴⁴⁵
557	amoorinin	R = OH	<i>Amoora rohituka</i> ^{534,535}
558	amoorinin-3-O- α -L-rhamnopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside	R = 3-O- α -L-Rha-(1 \rightarrow 6)- β -D-Glc	<i>Aphanamixis polystachya</i> ⁵³⁶
559	deoxyandirobin	R = H; $\Delta^{1,2}$	<i>Soymida febrifuga</i> ; ⁵³⁷ <i>Khaya grandifoliola</i> ¹⁶⁴
560	swietmanin J	R = OH	<i>Swietenia mahagoni</i> ⁴⁵⁸
561	domesticulide A	R = H	<i>Lansium domesticum</i> ¹⁰⁰
562	domesticulide B	R = Ac	<i>L. domesticum</i> ¹⁰⁰
563			<i>Soymida febrifuga</i> ⁵³⁸
564	dihydroamoorinin	R = OH	<i>Aphanamixis polystachya</i> ⁵³⁹
565	aphanamixinin	R = O	<i>A. polystachya</i> ^{536,540–542}
566	astrotrichilin	R = cinnamate/nicotinate ester	<i>Astrotrichilia asterotricha</i> ⁵⁴³
567	cipadonoid B		<i>Cipadessa cinerascens</i> ⁵⁴⁴
568	methyl angolensate	R ₁ = O; R ₂ = R ₃ = R ₄ = H	<i>Entandrophragma angolense</i> ; ^{423,545} <i>E. macrophyllum</i> ; ⁵³⁰ <i>Guarea thompsonii</i> ; ⁴⁷⁵ <i>Soymida febrifuga</i> ; ^{537,546} <i>Khaya senegalensis</i> ; ^{451,464,547–551} <i>K. anthotheca</i> ; ⁵⁵² <i>K. grandifoliola</i> ; ^{164,436,553} <i>K. ivorensis</i> ; ^{446,447,554} <i>Cedrela odorata</i> ; ^{98,168} <i>C. fissilis</i> ; ¹³² <i>Lansium domesticum</i> ; ¹⁰⁰ <i>Swietenia mahagoni</i> ; ^{112,458,555} <i>Ruagea glabra</i> ; ⁵⁵⁶ <i>Carapa guianensis</i> ; ^{113,137,437} <i>Cabralea eichleriana</i> ; ⁴³⁰ <i>Neobeguea mahafalensis</i> ; ⁵⁵⁷ <i>Melia azedarach</i> ; ⁴⁵² <i>Trichilia catigua</i> ; ¹⁶⁵ <i>Xylocarpus granatum</i> ; ⁴⁴⁸ <i>X. moluccensis</i> ⁵⁵⁸
569	methyl 6-hydroxyangolensate	R ₁ = O; R ₂ = OH; R ₃ = R ₄ = H	<i>Khaya senegalensis</i> ; ^{451,467,468,472,547–550,559} <i>K. anthotheca</i> ; ⁵⁵² <i>K. ivorensis</i> ; ^{446,447,554} <i>K. grandifoliola</i> ; ^{164,436,553,560} <i>Swietenia mahagoni</i> ; ^{457,458,555} <i>S. aubrevilleana</i> ; ⁴⁴⁵ <i>Lansium domesticum</i> ¹⁰⁰
570	methyl 6-acetoxyangolensate	R ₁ = O; R ₂ = OAc; R ₃ = R ₄ = H	<i>L. domesticum</i> ; ¹⁰⁰ <i>Khaya grandifoliola</i> ; ^{560,561} <i>K. senegalensis</i> ^{451,547,549,550,559}
571	methyl 6,12 α -diacetoxyangolensate	R ₁ = O; R ₂ = R ₃ = OAc; R ₄ = H	<i>Guarea thompsonii</i> ⁵³¹
572	azecin 1	R ₁ = OAc; R ₂ = H; R ₃ = OAc; R ₄ = O-L-rha (1 \rightarrow 6)- β -D-glc	<i>Melia azedarach</i> ¹⁷³
573	sandoricin	R ₁ = OAc; R ₂ = H; R ₃ = OAc; R ₄ = OH	<i>Sandoricum koetjape</i> ⁵³²
574	6-hydroxysandoricin	R ₁ = OAc; R ₂ = R ₄ = OH; R ₃ = OAc	<i>S. koetjape</i> ⁵³²
575	[2 α -(2-methylbutanoyl)oxy]sandoricin	R ₁ = α -Opiv; R ₂ = OAc; R ₃ = OH	<i>S. koetjape</i> ⁵⁶²
576	[2 α -(2-methylpropanoyl)oxy]sandoricin	R ₁ = α -OiBu; R ₂ = OAc; R ₃ = OH	<i>S. koetjape</i> ⁵⁶²
577	methyl 2 β ,3 β -diacetoxy-3-deoxoangolensate	R ₁ = β -OAc; R ₂ = R ₃ = H	<i>Cipadessa cinerascens</i> ⁵⁶³
578	cipadesin D	R ₁ = H; R ₂ = OH; R ₃ = β -OAc	<i>C. cinerascens</i> ⁵³
579	cipadesin F	R ₁ = OAc; R ₂ = OH; R ₃ = H	<i>C. cinerascens</i> ⁵⁴
580	cineracipadesin B	R ₁ = OAc; R ₂ = OH; R ₃ = α -OH	<i>C. cinerascens</i> ⁵⁶³
581	cineracipadesin C	R ₁ = H; R ₂ = OH; R ₃ = O	<i>C. cinerascens</i> ⁵⁶³
582	cineracipadesin D	R ₁ = R ₂ = H; R ₃ = α -OAc	<i>C. cinerascens</i> ⁵⁶³
583	cineracipadesin E	R ₁ = OAc; R ₂ = OH; R ₃ = α -OAc	<i>C. cinerascens</i> ^{563,564}
584	E.P.1	R ₁ = OAc; R ₂ = R ₃ = H	<i>Ekebergia pterophylla</i> ^{565,566}
585	E.P.2	R ₁ = H; R ₂ = Ac; R ₃ = OAc	<i>E. pterophylla</i> ⁵⁶⁶
586	E.P.3	R ₁ = R ₃ = OAc; R ₂ = H	<i>E. pterophylla</i> ^{565,566}
587	E.P.6	R ₁ = OTig; R ₂ = H; R ₃ = OH	<i>E. pterophylla</i> ⁵⁶⁵
588	ekebergin	R ₁ = OrVal; R ₂ = H; R ₃ = OAc	<i>E. capensis</i> ⁵⁶⁷
589	domesticulide C	R ₁ = OAc; R ₂ = O; R ₃ = OH	<i>Lansium domesticum</i> ¹⁰⁰
590	domesticulide D	R ₁ = OAc; R ₂ = OH; R ₃ = O	<i>L. domesticum</i> ¹⁰⁰
591	moluccensin N	R ₁ = H; R ₂ = O; R ₃ = OH	<i>Xylocarpus moluccensis</i> ⁵⁶⁸
592	moluccensin O	R ₁ = H; R ₂ = OH; R ₃ = O	<i>X. moluccensis</i> ⁵⁶⁸
593	sandoripin A	R = Piv	<i>Sandoricum koetjape</i> ⁵⁶⁹
594	sandoripin B	R = iBu	<i>S. koetjape</i> ⁵⁶⁹

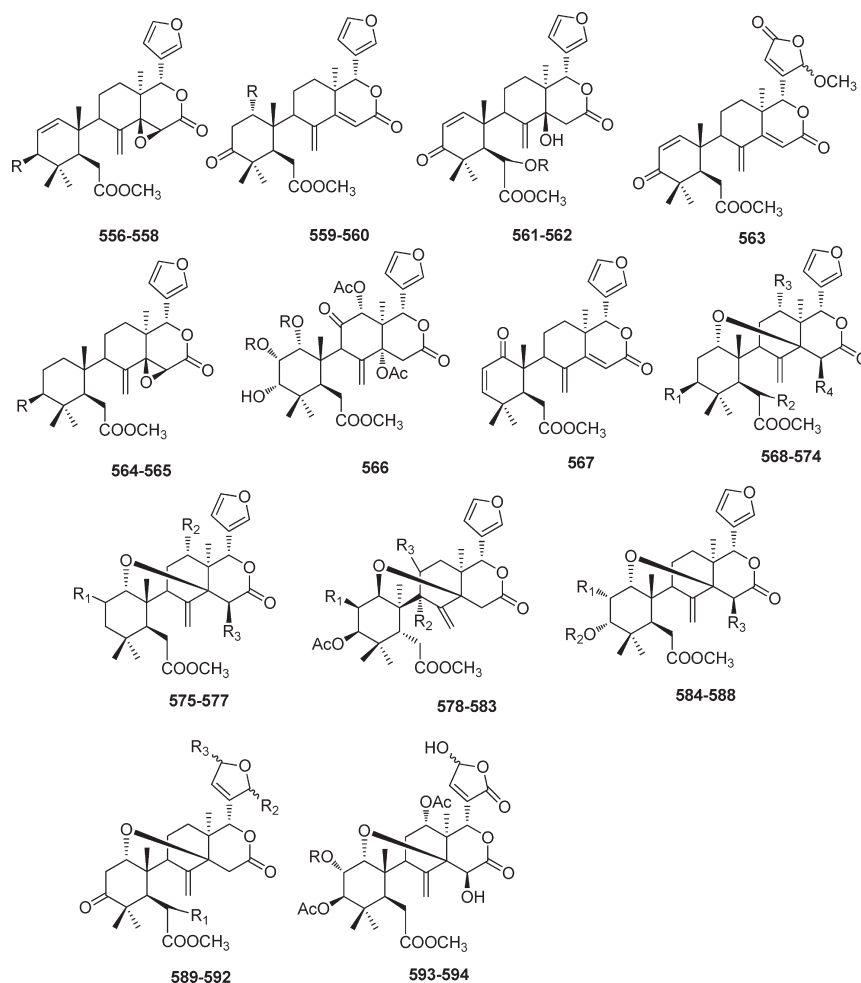


Figure 21. Structures of andirobin-class limonoids 556–594.

Table 20. Other Structures and Sources of Rings B,D-seco Limonoids 595–600

no.	compounds	substitution groups and others	sources
595	methyl 8 α -hydroxy-8,30-dihydroangolensate		<i>Trichilia connaroides</i> ⁵⁷³
596	secomahoganin	R = Ac	<i>Entandrophragma angolense</i> ; ⁵⁴⁵ <i>Swietenia mahagoni</i> ; ^{71,111,112} <i>S. macrophylla</i> ⁴⁵⁶
597	deacetylsecomahoganin	R = H	<i>S. mahagoni</i> ⁴⁵⁷
598	khayanoside	R = β -D-glucopyranoside	<i>Khaya senegalensis</i> ; ^{550,574,575} <i>K. ivorensis</i> ⁵⁵⁴
599	cedrelanolide I		<i>Cedrela salvadorensis</i> ^{570,571}
600	swiemahogin A		<i>Swietenia mahagoni</i> ; ⁵⁷² <i>Khaya ivorensis</i> ⁵⁵⁴

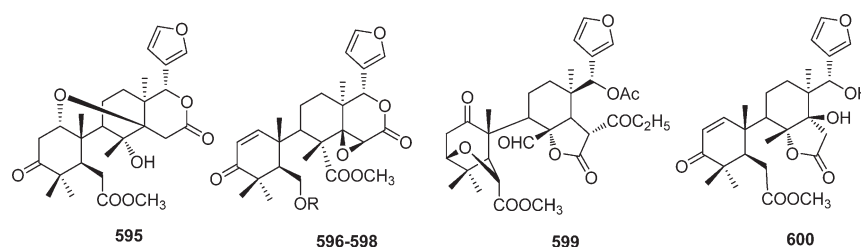


Figure 22. Other structures of rings B,D-seco limonoids 595–600.

292 have been continuing for more than twenty years in several research groups. This was undoubtedly due to its complex molecular architecture, which comprised sixteen contiguous

stereogenic centers, seven of which were tetrasubstituted carbon atoms, and a diverse array of oxygenated functionalities in addition to a rigid conformation imposed by intramolecular

Table 21. Structures and Sources of Rings A,B,D-seco Limonoids 601–606

no.	compounds	substitution groups and others	sources
601	methyl ivorenate		<i>Khaya ivorensis</i> ; ^{446,576} <i>Dysoxylum spectabile</i> ⁵¹⁶
602			<i>Soymida febrifuga</i> ⁵³⁸
603	elegantin A	R ₁ = O; R ₂ = OH	<i>Trichilia elegans</i> ssp. <i>elegans</i> ⁵²⁰
604	elegantin B	R ₁ = OH; R ₂ = O	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰
605	1,2-dihydro-1 α -acetoxyelegantin A	R ₁ = O; R ₂ = OH	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰
606	1,2-dihydro-1 α -acetoxyelegantin B	R ₁ = OH; R ₂ = O	<i>T. elegans</i> ssp. <i>elegans</i> ⁵²⁰

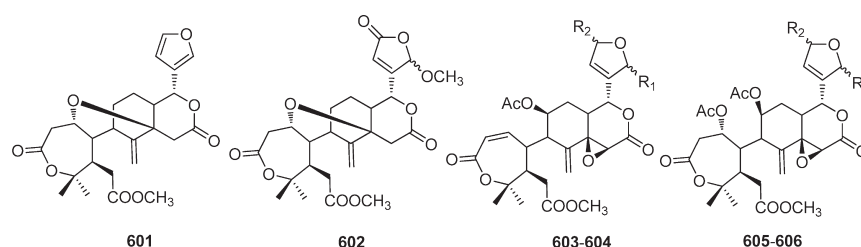


Figure 23. Structures of rings A,B,D-seco limonoids 601–606.

Table 22. Structures and Sources of 1,*n*-Linkage Rearranged Limonoids 607–625

no.	compounds	substitution groups and others	sources
607			<i>Carapa procera</i> ⁵⁸⁰
608	carapolide B		<i>C. procera</i> ⁵⁸¹
609	carapolide C		<i>C. procera</i> ; ⁵⁸¹ <i>C. grandiflora</i> ²⁷⁶
610	carapolide D	R ₁ R ₂ = CH ₂	<i>C. grandiflora</i> ^{276,582}
611	carapolide E	R ₁ = CH ₃ ; R ₂ = OH	<i>C. grandiflora</i> ^{276,582}
612	carapolide F	R = OH	<i>C. grandiflora</i> ^{276,582}
613	carapolide G	R = H	<i>C. grandiflora</i> ²⁷⁶
614	dukunolide A	R ₁ = R ₂ = α -OH; R ₃ = H; 5,6-epoxy; $\Delta^{8,9}$	<i>Lansium domesticum</i> ^{577,578}
615	dukunolide B	R ₁ = R ₂ = α -OH; R ₃ = H; 5,6; 8,9-diepoxy	<i>L. domesticum</i> ^{100,577}
616	dukunolide C	R ₁ = R ₂ = α -OH; R ₃ = OAc; 5,6-epoxy; $\Delta^{8,9}$	<i>L. domesticum</i> ^{100,577}
617	dukunolide D	R ₁ = R ₂ = α -OH; R ₃ = H; $\Delta^{8,9}$	<i>L. domesticum</i> ^{100,583}
618	dukunolide E	R ₁ = R ₂ = α -OH; R ₃ = H; 8,9-epoxy	<i>L. domesticum</i> ⁵⁸³
619	dukunolide F	R ₁ = R ₂ = β -OH; R ₃ = H; 8,9-epoxy	<i>L. domesticum</i> ⁵⁸³
620	seco-dukunolide F		<i>L. domesticum</i> ⁵⁸⁴
621	7 α , 12 α -diacetoxy-11 β -hydroxyneotectanin	R ₁ = OAc; R ₂ = H	<i>Turraea wakefieldii</i> ⁵⁷⁹
622	11 β , 12 α -diacetoxyneotectanin	R ₁ = O; R ₂ = Ac	<i>T. wakefieldii</i> ⁵⁷⁹
623	11 β , 12 α -diacetoxy-14 β , 15 β -epoxyneotectanin	R ₁ = O; R ₂ = Ac	<i>T. wakefieldii</i> ⁵⁷⁹
624	7 α , 12 α -diacetoxy-14 β , 15 β -epoxy-11 β -hydroxyneotectanin	R ₁ = OAc; R ₂ = H	<i>T. wakefieldii</i> ⁵⁷⁹
625	11 β , 12 α -diacetoxy-1-deoxy-14 β , 15 β -epoxy-3 β -hydroxy-2-oxo-neotectanin		<i>T. wakefieldii</i> ⁵⁷⁹

hydrogen bonding. Furthermore its sensitivity to acid and base together with its photoinstability made it particularly prone to rearrangement, thereby frustrating many synthesis plans.⁷⁷⁰ The strategy applied to the total synthesis of **292**, called “relay route” or “relay synthesis”, consisted of attempting to degrade **292** to a specific potential synthetic intermediate and then transform this back into the natural product. For example, one application of this strategy involved the degradation of the enol double bond to give an advanced intermediate and development of methods to convert this intermediate back into the natural product by reintroduction of the enol double bond using an acetal exchange process. In addition, the strategy focused on a convergent

approach, which would bring together a decalin fragment with a hydroxydihydrofuran acetal portion (Scheme 1).⁷⁷¹

The strategy in the formation of the decalin unit of **292** included two different ways. One is the employment of a silyl group to control the stereoselectivity of several key steps and to introduce C-3 hydroxyl functionality in decalin motif,^{772–774} and another is the cleavage of C8–C14 bond via a base-mediated retro-Aldol reaction of natural product **292**, in which macrocyclic carbonate is a key intermediate.^{774–776} The degradation of **292** to the demethylated decalin and the subsequent remethylation to the protected fragment has been presented. This not only connected the total synthesis and the degradation route of **292**,

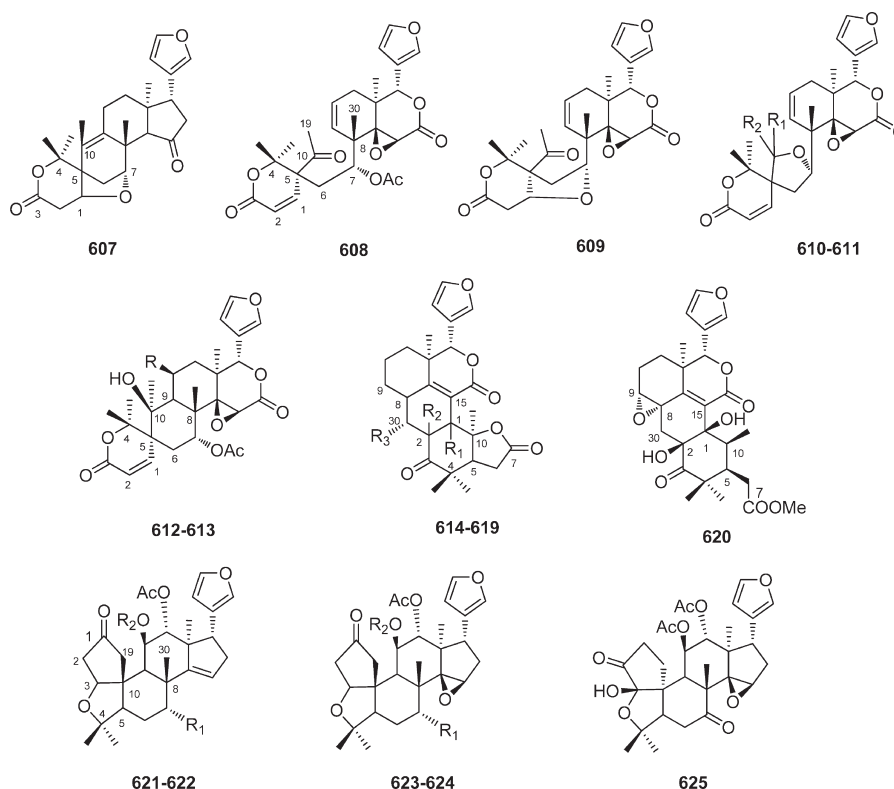


Figure 24. Structures of 1,*n*-linkage rearranged limonoids 607–625.

Table 23. Structures and Sources of Mexicanolide-Class Limonoids 626–845

no.	compounds	substitution groups and others	sources
626	mexicanolide	$R_1 = R_3 = H; R_2 = O$	<i>Carapa procera</i> ; ¹⁶⁷ <i>Cedrela mexicana</i> ; ⁵⁸⁷ <i>C. odorata</i> ; ^{533,641} <i>C. fissilis</i> ; ⁶⁴² <i>Khaya senegalensis</i> ; ^{451,467,603} <i>K. ivorensis</i> ; ⁴⁴⁶ <i>K. grandifoliola</i> ; ¹⁶⁴ <i>Neobeguea mahafalensis</i> ; ⁵⁵⁷ <i>Cipadessa fruticosa</i> ; ^{617,643} <i>Swietenia mahagoni</i> ; ⁴⁵⁸ <i>Xylocarpus granatum</i> ; ⁴⁴⁸
627	2 α -hydroxymexicanolide	$R_1 = OH; R_2 = O; R_3 = H$	<i>Khaya senegalensis</i> ; ^{467,603}
628	2 $\alpha,3\beta$ -dihydroxy-3-deoxymexicanolide	$R_1 = R_2 = OH; R_3 = H$	<i>K. senegalensis</i> ; ^{467,468,603} <i>Swietenia mahagoni</i> ; ⁴⁵⁸
629	3 β -hydroxy-3-deoxymexicanolide	$R_1 = R_3 = H; R_2 = OH$	<i>Khaya senegalensis</i> ; ^{467,603} <i>Cabralea eichleriana</i> ; ⁶⁴⁴
630	6-hydroxymexicanolide	$R_1 = H; R_2 = O; R_3 = OH$	<i>Cedrela odorata</i> ; ⁵³³ <i>Khaya senegalensis</i> ; ¹⁶⁴ <i>Lansium domesticum</i> ; ^{100,645}
631	6-acetoxymexicanolide	$R_1 = H; R_2 = O; R_3 = OAc$	<i>L. domesticum</i> ; ¹⁰⁰
632	6-deoxyswietenolide (proceranolide)	$R_1 = R_3 = H; R_2 = OH$	<i>Carapa procera</i> ; ⁵⁹⁰ <i>Swietenia macrophylla</i> ; ⁴⁴⁵ <i>S. mahagoni</i> ; ¹¹² <i>Cedrela odorata</i> ; ⁵³³ <i>Quivisia papinae</i> ; ⁶⁴⁶ <i>Xylocarpus granatum</i> ; ^{448,633}
633	2' <i>R</i> -methylbutanoylproceranolide	$R_1 = R_3 = H; R_2 = 2'R\text{-OPiv}$	<i>Cipadessa baccifera</i> ; ⁵⁹¹ <i>C. cinerascens</i> ; ⁶⁴⁷
634	2' <i>S</i> -methylbutanoylproceranolide	$R_1 = R_3 = H; R_2 = 2'S\text{-OPiv}$	<i>C. baccifera</i> ; ⁵⁹¹ <i>C. cinerascens</i> ; ⁶⁴⁷ <i>Xylocarpus moluccensis</i> ; ⁵⁵⁸
635	proceranolide butanoate	$R_1 = R_3 = H; R_2 = OBu$	<i>Khaya ivorensis</i> ; ⁶⁴⁸
636	2-hydroxy-3- <i>O</i> -isobutrylproceranolide	$R_1 = OH; R_2 = OiBu; R_3 = H$	<i>Swietenia mahagoni</i> ; ⁴⁵⁸
637	2-hydroxy-3- <i>O</i> -benzoylproceranolide	$R_1 = OH; R_2 = OBz; R_3 = H$	<i>S. mahagoni</i> ; ⁴⁵⁸
638	swietenolide	$R_1 = H; R_2 = R_3 = OH$	<i>S. mahagoni</i> ; ^{112,603,649} <i>S. macrophylla</i> ; ^{55,445} <i>Khaya grandifoliola</i> ; ⁴³⁶ <i>Cedrela odorata</i> ; ⁵¹⁰ <i>Quivisia papinae</i> ; ⁶⁴⁶ <i>Q. papinae</i> ; ⁶⁴⁶
639	2 α -hydroxyswietenolide	$R_1 = R_2 = R_3 = OH$	<i>Trichilia connaroides</i> ; ⁶⁵⁰
640	2-hydroxy-3- <i>O</i> -tigloyl-6- <i>O</i> -acetylswietenolide	$R_1 = OH; R_2 = OTig; R_3 = OAc$	

Table 23. Continued

no.	compounds	substitution groups and others	sources
641	2-hydroxy-3-tigloyl-6-deoxyswietenolide	$R_1 = \text{OH}; R_2 = \text{OTig}; R_3 = \text{H}$	<i>Capurionanthus mahafalensis</i> ; ⁶¹³ <i>Trichilia connaroides</i> ; ⁶⁵¹ <i>Swietenia mahagoni</i> ⁴⁵⁸
642	2-hydroxy-3-O-tigloylswietenolide	$R_1 = R_3 = \text{OH}; R_2 = \text{OTig}$	<i>S. mahagoni</i> ^{457,649}
643	3-acetylswietenolide	$R_1 = \text{H}; R_2 = \text{OAc}; R_3 = \text{OH}$	<i>S. mahagoni</i> ; ^{112,652} <i>Khaya ivorensis</i> ; ⁴⁴⁷ <i>K. senegalensis</i> ⁶²³
644	3-tigloylswietenolide	$R_1 = \text{H}; R_2 = \text{OTig}; R_3 = \text{OH}$	<i>Swietenia mahagoni</i> ; ^{112,603} <i>S. macrophylla</i> ^{55,653}
645	6-acetylswietenolide	$R_1 = \text{H}; R_2 = \text{OH}; R_3 = \text{OAc}$	<i>S. mahagoni</i> ; ¹¹² <i>S. macrophylla</i> ; ⁴⁴⁵ <i>Khaya grandifoliola</i> ⁴³⁶
646	6-acetyl-3-tigloylswietenolide	$R_1 = \text{H}; R_2 = \text{OTig}; R_3 = \text{OAc}$	<i>Swietenia mahagoni</i> ; ^{112,603} <i>S. macrophylla</i> ⁶⁵³
647	diacetylswietenolide	$R_1 = \text{H}; R_2 = R_3 = \text{OAc}$	<i>S. macrophylla</i> ; ^{55,445,653,654} <i>S. mahagoni</i> ; ^{112,603} <i>Khaya ivorensis</i> ; ⁴⁴⁶ <i>K. senegalensis</i> ⁶²³
648	fissinolide (grandifoliolin, angustinolide, 3 β -acetoxymexicanolide)	$R_1 = R_3 = \text{H}; R_2 = \text{OAc}$	<i>K. nyasica</i> ; ^{164,184} <i>K. senegalensis</i> ; ^{601,603,623} <i>K. grandifoliola</i> ; ⁶⁰² <i>K. madagascariensis</i> ; ⁴⁶⁹ <i>Cedrela fissilis</i> ; ⁵⁹⁶ <i>Cabralea eichleriana</i> ; ^{430,644} <i>Swietenia mahagoni</i> ⁴⁵⁸
649	2-hydroxyfissinolide	$R_1 = \text{OH}; R_2 = \text{OAc}; R_3 = \text{H}$	<i>S. mahagoni</i> ; ⁴⁵⁸ <i>Khaya ivorensis</i> ; ^{164,446} <i>K. senegalensis</i> ⁶²³
650	2,6-dihydroxyfissinolide	$R_1 = R_3 = \text{OH}; R_2 = \text{OAc}$	<i>K. senegalensis</i> ^{601,623}
651	3 β -deacetyl fissinolide	$R_1 = R_3 = \text{H}; R_2 = \text{OH}$	<i>Cabralea eichleriana</i> ; ⁴³⁰ <i>Cedrela odorata</i> ⁹⁸
652	khayasin (3 β -isobutyryloxymexicanolide)	$R_1 = R_3 = \text{H}; R_2 = \text{OiBu}$	<i>C. odorata</i> ; ⁶⁴¹ <i>Neobeguea mahafalensis</i> ; ⁵⁵⁷ <i>Cipadessa baccifera</i> ; ⁵⁹¹ <i>Xylocarpus moluccensis</i> ; ⁵⁵⁸ <i>Khaya senegalensis</i> ; ^{451,655} <i>K. grandifoliola</i> ¹⁶⁴
653	2-hydroxykhayasin	$R_1 = \text{OH}; R_2 = \text{OiBu}; R_3 = \text{H}$	<i>K. madagascariensis</i> ¹⁶⁴
654	khayasin B	$R_1 = R_3 = \text{H}; R_2 = \text{OBz}$	<i>K. senegalensis</i> ⁴⁵¹
655	khayasin T	$R_1 = R_3 = \text{H}; R_2 = \text{OTig}$	<i>K. senegalensis</i> ; ⁴⁵¹ <i>Cipadessa fruticosa</i> ; ^{617,656} <i>C. baccifera</i> ; ^{591,657} <i>C. cinerascens</i> ; ⁶⁴⁷ <i>Xylocarpus granatum</i> ; ^{426,633} <i>X. moluccensis</i> ; ⁵⁵⁸ <i>Toona ciliata</i> ; ²⁹⁰ <i>Swietenia macrophylla</i> ; ^{445,653} <i>S. mahagoni</i> ^{112,458}
656	augustineolide	$R_1 = \text{Tig}; R_2 = \text{OH}; R_3 = \text{OAc}; R_4 = \text{OiBu}$	<i>S. macrophylla</i> ⁴⁴⁵
657	swietmanin E	$R_1 = \text{Tig}; R_2 = R_4 = \text{H}; R_3 = \text{OH}$	<i>S. mahagoni</i> ⁴⁵⁸
658	swietmanin F	$R_1 = \text{Ac}; R_2 = R_4 = \text{H}; R_3 = \text{OH}$	<i>S. mahagoni</i> ; ⁴⁵⁸ <i>Khaya senegalensis</i> ⁶²³
659	khayalenoid G	$R_1 = \text{Ac}; R_2 = \text{OAc}; R_3 = \text{OH}; R_4 = \text{H}$	<i>K. senegalensis</i> ⁶²³
660	khayalenoid H	$R_1 = \text{Ac}; R_2 = \text{OAc}; R_3 = R_4 = \text{H}$	<i>K. senegalensis</i> ⁶²³
661	khayalenoid I	$R_1 = \text{Ac}; R_2 = R_3 = R_4 = \text{H}; 11\alpha\text{-OAc}$	<i>K. senegalensis</i> ⁶²³
662	cabralin	$R_1 = \text{OAc}; R_2 = \text{H}; R_3 = \text{O}; R_4 = \text{OH}$	<i>Cabralea eichleriana</i> ⁴³⁰
663	isocabralin	$R_1 = \text{OAc}; R_2 = \text{H}; R_3 = \text{OH}; R_4 = \text{O}$	<i>C. eichleriana</i> ⁴³⁰
664	domesticulide E	$R_1 = R_3 = \text{O}; R_2 = R_4 = \text{OH}$	<i>Lansium domesticum</i> ¹⁰⁰
665	2-hydroxy-8(14)-dihydrofissinolide	$R_1 = R_2 = \text{OH}; R_3 = R_4 = \text{H}$	<i>Khaya madagascariensis</i> ¹⁶⁴
666	methyl 3 β -acetoxo-2-hydroxy-1-oxomeliacate	$R_1 = \text{OH}; R_2 = \text{OAc}; R_3 = R_4 = \text{H}$	<i>K. madagascariensis</i> ⁴⁶⁹
667	dihydrokhayasin	$R_1 = R_3 = R_4 = \text{H}; R_2 = \text{OiBu}$	<i>K. anthotheca</i> ; ¹⁶³ <i>K. madagascariensis</i> ¹⁶⁴
668	khayanone	$R_1 = \text{H}; R_2 = \text{O}; R_3 = \text{OH}; R_4 = \beta\text{-OH}$	<i>K. senegalensis</i> ^{470,550,559,575,623,658}
669	xylocensin N	$R_1 = R_3 = \text{H}; R_2 = \text{OAc}; R_4 = \text{OH}$	<i>Xylocarpus granatum</i> ^{604,659}
670	3-deacetylxylocensin N	$R_1 = R_3 = \text{H}; R_2 = R_4 = \text{OH}$	<i>X. granatum</i> ⁶⁰⁵
671	xylocarpin B	$R_1 = R_3 = \text{H}; R_2 = \text{OTig}; R_4 = \text{OH}$	<i>X. granatum</i> ⁶⁶⁰
672	angolensin A	$R_1 = R_3 = R_4 = \text{H}; R_2 = \text{OTig}; \Delta^{14,15}$	<i>Entandrophragma angolense</i> ⁵⁴⁵
673	angolensin C	$R_1 = \text{H}; R_2 = \text{O}; R_3 = \alpha\text{-OAc}; R_4 = \text{OH}$	<i>E. angolense</i> ⁵⁴⁵
674	8 β ,14 α -dihydroxyswietenolide	$R_1 = R_4 = \text{H}; R_2 = \text{OH}; R_3 = \beta\text{-OH}$	<i>Cedrela odorata</i> ⁵¹⁰
675	granatum D	$R_1 = R_3 = R_4 = \text{H}; R_2 = \text{OTig}$	<i>Xylocarpus granatum</i> ⁴²⁶
676	3 β -hydroxyisomexicanolide		<i>Cedrela fissilis</i> ⁶⁴²
677	swietenine	$R_1 = \text{H}; R_2 = \text{OTig}; R_3 = \text{OH}$	<i>Swietenia macrophylla</i> ; ^{55,445,612,653,661,662} <i>S. mahagoni</i> ; ^{112,603,663} <i>Khaya ivorensis</i> ⁴⁴⁷
678	swietenine B	$R_1 = \text{H}; R_2 = \text{propanate}; R_3 = \text{OH}$	<i>Swietenia mahagoni</i> ¹¹²
679	swietenine C	$R_1 = \text{H}; R_2 = \text{OiBu}; R_3 = \text{OH}$	<i>S. mahagoni</i> ; ¹¹² <i>S. macrophylla</i> ; ⁶¹⁴ <i>S. humilis</i> ⁴³⁴
680	swietenine D	$R_1 = \text{H}; R_2 = \text{methacrylyl}; R_3 = \text{OH}$	<i>S. mahagoni</i> ¹¹²
681	swietenine E	$R_1 = \text{H}; R_2 = \text{OPiv}; R_3 = \text{OH}$	<i>S. mahagoni</i> ¹¹²

Table 23. Continued

no.	compounds	substitution groups and others	sources
682	swietenine F	R ₁ = H; R ₂ = OBz; R ₃ = OH	<i>S. mahagoni</i> ¹¹²
683	sweetenine acetate	R ₁ = H; R ₂ = OTig; R ₃ = OAc	<i>S. mahagoni</i> ; ¹¹² <i>S. macrophylla</i> ^{55,653}
684	6-deoxydestigloylswietenine (3 β -hydroxymexicanolide, $\Delta^{8,30}$)	R ₁ = R ₃ = H; R ₂ = OH	<i>Khaya senegalensis</i> ^{451,464,467,468}
685	6-deoxydestigloylswietenine acetate	R ₁ = R ₃ = H; R ₂ = OAc	<i>K. senegalensis</i> ; ^{451,464,466} <i>Xylocarpus granatum</i> ¹⁶²
686	3-O-detigloyl-3-O-acetylswietenine	R ₁ = H; R ₂ = OAc; R ₃ = OH	<i>Khaya ivorensis</i> ⁴⁴⁷
687	6-acetylswietenine	R ₁ = H; R ₂ = OTig; R ₃ = OAc	<i>Swietenia mahagoni</i> ⁶⁰³
688	6-O-acetyl-2-hydroxyswietenine	R ₁ = OH; R ₂ = OTig; R ₃ = OAc	<i>S. mahagoni</i> ⁶³⁰
689	2-hydroxyswietenine	R ₁ = R ₃ = OH; R ₂ = OTig	<i>S. mahagoni</i> ; ^{559,630,663,664} <i>S. macrophylla</i> ⁴⁴⁵
690	2-hydroxy-6-deoxyswietenine (methyl 3 β - tigloyloxy-2-hydroxy-1-oxo- meliac-8(30)-enate)	R ₁ = OH; R ₂ = OTig; R ₃ = H	<i>S. macrophylla</i> ; ⁶¹⁴ <i>Capuronianthus mahafalensis</i> ⁶¹³
691	6-dexoxyswietenine isobutyrate	R ₁ = R ₃ = H; R ₂ = OiBu	<i>Khaya nyasica</i> ¹⁶⁴
692	2-hydroxydestigloyl-6- deoxyswietenine acetate	R ₁ = OH; R ₂ = OAc; R ₃ = H	<i>Xylocarpus molluccensis</i> ¹⁶²
693	12 β -hydroxy-6-deoxy- destigloylswietenine diacetate	R ₁ = R ₃ = H; R ₂ = OAc; 12 β -OAc	<i>Khaya senegalensis</i> ⁴⁵¹
694	febrifugin (6-desoxyswietenine)	R ₁ = R ₃ = H; R ₂ = OTig	<i>Soymida febrifuga</i> ; ⁶¹⁵ <i>Cedrela odorata</i> ; ⁹⁸ <i>Cipadessa baccifera</i> ; ^{591,618,657} <i>C. fruticosa</i> ; ^{617,643,656} <i>C. cinerascens</i> ; ⁶⁴⁷ <i>Toona ciliata</i> ; ²⁹⁰ <i>Xylocarpus granatum</i> ; ⁴²⁶ <i>Swietenia mahagoni</i> ; ^{603,616} <i>S. macrophylla</i> ^{445,653}
695	humilinolide C	R ₁ = OAc; R ₂ = OTig; R ₃ = H	<i>S. humilis</i> ; ^{434,629,665}
696	6-acetoxhumilinolide C	R ₁ = R ₃ = OAc; R ₂ = OTig	<i>S. aubrevilleana</i> ⁴⁴⁵
697	humilinolide D	R ₁ = OH; R ₂ = OAc; R ₃ = OAc	<i>S. humilis</i> ; ^{434,629,665}
698	humilinolide E	R ₁ = OH; R ₂ = OTig; R ₃ = OAc	<i>S. humilis</i> ⁴³⁴
699	methyl-2-hydroxy-3 β -isobutyroxy-1- oxomeliac-8(30)-enate	R ₁ = OH; R ₂ = OiBu; R ₃ = H	<i>S. humilis</i> ; ^{434,619}
700	methyl-2-hydroxy-3 β -tigloyloxy-1- oxomeliac-8(30)-enate	R ₁ = OH; R ₂ = OTig; R ₃ = H	<i>S. humilis</i> ⁴³⁴
701	methyl 3 β -tigloyloxy-2,6-dihydroxy-1- oxo-meliac-8(30)-enate	R ₁ = OH; R ₂ = OTig; R ₃ = β -OH	<i>S. macrophylla</i> ⁶¹⁴
702	methyl 3 β -isobutyryloxy-1-oxomeliac- 8(30)-enate	R ₁ = R ₃ = H; R ₂ = OiBu	<i>Carapa procera</i> ; ⁶⁶⁶ <i>Khaya nyasica</i> ; ¹⁸⁴ <i>Cipadessa baccifera</i> ⁵⁹¹
703	cipadesin	R ₁ = R ₃ = H; R ₂ = OPiv	<i>C. baccifera</i> ; ^{618,657} <i>C. fruticosa</i> ^{617,643,656}
704	2' <i>R</i> -cipadesin	R ₁ = R ₃ = H; R ₂ = 2' <i>R</i> -OPiv	<i>C. baccifera</i> ⁵⁹¹
705	2' <i>S</i> -cipadesin	R ₁ = R ₃ = H; R ₂ = 2' <i>S</i> -OPiv	<i>C. baccifera</i> ⁵⁹¹
706	ruageanin D	R ₁ = OH; R ₂ = OAc; R ₃ = H	<i>Ruagea glabra</i> ⁵⁵⁶
707	6-epidestigloylswietenine diacetate	R ₁ = H; R ₂ = OAc; R ₃ = OAc	<i>Khaya senegalensis</i> ⁴⁶⁴
708	khayalenoid E	R ₁ = H; R ₂ = O; R ₃ = OAc	<i>K. senegalensis</i> ⁶²³
709	swietmanin A	R ₁ = R ₃ = H; R ₂ = OiBu; 11 α -OAc	<i>Swietenia mahagoni</i> ⁴⁵⁸
710	swietmanin B	R ₁ = R ₃ = H; R ₂ = OAc; 11 α -OAc	<i>S. mahagoni</i> ⁴⁵⁸
711	swietmanin C	R ₁ = R ₃ = H; R ₂ = OH; 11 α -OAc	<i>S. mahagoni</i> ⁴⁵⁸
712	swietmanin D	R ₁ = R ₂ = OAc; R ₃ = H; 11 α -OAc	<i>S. mahagoni</i> ⁴⁵⁸
713	11 α -acetox-2 α -hydroxy-6-deoxy- destigloylswietenine acetate	R ₁ = OH; R ₂ = OAc; R ₃ = H; 11 α -OAc	<i>Khaya ivorensis</i> ⁵⁵⁴
714	erythrocarpine B	R = Bz	<i>Chisocheton erythrocarpus</i> ⁶⁶⁷
715	erythrocarpine C	R = Cin	<i>C. erythrocarpus</i> ⁶⁶⁷
716	febrifugin A	R ₁ = O; R ₂ = OH	<i>Cipadessa fruticosa</i> ; ^{617,656} <i>Xylocarpus granatum</i> ^{426,633}
717	granatumin E	R ₁ = OH; R ₂ = H	<i>X. granatum</i> ⁴²⁶
718	dehydrocarapin	R = O	<i>Cedrela odorata</i> ⁵⁰⁰
719	xylomexicanolide B	R = OiBu	<i>Xylocarpus moluccensis</i> ⁵⁵⁸
720	mahagonin		<i>Swietenia mahagoni</i> ⁶⁶⁸
721	angustidenolide	R ₁ = R ₃ = H; R ₂ = Ac	<i>Cedrela angustifolia</i> ⁵⁹⁷

Table 23. Continued

no.	compounds	substitution groups and others	sources
722	2 α -hydroxyangustidienolide	R ₁ = OH; R ₂ = Ac; R ₃ = H	<i>C. augustifolia</i> ⁵⁹⁷
723	seneganolide A	R ₁ = R ₂ = R ₃ = H	<i>Swietenia mahagoni</i> ; ⁴⁵⁸ <i>Khaya senegalensis</i> ⁴⁷²
724	2-hydroxyseneganolide A	R ₁ = OH; R ₂ = R ₃ = H	<i>K. senegalensis</i> ⁴⁷²
725	2-acetoxyseneganolide A	R ₁ = OAc; R ₂ = R ₃ = H	<i>K. senegalensis</i> ⁴⁷²
726	tigloylseneganolide A	R ₁ = R ₃ = H; R ₂ = Tig	<i>Cipadessa baccifera</i> ; ⁵⁹¹ <i>Xylocarpus granatum</i> ⁴²⁶
727	erythrocarpine A	R ₁ = R ₃ = H; R ₂ = Bz	<i>Chisocheton erythrocarpus</i> ⁶⁶⁷
728	granatumin A	R ₁ = R ₃ = H; R ₂ = methylacryl	<i>Xylocarpus granatum</i> ⁴²⁶
729	granatumin B	R ₁ = R ₃ = H; R ₂ = Piv	<i>X. granatum</i> ⁴²⁶
730	swietmanin G	R ₁ = OH; R ₂ = iBu; R ₃ = H	<i>Swietenia mahagoni</i> ⁴⁵⁸
731	swietmanin H	R ₁ = OH; R ₂ = Ac; R ₃ = H	<i>S. mahagoni</i> ⁴⁵⁸
732	swietmanin I	R ₁ = OH; R ₂ = Tig; R ₃ = H	<i>S. mahagoni</i> ⁴⁵⁸
733	xylomexanolide A	R ₁ = R ₃ = H; R ₂ = iBu	<i>Xylocarpus moluccensis</i> ⁵⁵⁸
734	khayalenoid F	R ₁ = OH; R ₂ = Ac; R ₃ = S-OAc	<i>Khaya senegalensis</i> ⁶²³
735	quivisianolide B	R ₁ = OH; R ₂ = Ang; $\Delta^{9,11}$	<i>Quivisia papinae</i> ⁶⁴⁶
736	granatumin C	R ₁ = H; R ₂ = Tig; $\Delta^{14,15}$	<i>Xylocarpus granatum</i> ⁴²⁶
737	xylogranatin A	R ₁ = R ₃ = R ₅ = H; R ₂ = OTig; R ₄ = α -OH	<i>X. granatum</i> ^{633,639}
738	30 α -hydroxylxylogranatin A	R ₁ = R ₃ = H; R ₂ = OTig; R ₄ = R ₅ = α -OH	<i>X. granatum</i> ⁶⁶⁹
739	carapin	R ₁ = R ₃ = R ₅ = H; R ₂ = O; R ₄ = β -H	<i>Carapa procera</i> ⁶⁷⁰
740	3 β -hydroxy-3-deoxycarapin	R ₁ = R ₃ = R ₅ = H; R ₂ = OH; R ₄ = β -H	<i>Khaya senegalensis</i> ; ⁴⁶⁷ <i>Entandrophragma angolense</i> ⁵⁴⁵
741	methyl-3 β -acetoxy-1-oxomeliac-14(15)-enate (3 β -acetoxycarapin)	R ₁ = R ₃ = R ₅ = H; R ₂ = OAc; R ₄ = β -H	<i>Khaya nyasica</i> ; ¹⁸⁴ <i>Toona ciliata</i> ; ¹⁴⁵ <i>Cedrela fissilis</i> ^{132,671}
742	6-hydroxycarapin	R ₁ = R ₅ = H; R ₂ = O; R ₃ = OH; R ₄ = β -H	<i>C. glaziovii</i> ⁶⁷²
743	methyl 3 β -acetoxy-6-hydroxy-1-oxomeliac-14-enoate (3 β -acetoxy-3-deoxo-6R-hydroxycarapin)	R ₁ = R ₅ = H; R ₂ = OAc; R ₃ = OH; R ₄ = β -H	<i>Khaya anthotheca</i> ; ⁵⁵² <i>K. senegalensis</i> ⁶⁰¹
744	8 α -hydroxycarapin	R ₁ = R ₃ = R ₅ = H; R ₂ = O; R ₄ = α -OH	<i>Swietenia mahagoni</i> ⁴⁵⁸
745	6R,8 α -dihydroxycarapin	R ₁ = R ₅ = H; R ₂ = O; R ₃ = R ₄ = α -OH	<i>Khaya anthotheca</i> ⁵⁵²
746	3 β ,6-dihydroxydihydrocarapin	R ₁ = R ₅ = H; R ₂ = OH; R ₃ = β -OH; R ₄ = β -H	<i>Swietenia macrophylla</i> ; ⁴⁴⁵ <i>Cedrela odorata</i> ⁵¹⁰
747	xylocensin X ₁	R ₁ = R ₅ = H; R ₂ = OH; R ₃ = β -OAc; R ₄ = α -OH	<i>Xylocarpus granatum</i> ⁶⁷³
748	xylocensin X ₂	R ₁ = R ₃ = R ₅ = H; R ₂ = OH; R ₄ = α -OH	<i>X. granatum</i> ⁶⁷³
749	utilin B	R ₁ = OH; R ₂ = R ₅ = OAc; R ₃ = H; R ₄ = α -OiBu	<i>Entandrophragma utile</i> ^{491,620,674}
750	xylomexanin B	R ₁ = R ₃ = R ₅ = H; R ₂ = OPiv; R ₄ = α -OH	<i>Xylocarpus granatum</i> ⁶⁷⁵
751	khayalenoid A	R = H; $\Delta^{8,9}$; $\Delta^{14,15}$	<i>Khaya senegalensis</i> ⁶²²
752	khayalenoid B	R = H; $\Delta^{8,14}$	<i>K. senegalensis</i> ⁶²²
753	khayalenoid C	R = OH; $\Delta^{8,14}$	<i>K. senegalensis</i> ⁶²³
754	khayalenoid D	R = H; $\Delta^{8,30}$	<i>K. senegalensis</i> ⁶²³
755	utilin C	R ₁ = α -OH; R ₂ = OAc; R ₃ = H; R ₄ = OiBu	<i>Entandrophragma utile</i> ^{491,621,674}
756	xylocensin A	R ₁ = R ₃ = H; R ₂ = R ₄ = OiVal	<i>Xylocarpus moluccensis</i> ⁶²⁵
757	xylocensin D	R ₁ = α -OH; R ₂ = R ₄ = OiBu; R ₃ = H	<i>X. moluccensis</i> ⁶²⁵
758	xylocensin X	R ₁ = α -OH; R ₂ = OPiv; R ₃ = H; R ₄ = OiBu	<i>X. moluccensis</i> ⁶²⁴
759	xylocensin Y	R ₁ = α -OH; R ₂ = OiBu; R ₃ = H; R ₄ = OPiv	<i>X. moluccensis</i> ⁶²⁴
760	xylocarpin F	R ₁ = β -H; R ₂ = R ₄ = OAc; R ₃ = H	<i>X. granatum</i> ⁶³³
761	xylocarpin G	R ₁ = β -H; R ₂ = OAc; R ₃ = H; R ₄ = OTig	<i>X. granatum</i> ⁶³³
762	xylogranatin B	R ₁ = β -H; R ₂ = OTig; R ₃ = H; R ₄ = OAc	<i>X. granatum</i> ⁶³⁹
763	xylogranatin C	R ₁ = β -H; R ₂ = OPiv; R ₃ = H; R ₄ = OAc	<i>X. granatum</i> ^{633,639}
764	xylogranatin D	R ₁ = β -H; R ₂ = OiBu; R ₃ = H; R ₄ = OAc	<i>X. granatum</i> ⁶³⁹
765	xylogranatin S	R ₁ = β -H; R ₂ = OAc; R ₃ = H; R ₄ = OPiv	<i>X. granatum</i> ⁶⁷⁶
766	angolensin B	R ₁ = α -OH; R ₂ = OTig; R ₃ = OAc; R ₄ = OiBu	<i>Entandrophragma angolense</i> ⁵⁴⁵
767	xylocensin B	R ₁ = R ₃ = H; R ₂ = R ₄ = OiBu	<i>Xylocarpus moluccensis</i> ⁶²⁵
768	xylocensin F	R ₁ = OH; R ₂ = R ₄ = OiBu; R ₃ = H	<i>X. moluccensis</i> ⁶²⁵
769	xylocensin I	R ₁ = OH; R ₂ = OAc; R ₃ = H; R ₄ = OPiv	<i>X. granatum</i> ; ⁶²⁶ <i>X. moluccensis</i> ⁶²⁶

Table 23. Continued

no.	compounds	substitution groups and others	sources
770	xyloccensin J	R ₁ = OH; R ₂ = OAc; R ₃ = H; R ₄ = OiBu	<i>X. granatum</i> ; ⁶²⁶ <i>X. moluccensis</i> ⁶²⁶
771	xyloccensin M	R ₁ = R ₃ = R ₄ = H; R ₂ = OAc	<i>X. granatum</i> ^{604,659,677}
772	3-deacetylxyloccensin M	R ₁ = R ₃ = R ₄ = H; R ₂ = OH	<i>X. granatum</i> ⁶⁰⁵
773	xylocarpin A	R ₁ = R ₃ = R ₄ = H; R ₂ = OTig	<i>X. granatum</i> ⁶⁶⁰
774	khayalactol	R ₁ = R ₃ = OH; R ₂ = O; R ₄ = H	<i>Khaya ivorensis</i> ; ⁵⁵⁴ <i>K. senegalensis</i> ^{547,550,559,575,678}
775	grandifoliolide A	R ₁ = R ₃ = OH; R ₂ = OAc; R ₄ = H	<i>K. grandifoliola</i> ⁶⁷⁹
776	xylocarpin J		<i>Xylocarpus granatum</i> ⁶⁷⁷
777	seneganolide	R ₁ = R ₃ = H; R ₂ = O	<i>Khaya ivorensis</i> ; ⁵⁵⁴ <i>K. senegalensis</i> ^{549–551,559}
778	2-hydroxyseneganolide	R ₁ = OH; R ₂ = O; R ₃ = H	<i>K. senegalensis</i> ^{550,559,658}
779	anthothecanolide	R ₁ = R ₂ = R ₃ = OH	<i>K. grandifoliola</i> ; ⁶⁷⁹ <i>K. anthotheca</i> ⁵⁵²
780	3-O-acetylanthothecanolide	R ₁ = R ₃ = OH; R ₂ = OAc	<i>K. grandifoliola</i> ; ⁶⁷⁹ <i>K. anthotheca</i> ⁵⁵²
781	2,3-di-O-acetylanthothecanolide	R ₁ = R ₂ = OAc; R ₃ = OH	<i>K. anthotheca</i> ⁵⁵²
782	1 α ,8 α -oxido-3 β -acetoxy-2 α -acylperoxy-1 α ,14 α -dihydroxy[3,3,1 ^{10,2}]-bicyclomeliac-7,19-olide	R ₁ = OOAc; R ₂ = OAc; R ₃ = OH	<i>K. anthotheca</i> ⁶⁸⁰
783	3,8-hemiketalcarapin		<i>Swietenia mahagoni</i> ⁴⁵⁸
784	cedrodorin	R ₁ = OH; R ₂ = R ₃ = H	<i>Cedrela odorata</i> ^{510,681}
785	6-acetoxycedrodorin	R ₁ = OAc; R ₂ = R ₃ = H	<i>C. odorata</i> ; ⁶⁸¹ <i>Xylocarpus granatum</i> ^{627,628,659}
786	6-deoxy-9 α -hydroxycedrodorin	R ₁ = R ₃ = H; R ₂ = OH	<i>Cedrela odorata</i> ⁶⁸¹
787	9 α -hydroxycedrodorin	R ₁ = R ₂ = OH; R ₃ = H	<i>C. odorata</i> ⁶⁸¹
788	xyloccensin K	R ₁ = R ₂ = R ₃ = H	<i>C. guianensis</i> ; ¹¹³ <i>C. odorata</i> ; ⁵¹⁰ <i>Entandrophragma angolense</i> ; ⁵⁴⁵ <i>Xylocarpus granatum</i> ^{448,627,628,633,659,682}
789	xyloccensin W	R ₁ = R ₂ = H; R ₃ = OAc	<i>X. granatum</i> ^{628,659}
790	xyloccensin G	R = OPiv	<i>X. moluccensis</i> ⁶⁸³
791	xyloccensin H	R ₁ = H	<i>X. moluccensis</i> ⁶⁸³
792	swietemahonolide	R ₁ = R ₃ = H; R ₂ = Tig	<i>X. granatum</i> ; ⁴²⁶ <i>Cipadessa fruticosa</i> ; ⁶⁷¹ <i>C. baccifera</i> ; ⁵⁹¹ <i>C. cinerascens</i> ; ⁶⁴⁷ <i>Swietenia mahagoni</i> ^{56,112}
793	humilinolide A (methyl 3 β -isobutyryloxy-2,6-dihydroxy-8 α ,30 α -epoxy-1-oxo-meliacate)	R ₁ = R ₃ = OH; R ₂ = iBu	<i>S. humilis</i> ; ^{434,629,665,684} <i>S. macrophylla</i> ⁶¹⁴
794	humilinolide B	R ₁ = OH; R ₂ = iBu; R ₃ = OAc	<i>S. humilis</i> ^{434,629,665}
795	humilinolide F	R ₁ = R ₃ = OAc; R ₂ = Tig	<i>S. humilis</i> ⁴³⁴
796	methyl 3 β -acetoxy-2,6-dihydroxy-8 α ,30 α -epoxy-1-oxo-meliacate	R ₁ = R ₃ = OH; R ₂ = Ac	<i>S. macrophylla</i> ⁶¹⁴
797	methyl 3 β -tigloyloxy-2-hydroxy-8 α ,30 α -epoxy-1-oxo-meliacate (2-hydroxyswietemahonolide)	R ₁ = OH; R ₂ = Tig; R ₃ = H	<i>S. macrophylla</i> ; ^{614,653} <i>S. mahagoni</i> ; ⁶³⁰ <i>Khaya senegalensis</i> ⁵⁵⁹
798	methyl 2-hydroxy-3 β -isobutyryl-8 α ,30 α -epoxy-1-oxo-meliacate	R ₁ = OH; R ₂ = iBu; R ₃ = H	<i>Swietenia humilis</i> ⁶¹⁹
799	xylocarpin	R ₁ = R ₃ = H; R ₂ = Ac	<i>Xylocarpus granatum</i> ; ^{162,685} <i>Ruagea glabra</i> ⁵⁵⁶
800	swietemahonin A	R ₁ = H; R ₂ = propanoyl; R ₃ = OH	<i>Swietenia mahagoni</i> ^{56,112,652}
801	swietemahonin B	R ₁ = H; R ₂ = propanoyl; R ₃ = OAc	<i>S. mahagoni</i> ^{56,112}
802	swietemahonin C	R ₁ = H; R ₂ = iBu; R ₃ = OAc	<i>S. mahagoni</i> ; ^{56,112} <i>S. humilis</i> ⁴³⁴
803	swietemahonin D	R ₁ = H; R ₂ = Ac; R ₃ = OH	<i>S. mahagoni</i> ^{56,112}
804	swietemahonin E	R ₁ = H; R ₂ = Tig; R ₃ = OH	<i>S. mahagoni</i> ; ^{56,112,652} <i>S. macrophylla</i> ^{445,653}
805	8,30-epoxy swietenine acetate (swietemahonin F)	R ₁ = H; R ₂ = Tig; R ₃ = OAc	<i>S. mahagoni</i> ; ^{56,112} <i>S. macrophylla</i> ^{55,445}
806	swietemahonin G	R ₁ = R ₃ = OH; R ₂ = Tig	<i>S. mahagoni</i> ; ^{56,112,457,559,630} <i>S. macrophylla</i> ⁴⁴⁵
807	6-O-acetylswietemahonin G	R ₁ = OH; R ₂ = Tig; R ₃ = OAc	<i>S. mahagoni</i> ; ^{559,630} <i>S. macrophylla</i> ⁶⁵³
808	ruageanin A	R ₁ = R ₃ = H; R ₂ = iBu	<i>Cipadessa baccifera</i> ; ⁵⁹¹ <i>C. fruticosa</i> ; ^{617,647,656} <i>Ruagea glabra</i> ⁵⁵⁶
809	ruageanin B	R ₁ = OH; R ₂ = Tig; R ₃ = H	<i>R. glabra</i> ⁵⁵⁶
810	3-angeloyl-3-detigloylruageanin B	R ₁ = OH; R ₂ = Ang; R ₃ = H	<i>Quivisia papinae</i> ⁶⁴⁶

Table 23. Continued

no.	compounds	substitution groups and others	sources
811	ruageanin C	R ₁ = OH; R ₂ = Ac; R ₃ = H	<i>Ruagea glabra</i> ⁵⁵⁶
812	humilin B	R ₁ = H; R ₂ = <i>i</i> Bu; R ₃ = OH	<i>Swietenia humilis</i> ; ⁴³⁴ <i>Xylocarpus moluccensis</i> ¹⁶²
813	2'- <i>R</i> -cipadesin A	R ₁ = R ₃ = H; R ₂ = 2'- <i>R</i> -pivaloyl	<i>Cipadessa baccifera</i> ; ⁵⁹¹ <i>C. cinerascens</i> ⁶⁴⁷
814	2'- <i>S</i> -cipadesin A	R ₁ = R ₃ = H; R ₂ = 2'- <i>S</i> -pivaloyl	<i>C. baccifera</i> ⁵⁹¹
815	cipadesin A	R ₁ = R ₃ = H; R ₂ = Piv	<i>C. fruticosa</i> ; ^{617,643,656} <i>C. cinerascens</i> ⁶⁴⁷
816	cineracipadesin A	R ₁ = H; R ₂ = Piv	<i>C. cinerascens</i> ⁵⁶³
817	quivisianolide A	R ₁ = OH; R ₂ = Ang	<i>Quivisia papinae</i> ⁶⁴⁶
818	quivisianone		<i>Q. papinae</i> ⁶⁴⁶
819	granaxylocarpin A	R ₁ = OPiv; R ₂ = Ac	<i>Xylocarpus granatum</i> ⁶³²
820	xylogranatin B	R ₁ = OTig; R ₂ = Ac	<i>X. granatum</i> ⁶³⁷
821	xylomexicanin A	R ₁ = H; R ₂ = <i>i</i> Bu; Δ ^{2,3}	<i>X. granatum</i> ⁶⁷⁵
822	granaxylocarpin B (xylocarpin H)	R ₁ = H; R ₂ = Tig; Δ ^{2,3}	<i>X. granatum</i> ^{632,633}
823	xylogranatin C	R ₁ = H; R ₂ = Ac; Δ ^{2,3}	<i>X. granatum</i> ^{448,637,638}
824	ecuadorin		<i>Guarea kunthiana</i> ⁶⁸⁶
825	xylocarpanoid A		<i>Xylocarpus granatum</i> ⁶³⁴
826	xylogranatin E		<i>X. granatum</i> ⁶⁸⁷
827	erythrocarpine D	R ₁ = Cin; R ₂ = H; Δ ^{8,30} , Δ ^{14,15}	<i>Chisocheton erythrocarpus</i> ⁶⁶⁷
828	erythrocarpine E	R ₁ = Cin; R ₂ = OH; Δ ^{8,30}	<i>C. erythrocarpus</i> ⁶⁶⁷
829	xyloactone (xylocensin L)	R ₁ = Tig; R ₂ = H; 8,30-epoxy	<i>Xylocarpus granatum</i> ^{635,636,659}
830	granaxylocarpin C	R ₁ = Tig; R ₂ = OH; 8,30-epoxy	<i>X. granatum</i> ⁶³²
831	grandifolin		<i>Khaya grandifoliola</i> ⁵⁶¹
832	xylogranatin A		<i>Xylocarpus granatum</i> ⁶³⁷
833	xylogranatin D		<i>X. granatum</i> ^{637,638}
834	xylogranatin I	R ₁ = R ₂ = H	<i>X. granatum</i> ⁶³⁸
835	xylogranatin J	R ₁ = R ₂ = CH ₃	<i>X. granatum</i> ⁶³⁸
836	xylogranatin K	R ₁ = H; R ₂ = CH ₃	<i>X. granatum</i> ⁶³⁸
837	xylogranatin L	R ₁ = H; R ₂ = CH ₂ CH ₃	<i>X. granatum</i> ⁶³⁸
838	xylogranatin M	R ₁ = CH ₃ ; R ₂ = Ac	<i>X. granatum</i> ⁶³⁸
839	xylogranatin N	R ₁ = H; R ₂ = 2'- <i>S</i> -methylbutyryl	<i>X. granatum</i> ⁶³⁸
840	xylogranatin O	R ₁ = H; R ₂ = Tig	<i>X. granatum</i> ⁶³⁸
841	xylogranatin P	R ₁ = H; R ₂ = <i>i</i> Bu	<i>X. granatum</i> ⁶³⁸
842	xylogranatin Q		<i>X. granatum</i> ⁶³⁸
843	xylogranatin R		<i>X. granatum</i> ⁶³⁸
844			<i>Khaya ivorensis</i> ⁶⁸⁸
845	grandifotane A		<i>K. grandifoliola</i> ⁶⁴⁰

but also gave ready access to the demethylated decalin with the hydroxydihydrofuran acetal unit (right-hand side of the molecule as drawn) and the synthesis of important model compounds.⁷⁷⁷ Several research groups have proposed the construction of a highly functionalized tricyclic *trans*-decalin system by IMDA (intramolecular Diels–Alder) cycloaddition.^{778–784} In addition, the tetracyclic decalin portion was synthesized in an optically pure form *via* reduction of a silyloxyfuran derivative, and the key reactions involved the CBS (Corey–Bakshi–Shibata) asymmetric reduction of a ketone and an IMDA reaction.^{785,786} The development of a strategy for the functionalization of the decalin portion based on the thermal Claisen rearrangement represented significant progress toward the total synthesis of **292**.⁷⁸⁷ For a more advanced decalin system, both the total synthesis and semisynthesis with efficient and stereoselective construction of the ABCD rings,⁷⁸⁸ ABC rings,⁷⁸⁹ AB rings,⁷⁹⁰ and B-ring,⁷⁹¹ all with full functionality, were reported.

For biological evaluation and a total synthesis study directed toward azadirachtin (**292**), the hydroxyfuran acetal functional group related to **292** have been prepared^{792–796} using some reactions which involved an enantioselective route.^{797,798} An extensive body

of work has been completed on the preparation of models for the decalin portion of **292** and has led to the design of an effective route to the fragment methyl (3*SR**,3*aR**,6*aR**,10*aR**)-3-hydroxy-5-oxoperhydronaphtho[1,8*a-c*]furan-3-carboxylate, containing some of the functionality required for antifeedant activity.⁷⁹⁹ A model substance for **292**, 9-hydroxy-dihydrofuro-2,3-tetrahydropyran, was synthesized by a route in which the key step involved cyclization of hydroxyl-dialdehyde precursors, acetylation and pyrolysis.⁸⁰⁰ A tricyclic lactone derived from D-galactal *via* tin hydride mediated transannular radical cyclization was easily converted into an advanced precursor of the tricyclic dihydrofuran portion of **292**.⁸⁰¹ The Diels–Alder adduct formed using Evans' chiral Cu-bisoxazoline complex catalyst was easily converted to the tricyclic dihydrofuran moiety *via* SmI₂ reductive cleavage and selective functionalization.⁸⁰² Furthermore, a synthesis route to mimics of **292** containing the hydrotetrahydrofuran-carboxylate hemiketal functional moiety was developed.^{803,804} A key tricyclic acetal intermediate has been prepared in optically pure form in 12 steps from the known (-)-3-endobromotricyclo-[3.2.0.0^{2,7}]heptan-6-one.⁸⁰⁵

The extreme steric congestion at the C8–C14 bond has resulted in the failure of many attempted coupling strategies. The convergent synthetic approach toward **292** and functionalized analogs was based on the construction of the C8–C14 bond through a diastereoselective Claisen rearrangement,^{806–809} or through a transition metal chemistry strategy,⁸¹⁰ or through an

intramolecular radical reaction followed by a cation-induced rupture of an initially formed bridge.^{811,812} Finally, Ley placed particular emphasis on the key coupling of a left-hand decalin fragment with a right-hand hydroxydihydrofuran acetal unit via a Claisen rearrangement reaction of an intermediate propargylic enol ether.²³

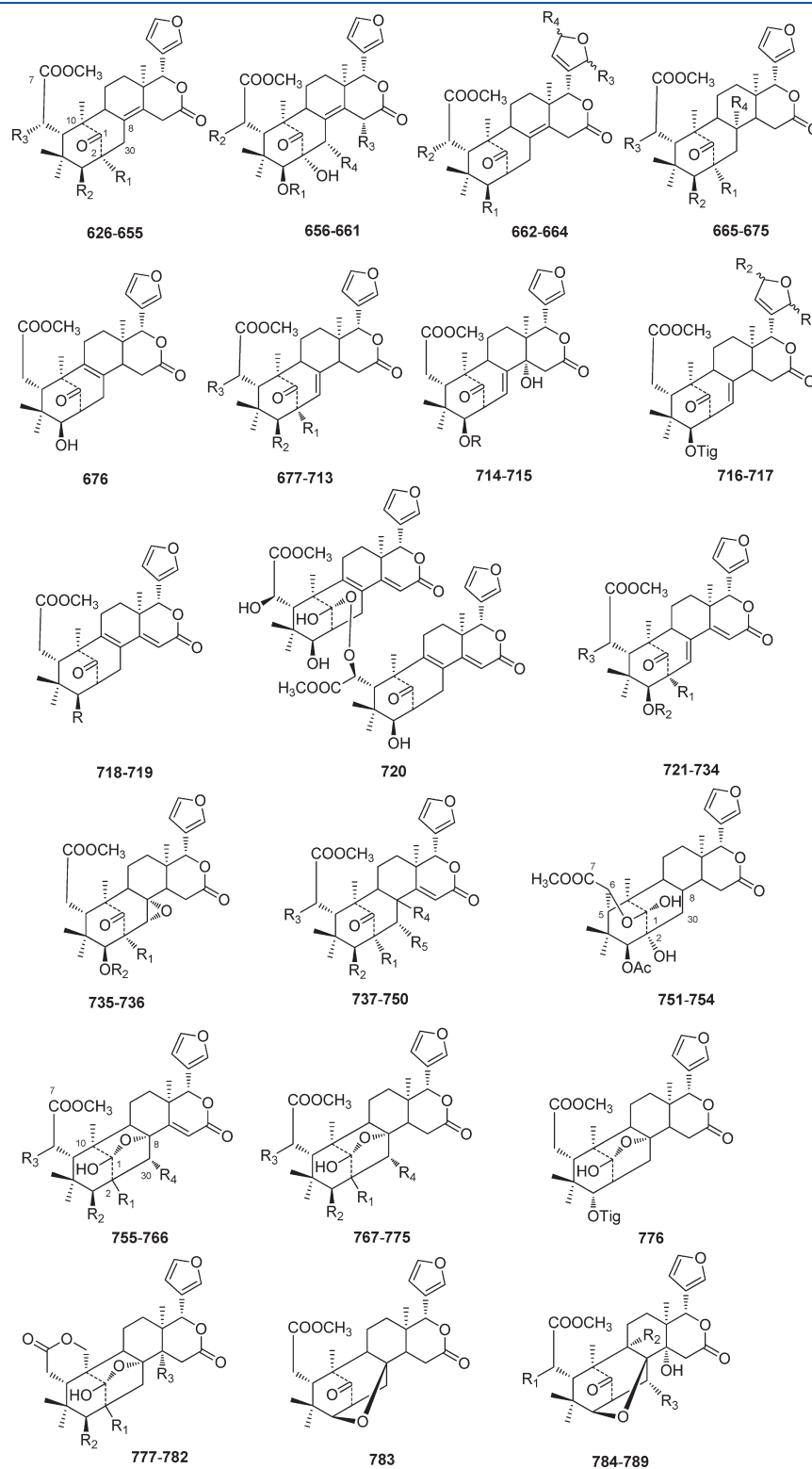


Figure 25. Continued

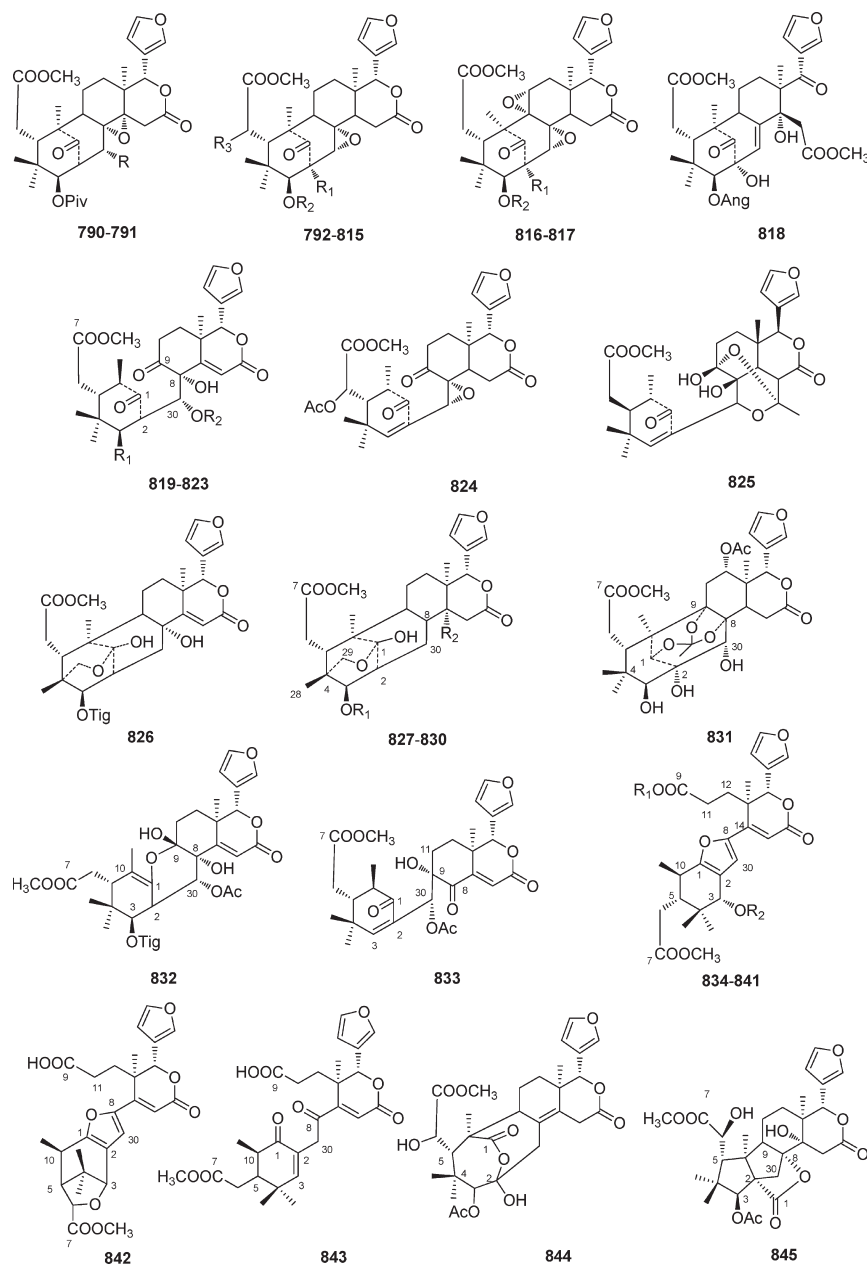


Figure 25. Structures of mexicanolide-class limonoids **626**–**845**.

After a long journey of 22 years, the total synthesis of **292** was finally completed. It could be produced from the key intermediate through a series of selective transformations.^{770,813} Jauch summarized the retrosynthetic analysis, the key Ireland-Claisen rearrangement, radical cyclization, epoxidation, and completion of the total synthesis of **292** through relay synthesis, which contained 71 steps with a total yield of 0.00015%, and commented this work was a real highlight of organic chemistry.⁸¹⁴ In addition, Devakumar et al. summarized the decalin scaffold synthesis, pyran fragment construction, and the ‘last summit’ of the total synthesis of **292**, and called it a chemical odyssey.²⁴

Azadirachtin (**292**), along with another four limonoids vepaol (**303**), isovepaol (**304**), 3-desacetylazadirachtin, and 1-tigloyl-3-acetyl-11-methoxyazadirachtin (**318**), was synthesized from a

common intermediate, and the judicious choice of transacetalization conditions allowed efficient access to both the azadirachtin and the azadirachtinin skeleton (Scheme 2).⁸¹⁵

The conversion of **292** derivatives to the corresponding azadirachtinin skeletons could be achieved in high yield under mild conditions (Scheme 3).⁸¹⁶ Dinitrophenylamino, dansyl, and biotin groups were covalently attached to several derivatives of **292** via a linker group to give fluorescent or immunogenic compounds that generally retain the biological properties of **292**, which were potential tools for the determination of the mechanisms of **292** in living systems.⁸¹⁷

Some derivatives related to naturally occurring limonoids were prepared for the purpose of either biological activity evaluation or reaction mechanistic investigation. On the basis

Table 24. Structures and Sources of Phragmalin-*ortho* Ester Limonoids 846–962

no.	compounds	substitution groups and others	sources
846	phragmalin	$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = H$	<i>Entandrophragma caudatum</i> ; ⁶⁸⁹ <i>Khaya senegalensis</i> ⁵⁵⁹
847	12-acetoxypfragmalin	$R_1 = R_2 = R_3 = R_5 = R_6 = H$; $R_4 = OAc$	<i>Chukrasia tabularis</i> ⁷⁰²
848	phragmalin 3,30-di-isobutyrate	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = R_6 = iBu$	<i>C. tabularis</i> ; ⁷⁰² <i>Entandrophragma caudatum</i> ⁷⁰³
849	phragmalin 3,30-diacetate	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = R_6 = Ac$	<i>Xylocarpus moluccensis</i> ¹⁶²
850	xylocensin E (phragmalin 2,3,30-triacetate)	$R_1 = R_2 = R_6 = Ac$; $R_3 = R_4 = R_5 = H$	<i>X. moluccensis</i> ^{162,625}
851	12-acetoxypfragmalin 3,30-di-isobutyrate	$R_1 = R_3 = R_5 = H$; $R_2 = R_6 = iBu$; $R_4 = OAc$	<i>Chukrasia tabularis</i> ⁷⁰²
852	phragmalin 3-isobutyrate 30-propionate	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = iBu$; $R_6 = propanoyl$	<i>C. tabularis</i> ; ⁷⁰² <i>Entandrophragma caudatum</i> ⁷⁰³
853	12-acetoxypfragmalin 3-isobutyrate 30-propionate	$R_1 = R_3 = R_5 = H$; $R_2 = iBu$; $R_4 = OAc$; $R_6 = propanoyl$	<i>E. caudatum</i> ; ⁷⁰³ <i>Chukrasia tabularis</i> ⁷⁰²
854	leandranin C	$R_1 = R_2 = R_6 = Ac$; $R_3 = R_4 = H$; $R_5 = OAc$	<i>Neobegonia leandrea</i> ⁷⁰⁴
855	14,15-dihydroepoxyfebrinin B	$R_1 = R_6 = Ac$; $R_2 = epoxytigloyl$; $R_3 = R_4 = R_5 = H$	<i>Soymida febrifuga</i> ⁷⁰⁵
856	tabulalide C	$R_1 = R_2 = R_6 = H$; $R_3 = OH$; $R_4 = R_5 = OAc$	<i>Chukrasia tabularis</i> ⁷⁰⁶
857	tabulalide D	$R_1 = R_6 = H$; $R_2 = Ac$; $R_3 = OH$; $R_4 = R_5 = OAc$	<i>C. tabularis</i> ^{559,706}
858	2-O-acetyltabulalide D	$R_1 = R_2 = Ac$; $R_3 = OH$; $R_4 = R_5 = OAc$ $R_6 = H$	<i>C. tabularis</i> ⁵⁵⁹
859	tabularisin N	$R_1 = H$; $R_2 = R_6 = Ac$; $R_3 = OH$; $R_4 = R_5 = OAc$	<i>C. tabularis</i> ⁷⁰⁷
860	febrinin A	$R_1 = Ac$; $R_2 = Tig$; $R_3 = R_4 = R_5 = H$; $R_6 = propanoyl$; $\Delta^{14,15}$	<i>Soymida febrifuga</i> ⁷⁰⁸
861	febrinin B	$R_1 = R_6 = Ac$; $R_2 = Tig$; $R_3 = R_4 = R_5 = H$; $\Delta^{14,15}$	<i>S. febrifuga</i> ⁷⁰⁸
862	epoxyfebrinin B	$R_1 = R_6 = Ac$; $R_2 = epoxytigloyl$; $R_3 = R_4 = R_5 = H$; $\Delta^{14,15}$	<i>S. febrifuga</i> ⁷⁰⁵
863	xylocarpin I		<i>Xylocarpus granatum</i> ⁶³³
864	neobeguina	$R_1 = R_3 = R_4 = R_5 = H$; $R_2 = R_6 = Ac$; $R_7 = CH_3$	<i>Neobegonia mahafalensis</i> ⁷⁰⁹
865	bussein A	$R_1 = R_3 = H$; $R_2 = Piv$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>Entandrophragma bussei</i> ^{424,691,693}
866	bussein B	$R_1 = R_3 = H$; $R_2 = iBu$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ^{424,691,693}
867	bussein C	$R_1 = R_3 = R_7 = H$; $R_2 = Piv$; $R_4 = R_5 = OAc$; $R_6 = Ac$	<i>E. bussei</i> ⁶⁹³
868	bussein D	$R_1 = R_3 = H$; $R_2 = epoxytigloyl$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
869	bussein E	$R_1 = R_3 = H$; $R_2 = Tig$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
870	bussein F	$R_1 = R_3 = R_7 = H$; $R_2 = iBu$; $R_4 = R_5 = OAc$; $R_6 = Ac$	<i>E. bussei</i> ⁶⁹³
871	bussein G	$R_1 = R_3 = H$; $R_2 = 2'-hydroxypivaloyl$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
872	bussein H	$R_1 = R_3 = H$; $R_2 = R_6 = Ac$; $R_4 = R_5 = OAc$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
873	bussein J	$R_1 = R_3 = H$; $R_2 = Piv$; $R_4 = OH$; $R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
874	bussein K	$R_1 = R_3 = H$; $R_2 = iBu$; $R_4 = OH$; $R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
875	bussein L	$R_1 = R_3 = H$; $R_2 = iBu(OH)$; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
876	bussein M	$R_1 = R_3 = H$; $R_2 = 2',3'$ -dihydroxypivaloyl; $R_4 = R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. bussei</i> ⁶⁹³
877	spicata 2	$R_1 = R_3 = H$; $R_2 = Piv$; $R_4 = OiBu$; $R_5 = OAc$; $R_6 = Ac$; $R_7 = CH_3$	<i>E. spicatum</i> ⁷¹⁰
878	tabularisin P	$R_1 = R_4 = R_6 = R_7 = H$; $R_2 = iBu$; $R_3 = R_5 = OAc$	<i>Chukrasia tabularis</i> ⁷⁰⁷
879	chukrasin A	$R_1 = H$; $R_2 = Ac$; $R_3 = OH$; $R_4 = OAc/OiBu$; $R_5 = OiBu$; $R_6 = Ac/iBu$; $R_7 = CH_3$	<i>C. tabularis</i> ⁷¹¹
880	chukrasin B	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = R_5 = OiBu$; $R_6 = iBu$; $R_7 = CH_3$	<i>C. tabularis</i> ⁷¹¹

Table 24. Continued

no.	compounds	substitution groups and others	sources
881	chukrasin C	$R_1 = R_3 = H$; $R_2 = Ac$; $R_4 = OAc/OiBu$; $R_5 = OiBu$; $R_6 = Ac/iBu$; $R_7 = CH_3$	<i>C. tabularis</i> ⁷¹¹
882	chukrasin D	$R_1 = R_2 = Ac$; $R_3 = H$; $R_4 = OAc/OiBu$; $R_5 = OiBu$; $R_6 = Ac/iBu$; $R_7 = CH_3$	<i>C. tabularis</i> ⁷¹¹
883	chukrasin E	$R_1 = R_2 = Ac$; $R_3 = H$; $R_4 = R_5 = OiBu$; $R_6 = iBu$; $R_7 = CH_3$	<i>C. tabularis</i> ⁷¹¹
884	tabularisin O		<i>C. tabularis</i> ⁷⁰⁷
885	leandranin A	$R_1 = H$; $R_2 = OAc$; $R_3 = O$; $R_4 = Ac$	<i>Neobegonia leandreana</i> ⁷⁰⁴
886	leandranin B	$R_1 = R_4 = Ac$; $R_2 = OAc$; $R_3 = O$	<i>N. leandreana</i> ⁷⁰⁴
887	kotschyin B	$R_1 = Ac$; $R_2 = H$; $R_3 = OAc$; $R_4 = iBu$	<i>Pseudocedrela kotschyii</i> ⁴⁴³
888	kotschyin C	$R_1 = Ac$; $R_2 = OAc$; $R_3 = O$; $R_4 = iBu$	<i>P. kotschyii</i> ⁴⁴³
889	swietenialide D	$R_1 = H$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = OH$; $R_4 = propanoyl$	<i>Swietenia mahagoni</i> ; ⁶⁶⁴ <i>S. macrophylla</i> ⁴⁵⁶
890	2-acetoxyswietenialide D	$R_1 = Ac$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = OH$; $R_4 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
891	2,11-diacetoxyswietenialide D	$R_1 = Ac$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = OAc$; $R_4 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
892	11-deoxyswietenialide D	$R_1 = R_3 = H$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_4 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
893	swietenitin G	$R_1 = R_4 = Ac$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = OH$	<i>S. macrophylla</i> ⁴⁵⁶
894	swietenitin H	$R_1 = Ac$; $R_2 = Tig$; $R_3 = OAc$; $R_4 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
895	swietenialide E		<i>S. mahagoni</i> ⁶⁶⁴
896	kotschyin A	$R_1 = R_2 = Ac$; $R_3 = iBu$	<i>Pseudocedrela kotschyii</i> ⁴⁴³
897	swietenitin A	$R_1 = R_3 = Ac$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl	<i>S. macrophylla</i> ⁴⁵⁶
898	swietenitin B	$R_1 = R_3 = Ac$; $R_2 = 2'/\alpha,3'/\alpha$ -epoxytigloyl	<i>S. macrophylla</i> ⁴⁵⁶
899	swietenitin C	$R_1 = Ac$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
900	swietenitin D	$R_1 = H$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
901	swietenitin E	$R_1 = Ac$; $R_2 = Tig$; $R_3 = propanoyl$	<i>S. macrophylla</i> ⁴⁵⁶
902	swietenitin F	$R_1 = H$; $R_2 = Tig$; $R_3 = iBu$	<i>S. macrophylla</i> ⁴⁵⁶
903	pseudrelone B		<i>Pseudocedrela kotschyii</i> ⁶⁹⁴
904	chukvelutilide A	$R_1 = R_2 = H$	<i>Chukrasia tabularis</i> ⁶⁹⁶
905	chukvelutilide B	$R_1 = Ac$; $R_2 = H$	<i>C. tabularis</i> ⁶⁹⁶
906	chukvelutilide C	$R_1 = H$; $R_2 = CH_3$	<i>C. tabularis</i> ⁶⁹⁶
907	chukvelutilide D	$R_1 = Ac$; $R_2 = CH_3$	<i>C. tabularis</i> ⁶⁹⁶
908	chukvelutilide E	$R_1 = R_2 = Ac$; $R_3 = H$	<i>C. tabularis</i> ⁶⁹⁶
909	chukvelutilide F	$R_1 = H$; $R_2 = iBu$; $R_3 = CH_3$	<i>C. tabularis</i> ⁶⁹⁶
910	chuktabrin B		<i>C. tabularis</i> ⁶⁹⁷
911	tabularisin A	$R_1 = OAc$; $R_2 = Ac$	<i>C. tabularis</i> ^{707,712,713}
912	tabularisin B	$R_1 = OAc$; $R_2 = H$	<i>C. tabularis</i> ^{707,712,713}
913	tabularisin E	$R_1 = H$; $R_2 = Ac$	<i>C. tabularis</i> ^{707,712}
914	tabularisin F	$R_1 = R_2 = H$	<i>C. tabularis</i> ^{707,712}
915	tabularisin J	$R_1 = OH$; $R_2 = Ac$	<i>C. tabularis</i> ⁷⁰⁷
916	tabularisin K	$R_1 = OH$; $R_2 = H$	<i>C. tabularis</i> ⁷⁰⁷
917	candollein	$R_1 = H$; $R_2 = iBu$	<i>Entandrophragma candollei</i> ; ⁵³⁰ <i>E. cylindricum</i> ⁷¹⁴
918	β -dihydroentandrophragmin	$R_1 = OH$; $R_2 = iBu$	<i>E. cylindricum</i> ⁷¹⁴
919	entandrophragmin	$R = iBu$	<i>E. cylindricum</i> ; ^{168,423,530,714} <i>E. bussei</i> ; ^{424,530} <i>E. spicatum</i> ; ^{530,710} <i>E. caudatum</i> ⁵³⁰
920	utilin	$R = Ac$	<i>E. utile</i> ^{168,423,530}
921	swietenialide A	$R_1 = H$; $R_2 = Tig$; $R_3 = CH_3$	<i>Swietenia mahagoni</i> ⁶⁶⁴
922	swietenialide B	$R_1 = H$; $R_2 = Tig$; $R_3 = CH_2CH_3$	<i>S. mahagoni</i> ⁶⁶⁴
923	swietenialide C	$R_1 = H$; $R_2 = 2'/\beta,3'/\beta$ -epoxytigloyl; $R_3 = CH_3$	<i>S. mahagoni</i> ⁶⁶⁴
924	swietenitin I	$R_1 = H$; $R_2 = 2'/\beta, 3'/\beta$ -epoxytigloyl; $R_3 = CH_2CH_3$	<i>S. macrophylla</i> ⁴⁵⁶

Table 24. Continued

no.	compounds	substitution groups and others	sources
925	swietenitin J	R ₁ = Ac; R ₂ = 2'β, 3'β-epoxytigloyl; R ₃ = CH ₂ CH ₃	<i>S. macrophylla</i> ⁴⁵⁶
926	swietenitin K	R ₁ = Ac; R ₂ = Tig; R ₃ = CH ₂ CH ₃	<i>S. macrophylla</i> ⁴⁵⁶
927	procerin	R ₁ = propanoyl; R ₂ = H; R ₃ = OAc; R ₄ = Ac	<i>Carapa procera</i> ^{580,715}
928	swietenitin L	R ₁ = 2'β, 3'β-epoxytigloyl; R ₂ = OH; R ₃ = H; R ₄ = proanoyl	<i>Swietenia macrophylla</i> ⁴⁵⁶
929	swietenitin M	R ₁ = 2'β, 3'β-epoxytigloyl; R ₂ = OAc; R ₃ = H; R ₄ = proanoyl	<i>S. macrophylla</i> ⁴⁵⁶
930	febrinolide		<i>Soymida febrifuga</i> ⁷⁰⁵
931	swietephragmin A	R ₁ = Ac; R ₂ = Tig; R ₃ = R ₄ = H; R ₅ = CH(CH ₃) ₂	<i>Swietenia mahagoni</i> ⁴⁵⁷
932	swietephragmin B	R ₁ = Ac; R ₂ = Tig; R ₃ = R ₄ = H; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. mahagoni</i> ⁴⁵⁷
933	swietephragmin C	R ₁ = R ₃ = R ₄ = H; R ₂ = Tig; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. mahagoni</i> ⁴⁵⁷
934	12α-acetoxyswietephragmin C	R ₁ = R ₃ = H; R ₂ = Tig; R ₄ = OAc; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁶
935	3β-O-distigloyl-3β-O-benzoyl-12α-acetoxyswietephragmin C	R ₁ = R ₃ = H; R ₂ = Bz; R ₄ = OAc; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁶
936	swietephragmin D	R ₁ = R ₃ = R ₄ = H; R ₂ = Tig; R ₅ = CH(CH ₃) ₂	<i>S. mahagoni</i> ⁴⁵⁷
937	12α-acetoxyswietephragmin D	R ₁ = R ₃ = H; R ₂ = Tig; R ₄ = OAc; R ₅ = CH(CH ₃) ₂	<i>S. macrophylla</i> ⁷¹⁶
938	3β-O-distigloyl-3β-O-benzoyl-12α-acetoxyswietephragmin D	R ₁ = R ₃ = H; R ₂ = Bz; R ₄ = OAc; R ₅ = CH(CH ₃) ₂	<i>S. macrophylla</i> ⁷¹⁶
939	swietephragmin E	R ₁ = R ₄ = H; R ₂ = Tig; R ₃ = OH; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. mahagoni</i> ⁴⁵⁷
940	6-O-acetylswietephragmin E	R ₁ = R ₄ = H; R ₂ = Tig; R ₃ = OAc; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁶
941	3β-O-distigloyl-3β-O-benzoyl-6-O-acetylswietephragmin E	R ₁ = R ₄ = H; R ₂ = Bz; R ₃ = OAc; R ₅ = CH(CH ₃)CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁶
942	6-O-acetyl-3'-demethylswietephragmin E	R ₁ = R ₄ = H; R ₂ = Tig; R ₃ = OAc; R ₅ = CH(CH ₃) ₂	<i>S. macrophylla</i> ⁶⁵³
943	swietephragmin F	R ₁ = R ₃ = R ₄ = H; R ₂ = Tig; R ₅ = CH ₂ CH ₃	<i>S. mahagoni</i> ⁴⁵⁷
944	swietephragmin G	R ₁ = R ₃ = R ₄ = H; R ₂ = Tig; R ₅ = CH ₃	<i>S. mahagoni</i> ⁴⁵⁷
945	swietephragmin H	R ₁ = Ac; R ₂ = Tig; R ₃ = R ₄ = H; R ₅ = CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁷
946	swietephragmin I	R ₁ = Ac; R ₂ = Tig; R ₃ = R ₄ = H; R ₅ = CH ₃	<i>S. macrophylla</i> ⁷¹⁷
947	swietephragmin J	R ₁ = Ac; R ₂ = Tig; R ₃ = H; R ₄ = OH; R ₅ = CH ₂ CH ₃	<i>S. macrophylla</i> ⁷¹⁷
948	xyloccensin O	R ₁ = H; R ₂ = OAc	<i>Xylocarpus granatum</i> ^{448,659,699,718}
949	xyloccensin P	R ₁ = R ₂ = OAc	<i>X. granatum</i> ^{448,633,639,659,699,718}
950	xyloccensin Q (xyloccensin R)	R ₁ = OH; R ₂ = OAc	<i>X. granatum</i> ^{639,659,700,701,718}
951	xyloccensin R (xyloccensin Q)	R ₁ = R ₂ = OH	<i>X. granatum</i> ^{659,700,701}
952	xyloccensin S	R ₁ = OAc; R ₂ = OH	<i>X. granatum</i> ^{659,700,701}
953	xyloccensin T	R ₁ = H; R ₂ = OH	<i>X. granatum</i> ^{659,700}
954	xyloccensin U	R ₁ = OH; R ₂ = H	<i>X. granatum</i> ^{659,700}
955	xyloccensin V (xyloccensin T)	R ₁ = OAc; R ₂ = H	<i>X. granatum</i> ^{659,700,701}
956	tabularisin C	R ₁ = OAc; R ₂ = H; R ₃ = R ₄ = Ac	<i>Chukrasia tabularis</i> ^{707,712,713}
957	tabularisin D	R ₁ = R ₂ = R ₄ = H; R ₃ = Ac	<i>C. tabularis</i> ⁷¹³
958	tabularisin G	R ₁ = R ₂ = H; R ₃ = R ₄ = Ac	<i>C. tabularis</i> ^{707,712}
959	tabularisin H	R ₁ = OAc; R ₂ = H; R ₃ = Ac; R ₄ = iBu	<i>C. tabularis</i> ^{707,712}
960	tabularisin I	R ₁ = OAc; R ₂ = R ₃ = H; R ₄ = iBu	<i>C. tabularis</i> ^{707,712}
961	tabularisin L	R ₁ = OAc; R ₂ = R ₃ = H; R ₄ = Ac	<i>C. tabularis</i> ⁷⁰⁷
962	tabularisin M	R ₁ = OAc; R ₂ = R ₄ = Ac; R ₃ = H	<i>C. tabularis</i> ⁷⁰⁷

of an intramolecular cyclopropanation of a diazo ketone and subsequent selective cleavage of a cyclopropyl ketone, a stereoselective

synthesis of a model compound for azadiradione (**12**) was accomplished starting from α-cyclocitral in 12 steps with 15% overall

yield.⁸¹⁸ Early in 1989, Corey reported the synthesis of **12** from *trans,trans*-farnesol stereoselectively.⁸¹⁹ Sastry et al. prepared a series of nimbolide (**345**) derivatives modified on the lactone ring under catalyst-free conditions, and pointed out that the position

and nature of the substituent seemed to be crucial for the cytotoxic activity.⁸²⁰ The brief and stereoselective synthesis of havanensin-class limonoid models was based on a radical domino reaction converting an epoxyketone to a bicyclic hydroxyketone, and was

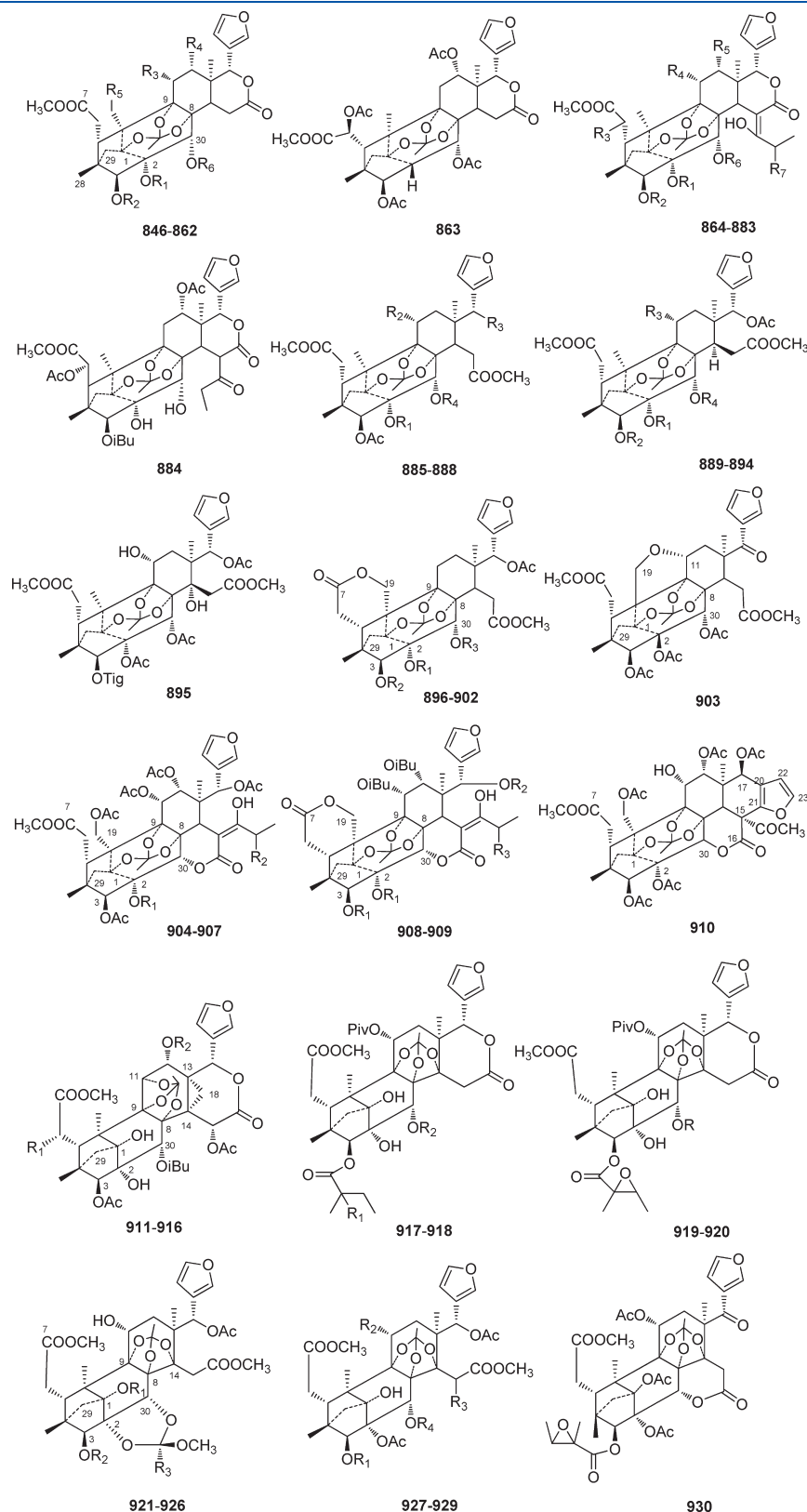


Figure 26. Continued

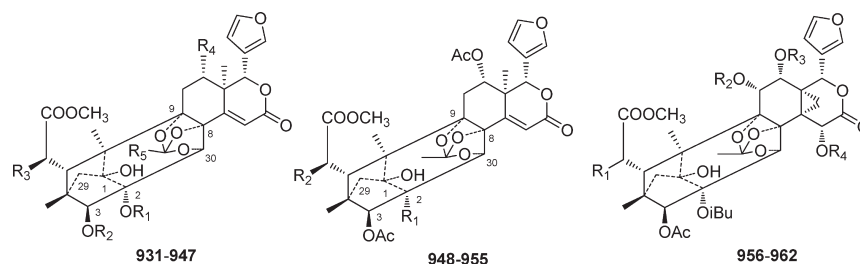


Figure 26. Structures of phragmalin-*ortho* ester limonoids 846–962.

achieved in six steps overall from simple cyclohexenones (Scheme 4).⁸²¹

A possible key intermediate in the biosynthesis of the ring D-*seco* limonoids was synthesized by the conversion of the side-chain of turraeanthin, a protolimonoid in *Turraeanthus africanus*, into a β -substituted furan in two steps with considerable yield.^{822,823} The tactics of the synthesis of fraxinellone (1142) included reaction of 6-formyl-2,6-dimethyl-cyclohex-2-enecarboxylates with furyllithium followed by double-bond isomerization with base,^{824,825} and conversion from fraxinellonone (1141) in short steps.⁸²⁶ After formation of the five-membered lactone, an aldol reaction and olefin metathesis established the bicyclic ring system, in which the catalytic diastereoselective Oshima–Utimoto reaction was employed as key step (Scheme 5).⁸²⁷ The short and stereo-controlled simple synthetic approach to the limonoids system was presented in 1987 by Corey et al., which introduced a high susceptibility for α -oxygenated, α -stannylated allylic systems to undergo free radical attack at the γ -carbon.⁸²⁸

Chemical transformation was considered to be an efficient method in structure elucidation and revision. A direct relationship between the melianes and meliacins (limonoids) was established through opening the 7 α ,8 α -epoxide ring of a melianone derivative.⁸²⁹ Swietenine (677) was converted into diacetyswietenolide (647), two compounds which differed mainly in the position of the double bond, in seven steps via 14 α -hydroxyswietenine and the $\Delta^{8,30}$, $\Delta^{14,15}$ diene intermediates.⁸³⁰ Khayanthone (111) was converted into khivorin (434) by oxidation with alkaline hydrogen peroxide followed by reacylation.⁸³¹ The preparations of methyl angolensate (568) and andirobin (556) from 7-deacetoxy-7-oxokhivorin (441)⁵²⁹ substantiated the suggestion that the characteristic bicycle[3.3.1]nonane ring system of the swietenine group was formed from the normal tetracyclic triterpene nucleus by oxidative cleavage of ring B followed by intramolecular Michael addition of a C-2 carbanion to the diene lactone system.⁶⁰⁹ Mexicanolide (626) was prepared from 7-deacetoxy-7-oxokhivorin (441) via a diene-lactone intermediate, which subsequently underwent intramolecular Michael addition by alkaline hydrolysis.^{832–834} E.P.1 (584) has been partially synthesized from gedunin (416), by a synthesis in which the key stage involved the Baeyer–Villiger oxidation of the 7-oxo group to a lactone.⁸³⁵ 416 was transformed along an unambiguous route into 6 β -hydroxygedunin (420) and the chemical and spectroscopy properties of the acetate of this product were different from the natural 6 α -acetoxygedunin (418).⁸³⁶ An investigation was made of the oxidation of 626 and related compounds with a view to the partial preparation of the 1,8-hemiacetal bridge characteristic of the limonoids such as xylocensin A (756) which originated from *Xylocarpus molccensis*.⁸³⁷

Besides chemical conversion, structural modification using biocatalysts was also documented. *Nocardia* sp. quantitatively converted salannin (332) and 3-deacetylsalannin (333) into 3-deacetoxy-1-de[(E)-2-methylbut-2-en-1-yl]salannin-1-en-3-one, a potentially bioactive compound with an α,β -unsaturated ketone moiety in ring A.⁸³⁸

5. BIOLOGICAL ACTIVITIES OF MELIACEOUS LIMONIDS

Meliaceous limonoids have been gaining global acceptance in agricultural applications and in contemporary medicine for their myriad but discrete properties. The need to protect our food supply from phytophagous insect attack using ecologically acceptable methods has led to a growing interest in behavior modifying chemicals from natural sources. For example, considering azadirachtin (292), we see that its potent activity against a broad range of insect species combined with its remarkable nontoxicity toward mammalian organism made 292 an attractive candidate as a natural pesticide.⁸³⁹ Miscellaneous activities of meliaceous limonoids have been investigated and some wonderful general reviews,^{840–842} and specific reviews on insect growth regulating activity,⁸⁴³ insecticidal activity,^{34,844} and the cytotoxic activity against the P388 cell line⁸⁴⁵ have been presented in the past decades. In addition, the biological activities of limonoids from *Melia azedarach*,^{37,44–47} *M. toosendan*,^{47,85} and *Azadirachta indica*,^{3,29,35–37,39,41–43,846} including especially the activities^{19,26–28,30,847} and commercial application of 292,⁸⁴⁸ have been reviewed. Furthermore, the modes and toxicity characteristics of the biological action of 292 were presented.^{32,33} For example, Mordue et al. proved that the mode of 292 involved (i) effects on deterrent and other chemoreceptors resulting in antifeedancy (ii) effects on ecdysteroid and juvenile hormone titers through a blockage of morphogenetic peptide hormone release, and (iii) direct effects on most other tissues studied resulting in an overall loss of fitness of the insect.²⁵ The biological activity of ring D and rings B,D-*seco* limonoids of Meliaceae,⁵⁰ and of gedunin (416) have also been summarized recently.⁴⁹ Furthermore, the activities of natural limonoids from plants have been presented including the meliaceous limonoids as one of their discussion topics.^{10,16–18}

In addition, the toxicity evaluation of meliaceous limonoids has been reported occasionally. Among the six limonoids from *Melia azedarach*, azedarachin B (160) showed remarkable BST (brine shrimp lethality test) activity with an LC₅₀ value of 0.0098 μ M.²¹⁸ 1-Methacrylyl-3-acetyl-11-methoxymeliacarpinin (326) exhibited significant lethal activity with an IC₅₀ value of 19 μ g/mL in the BST test.³⁴⁶ The highest dose of azadirachtin (292), 1500 mg/kg, was well tolerated by rats of both sexes thus could be used as a basal dose for the determination of the

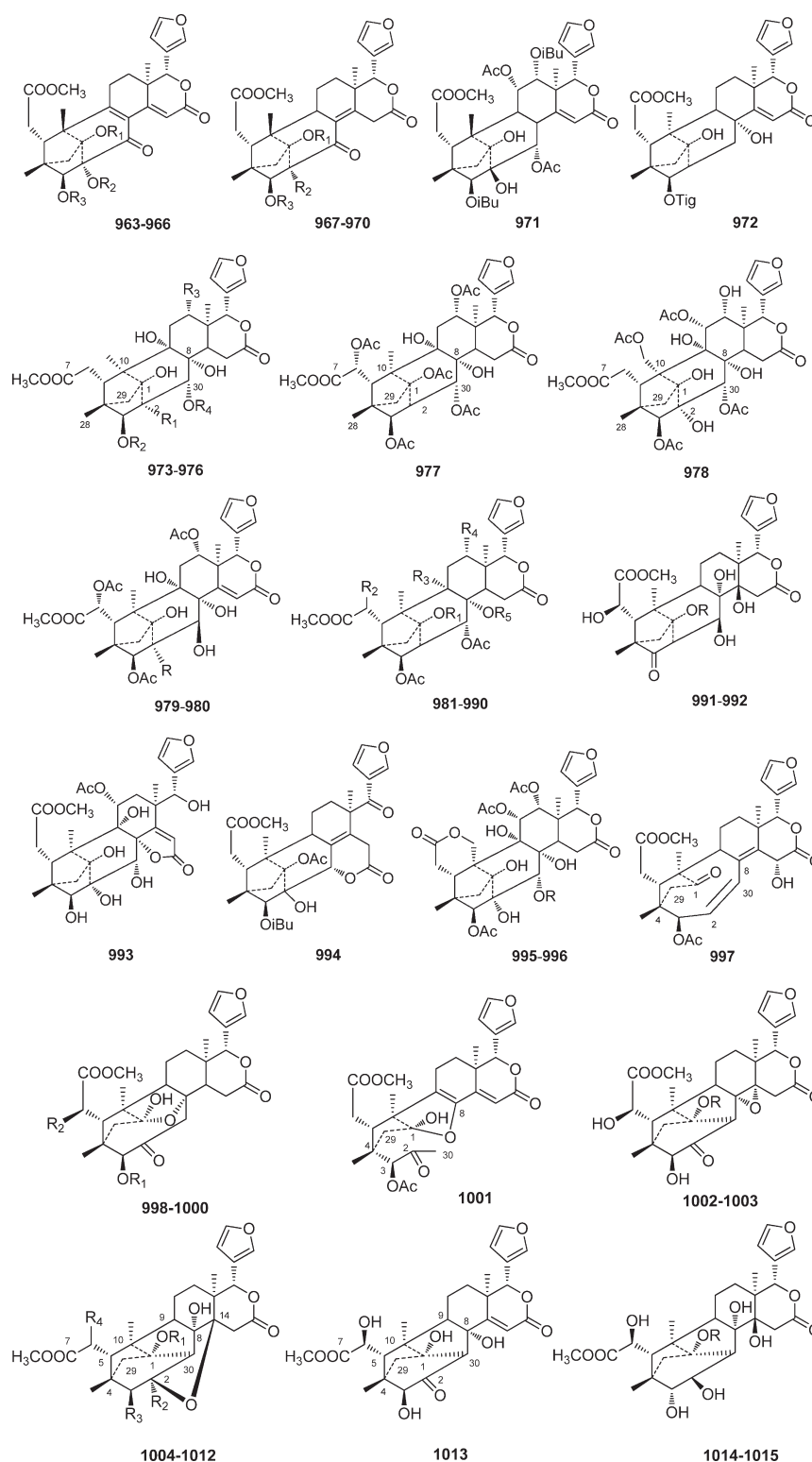


Figure 27. Structures of polyoxyphragmalin limonoids **963**–**1015**.

NOEL (no-observed-effect level) of **292** to calculate its safety margin.⁸⁴⁹ Nimbolide (**345**) was proved to be toxic to mice only when given i.p. and i.v., and less toxic to rats and hamsters, and it was supposed that when given i.v., the possible cause of death induced by it was a sudden hypotensive shock.⁸⁵⁰ Azedaralide (**1138**), fraxinellone (**1141**) and 12 α -acetoxyfraxinellone (**1147**) showed

ichthyotoxic activity at a concentration of 50 ppm, while fraxinellone (**1142**) required only 10 ppm.²³⁰

5.1. Biological Activities in Agricultural Use

5.1.1. Insects Antifeeding Activity. Insect antifeedant activity, the most potent activity of limonoids, has been extensively

Table 25. Structures and Sources of Polyoxyphragmalin Limonoids 963–1015

no.	compounds	substitution groups and others	sources
963	moluccensin H	R ₁ = R ₂ = H; R ₃ = Ac	<i>Xylocarpus moluccensis</i> ⁷²³
964	moluccensin H	R ₁ = Piv; R ₂ = H; R ₃ = iBu	<i>X. moluccensis</i> ⁵⁶⁸
965	moluccensin I	R ₁ = iBu; R ₂ = H; R ₃ = Piv	<i>X. moluccensis</i> ⁵⁶⁸
966	moluccensin J	R ₁ = Piv; R ₂ = iBu; R ₃ = H	<i>X. moluccensis</i> ⁵⁶⁸
967	moluccensin I	R ₁ = H; R ₂ = OCH ₃ ; R ₃ = Ac	<i>X. moluccensis</i> ⁷²³
968	moluccensin J	R ₁ = R ₂ = H; R ₃ = Ac	<i>X. moluccensis</i> ⁷²³
969	moluccensin K	R ₁ = H; R ₂ = Piv; R ₃ = iBu	<i>X. moluccensis</i> ⁵⁶⁸
970	moluccensin L	R ₁ = R ₃ = Piv; R ₂ = H	<i>X. moluccensis</i> ⁵⁶⁸
971	tabularin		<i>Chukrasia tabularis</i> ⁷²⁴
972	xylogranatin E ₂		<i>Xylocarpus granatum</i> ⁶⁶⁹
973	tabulalin	R ₁ = R ₃ = OH; R ₂ = Ac; R ₄ = H; $\Delta^{14,15}$	<i>Chukrasia tabularis</i> ⁷⁰⁶
974	atomasin A	R ₁ = OAc; R ₂ = Ac; R ₃ = H; R ₄ = iBu	<i>Entandrophragma candollei</i> ^{719,725}
975	atomasin B	R ₁ = OAc; R ₂ = Ac; R ₃ = H; R ₄ = propanoyl	<i>E. candollei</i> ^{719,725}
976	swietemacrophine	R ₁ = OH; R ₂ = R ₄ = Tig; R ₃ = OAc	<i>Swietenia macrophylla</i> ⁷¹⁷
977	xylocarpin K		<i>Xylocarpus granatum</i> ⁶⁷⁷
978	tabulalide E		<i>Chukrasia tabularis</i> ⁷⁰⁶
979	granatumin F	R = H	<i>Xylocarpus granatum</i> ⁴²⁶
980	granatumin G	R = OH	<i>X. granatum</i> ⁴²⁶
981	xylocarpin A (granaxylocarpin E)	R ₁ = Ac; R ₂ = OAc; R ₃ = R ₄ = R ₅ = H	<i>X. granatum</i> ^{632,633}
982	xylocarpin B	R ₁ = Ac; R ₂ = R ₃ = R ₄ = R ₅ = H	<i>X. granatum</i> ⁶³³
983	xylocarpin C	R ₁ = R ₂ = R ₃ = R ₅ = H; R ₄ = OAc	<i>X. granatum</i> ⁶³³
984	xylocarpin D (granaxylocarpin D)	R ₁ = Ac; R ₂ = OH; R ₃ = R ₅ = H; R ₄ = OAc	<i>X. granatum</i> ^{632,633}
985	xylocarpin E	R ₁ = Ac; R ₂ = OAc; R ₃ = R ₅ = H; R ₄ = OH	<i>X. granatum</i> ⁶³³

investigated with respect to many kinds of insects. For example, a number of evaluations of the well-known azadirachtin (**292**) were carried out, and some nice reviews described its antifeedancy against miscellaneous insects in detail.^{25–27} In addition, some antifeeding data of **292** are summarized in Table 32. With as little as 0.2 ppm of **292** incorporated into the diet of *Spodoptera frugiperda*, it showed antifeedant effects on first instar larvae and inhibited the molting of the nymphs to the adult stage when it was applied topically with 0.01 μg to newly molted fifth instar nymphs of *Oncopeltus fasciatus*.⁸⁵¹ **292** also elicited dose-dependent neural and antifeedant behavioral responses in *S. littoralis*, *Schistocerca gregaria*, and *Locusta migratoria* when it was used to investigate the mechanism of its effects on the feeding behavior of these three species.²⁶ The pathological effects of **292** on *S. gregaria* and *L. migratoria* were closely linked to a loss of feeding, with injections of 5, 10, and 15 $\mu\text{g/g}$ causing an increasingly rapid onset of the effects associated with an increasingly reduced food intake.⁸⁵² In greenhouse and seedbed tests, the feeding deterrence provided by **292** against the striped *Acalymma vittatum* was not as great as by carbaryl.⁸⁵³ Exposure of **292** to sunlight caused a rapid decrease in antifeedant potency against newly emerged first-instar (0.046 mg) of *Spodoptera frugiperda*, and acetone solutions of **292** exposed for seven days gave more than a 50% reduction in activity.⁸⁵⁴ Interestingly, *Crocidolomia binotalis* was capable of detoxifying the antifeedancy of **292** to a limited extent at the cost of poor weight gain and disruption in larval and pupal development.⁸⁵⁵ Feeding behavior of four slug species of *Deroceras reticulatum*, *Arion distinctus*, *Agriolimax caruanae*, and *Maximus* sp., as detected by the amount of leaf eaten compared to the controls, was not affected by the presence of **292** at those concentrations (<500 ppm) which deterred from feeding in *Rhopalosiphum padi* and *Sitobion avenae*.⁸⁵⁶

Using *Pericallia ricini* in dual choice bioassay, nymanina (**478**) was an effective antifeedant at concentrations of 1–10 $\mu\text{g}/\text{cm}^2$ leaf, which is half as active as **292**.⁴⁹⁷ Salannin (**332**) was less active than **292** in feeding suppression against the larvae of *Spodoptera littoralis* and *Earias insulana*.⁸⁵⁷ **292** was more potent as an antifeedant and growth inhibitor than any of five limonoids 17 β -hydroxyazadiradione (**18**), salannin (**332**), 6-deacetylnimbin (**392**), gedunin (**416**), and 7-deacetylgedunin (**421**) against *Helicoverpa armigera*,⁸⁵⁸ and produced almost 100% larval mortality at 1 ppm concentration.⁸⁵⁹ At 4 $\mu\text{g}/\text{cm}^2$ and 1 $\mu\text{g}/\text{cm}^2$, the isomeric mixture of meliartenin (**164**) was active as **292** in strongly inhibiting the larval feeding of *Epilachna paenulata* and *S. eridania*.²⁰⁸ 1-Tigloyl-3-acetylazadirachtol (**297**) and marrangin (**1067**) were reported as being more potent than **292** in the 24 h dual choice antifeedant test against *E. varivestis* (Table 33).³²² Similarly, the crop protection against *Schistocerca gregaria* afforded by **292** resulted from both antifeedancy and toxicity, whereas 3-tigloylazadirachtol (**296**) was more effective by direct toxicity after significant ingestion.⁸⁶⁰ *Cnaphalocrocis medinalis* larvae which were chronically exposed to any of 17 β -hydroxyazadiradione (**18**), **292**, salannin (**332**), deacetylnimbin (**392**), gedunin (**416**), or 7-deacetylgedunin (**421**), showed a reduction in weight of 59–89% and exhibited a significant reduction in activities of acid phosphatases (ACP), alkaline phosphatases (ALP), and adenosine triphosphatases (ATPase). These results indicate that neem limonoids affected gut enzyme activities.^{861,862}

The five limonoids 17 β -hydroxyazadiradione (**18**), salannin (**332**), 6-deacetylnimbin (**392**), gedunin (**416**), and 7-deacetylgedunin (**421**) affected feeding, development and reproduction in *Helicoverpa armigera*, and the reduced nutritional efficiency and fecundity were recorded as the consequence of postingested

Table 26. Structures and Sources of 8,11-Linkage Limonoids (Trijugin-Class) 1016–1043

no.	compounds	substitution groups and others	sources
1016	trijugin A	$R_1 = H; R_2 = O; R_3 = \beta\text{-OH}; R_4 = \text{OAc}$	<i>Heynea trijuga</i> ⁷²⁹
1017	trijugin G	$R_1 = O; R_2 = \text{OPiv}; R_3 = \beta\text{-OH}; R_4 = H$	<i>Trichilia connaroides</i> ⁵⁷³
1018	voamatin A	$R_1 = \text{OH}; R_2 = \text{OCin}; R_3 = \alpha\text{-OH}; R_4 = H$	<i>Astrotrichilia voamatata</i> ⁷³³
1019	voamatin B	$R_1 = \text{OH}; R_2 = \text{OCin}; R_3 = \beta\text{-OH}; R_4 = H$	<i>A. voamatata</i> ⁷³³
1020	trijugin B	$R = H$	<i>Heynea trijuga</i> ⁷²⁹
1021	trijugin B acetate	$R = \text{Ac}$	<i>H. trijuga</i> ⁷³⁴
1022	capensolactone 3	$R_1/R_2 = \text{ONic/OiBu}; R_3 = H; R_4 = R_5 = \text{OAc}$	<i>Ekebergia capensis</i> ⁷³⁰
1023	cipatrijugin A	$R_1 = R_3 = R_4 = R_5 = H; R_2 = \text{OAc}$	<i>Cipadessa cinerascens</i> ^{544,735}
1024	cipatrijugin B	$R_1 = R_4 = R_5 = H; R_2 = \text{OAc}; R_3 = \text{OH}$	<i>C. cinerascens</i> ^{563,735}
1025	cipatrijugin C	$R_1 = R_4 = R_5 = H; R_2 = R_3 = \text{OAc}$	<i>C. cinerascens</i> ^{563,735}
1026	cipatrijugin D	$R_1 = R_3 = R_5 = H; R_2 = R_4 = \text{OAc}$	<i>C. cinerascens</i> ^{563,735}
1027	sandrapin A	$R_1 = R_2 = R_5 = \text{OAc}; R_3 = H; R_4 = \text{OH}$	<i>Sandoricum koetjape</i> ^{736,737}
1028	sandrapin B	$R_1 = \text{OPiv}; R_2 = R_5 = \text{OAc}; R_3 = H; R_4 = \text{OH}$	<i>S. koetjape</i> ^{736,737}
1029	sandrapin C	$R_1 = \text{OiBu}; R_2 = R_5 = \text{OAc}; R_3 = H; R_4 = \text{OH}$	<i>S. koetjape</i> ^{736,737}
1030	sandrapin D	$R_1 = \text{OTig}; R_2 = R_5 = \text{OAc}; R_3 = H; R_4 = \text{OH}$	<i>S. koetjape</i> ^{737,738}
1031	sandrapin E	$R_1 = \text{methacrylate}; R_2 = R_5 = \text{OAc}; R_3 = H; R_4 = \text{OH}$	<i>S. koetjape</i> ^{737,738}
1032	E.P.4	$R_1 = R_4 = \text{OAc}; R_2 = \text{OAng}; R_3 = R_5 = H$	<i>Ekebergia pterophylla</i> ⁵⁶⁵
1033	capensolactone 1	$R_1 = \text{iBu}; R_2 = R_4 = H; R_3 = \text{OH}$	<i>E. capensis</i> ⁷³⁰
1034	capensolactone 2	$R_1/R_2 = \text{Nic/Piv}; R_3 = \text{OH}; R_4 = \text{Ac}$	<i>E. capensis</i> ⁷³⁰
1035	E.P.5	$R_1 = R_2 = R_4 = \text{Ac}; R_3 = H$	<i>E. pterophylla</i> ⁵⁶⁵
1036	trichilin A		<i>Trichilia connaroides</i> ⁷³¹
1037	trijugin H		<i>T. connaroides</i> ⁵⁷³
1038	cipadesin D	$R_1 = R_3 = H; R_2 = \text{OAc}$	<i>Cipadessa cinerascens</i> ^{54,544,564}
1039	cipadesin E	$R_1 = \text{OH}; R_2 = R_3 = H$	<i>C. cinerascens</i> ^{54,563}
1040	cineracipadesin F	$R_1 = \text{OAc}; R_2 = R_3 = H$	<i>C. cinerascens</i> ⁵⁶³
1041	cipadesin H	$R_1 = R_2 = R_3 = H$	<i>C. cinerascens</i> ⁵⁶⁴
1042	cipadesin I	$R_1 = H; R_2 = R_3 = \text{OAc}$	<i>C. cinerascens</i> ⁵⁶⁴
1043	trichilin B		<i>Trichilia connaroides</i> ⁷³¹

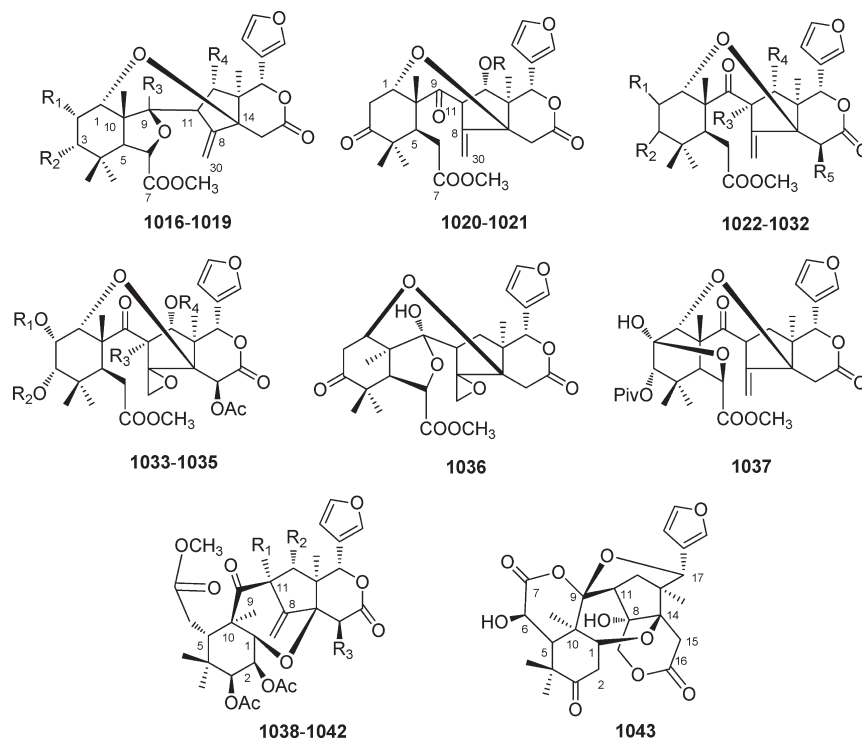


Figure 28. Structures of 8,11-linkage limonoids (trijugin-class) 1016–1043.

Table 27. Structures and Sources of 10,11-Linkage Limonoids (Cipadesin-Class) 1044–1053

no.	compounds	substitution groups and others	sources
1044	cipadesin C	R ₁ = OAc; R ₂ = H; R ₃ = OH	<i>Cipadessa cinerascens</i> ^{564,631}
1045	cipadesin E	R ₁ = R ₂ = H; R ₃ = OH	<i>C. cinerascens</i> ⁵³
1046	cipadonoid C	R ₁ = R ₂ = R ₃ = H	<i>C. cinerascens</i> ⁵⁴⁴
1047	cipadonoid D	R ₁ = R ₂ = H; R ₃ = OAc	<i>C. cinerascens</i> ⁵⁴⁴
1048	cipadonoid E	R ₁ = H; R ₂ = R ₃ = OAc	<i>C. cinerascens</i> ⁵⁴⁴
1049	cipadonoid F	R ₁ = H; R ₂ = OAc; R ₃ = α -CH ₃	<i>C. cinerascens</i> ⁵⁴⁴
1050	cipadonoid G	R ₁ = H; R ₂ = OAc; R ₃ = α -CH ₃ ; 11 α -OH	<i>C. cinerascens</i> ⁵⁴⁴
1051	cipadesin A	R ₁ = R ₂ = OAc; R ₃ = β -CH ₃	<i>C. cinerascens</i> ^{563,631,735}
1052	cipadesin B	R ₁ = OAc; R ₂ = H; R ₃ = β -CH ₃	<i>C. cinerascens</i> ⁶³¹ ; <i>C. fruticosa</i> ^{563,564,671}
1053	cipadesin G	R ₁ = R ₂ = H; R ₃ = β -CH ₃	<i>C. cinerascens</i> ⁵⁶⁴

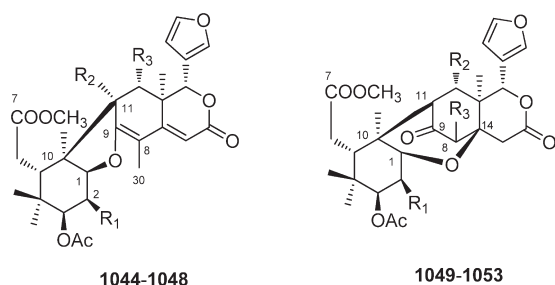


Figure 29. Structures of 10,11-linkage limonoids (cipadesin-class) 1044–1053.

toxic effects of these compounds.⁸⁶³ Both azecins 1 and 3 (572 and 101) were effective antifeedants when incorporated into the fourth-instar larvae of *Spodoptera litura* and third-instar larvae of *Henosepilachna vigintioctopunctata*, as was evidenced by the reduced growth rate, increased time of pupation, and even significant mortality.¹⁷³ Of the five limonoids 94–98 from *Trichilia pallida*, methyl 6,11 β -dihydroxy-12 α -(2-methylpropyloxy)-3,7-dioxo-14 β ,15 β -epoxy-1,5-meliacadien-29-oate (97) showed the greatest activity in tests against the larvae of *S. littoralis*, *S. exigua*, *Heliothis virescens*, and *Helicoverpa armigera* with feeding index (FI) values varying from 40 to 49.¹⁷¹ In the antifeeding percentage test against *S. littoralis*, khayalactol (774) showed the highest potential with 83.8% at 1000 μ g/mL, followed by 1-*O*-acetylkhayanolide A (1003) with 58.3% at 500 μ g/mL, khayanolide D (1006) with 55.8 at 200 μ g/mL and finally 1003 with 31.4% at 100 μ g/mL.⁵⁵⁰ The growth inhibitory activities after 7 days and antifeedant activities of 774, khayanolide A (1002), khayanolide B (1004), and 1-*O*-acetylkhayanolide B (1005) were evaluated against *S. littoralis*. Among these, 1004 was the most active antifeedant with an EC₅₀ value of 6.96 mg/kg for growth inhibitory activity and 2.19 mg/kg for antifeedancy.⁶⁷⁸ Xylogranatins F, G, and R (1156, 1157, and 843) exhibited marked antifeedant activity against the third-instar larvae of *Mythimna separata* at a concentration of 1 mg/mL. Among these, 1157 was the most potent with AFC₅₀ (concentration for 50% antifeedant activity) values of 0.31 and 0.30 mg/mL at exposure times of 24 and 48 h, respectively.⁶³⁸

Modes of action other than their useful antifeedant activity were also investigated for limonoids. Chuanliansu (167) stimulated a deterrent receptor cell located in the medial maxillary sensillum styloconicum, and inhibited responses of both the sugar and glucosinolate receptor cell which are localized in the

Table 28. Sources of Rearranged Limonoids with Other Linkage 1054–1062

no.	compounds	sources
1054	walsuronoid A	<i>Walsura robusta</i> ⁷³⁹
1055	4 α ,6 α -dihydroxy-A-homoazadirone	<i>Azadirachta indica</i> ⁷⁴²
1056	spirosendan	<i>Melia toosendan</i> ^{85,247,743}
1057	volkensinin	<i>M. volkensii</i> ⁷⁴⁴
1058	walsuronoid B	<i>Walsura robusta</i> ⁷³⁹
1059	walsuronoid C	<i>W. robusta</i> ⁷³⁹
1060	delevoyin C	<i>Entandrophragma delevoyi</i> ⁴²⁵
1061	cipadonoid A	<i>Cipadessa cinerascens</i> ^{740,741}
1062	cumindysoside B	<i>Dysoxylum cumingianum</i> ⁷⁴⁵

lateral sensillum styloconicum.^{864,865} In other experiments, when *Pieris brassicae* fed on its natural foodplant, the deterrent effect of 167 and salannin (332) were mediated solely via the medial deterrent receptor, whereas inhibitory effects on the sugar and glucosinolate receptors did not play a significant role.⁸⁶⁶ Investigation of the bioefficacy and mode of action of some salannin-class limonoids and their role in a multicomponent system against lepidopteran larvae led to the conclusion that nonazadirachtin limonoids having structural similarities and explicitly similar modes of action have no potentiating effect in any combination.³⁶⁶ Ortego et al. concluded that the effects of azadirone (1) and the mixture of 3,7-di-*O*-acetylhananensin (107) and 1,7-di-*O*-acetylhananensin (108) on digestive proteases and detoxication enzymes in the larval midgut of *Leptinotarsa decemlineata* larvae reflected their postulated mode of action.⁸⁶⁷ Salannin (332) and nimbinene (1099) showed no toxicity-mediated effects on *Spodoptera litura* larvae, and the antifeedant activity was a result of the effects on other chemoreceptors.⁸⁶⁸ Potentiation among nonazadirachtin limonoids having two explicitly different modes of action, such as feeding deterrence and physiological toxicity, might be playing a significant role in the potentiation effect.⁴⁴²

From studies in which the *Spodoptera* species insects were frequently used, the EC₅₀ (50% effective concentration), ED₅₀ (50% effective dosage), MAC (minimum antifeedant concentration), PC₅₀ (50% protective concentration), PC₉₅ (95% protective concentration), AR (antifeedant rate), FI₅₀ (50% feeding inhibition), and AI (antifeedant index, mean \pm SEM) values of antifeedant activity of meliaceous limonoids were summarized in detail (Tables 33 and 34). Unfortunately, some limonoids were declared to show antifeedant activity against

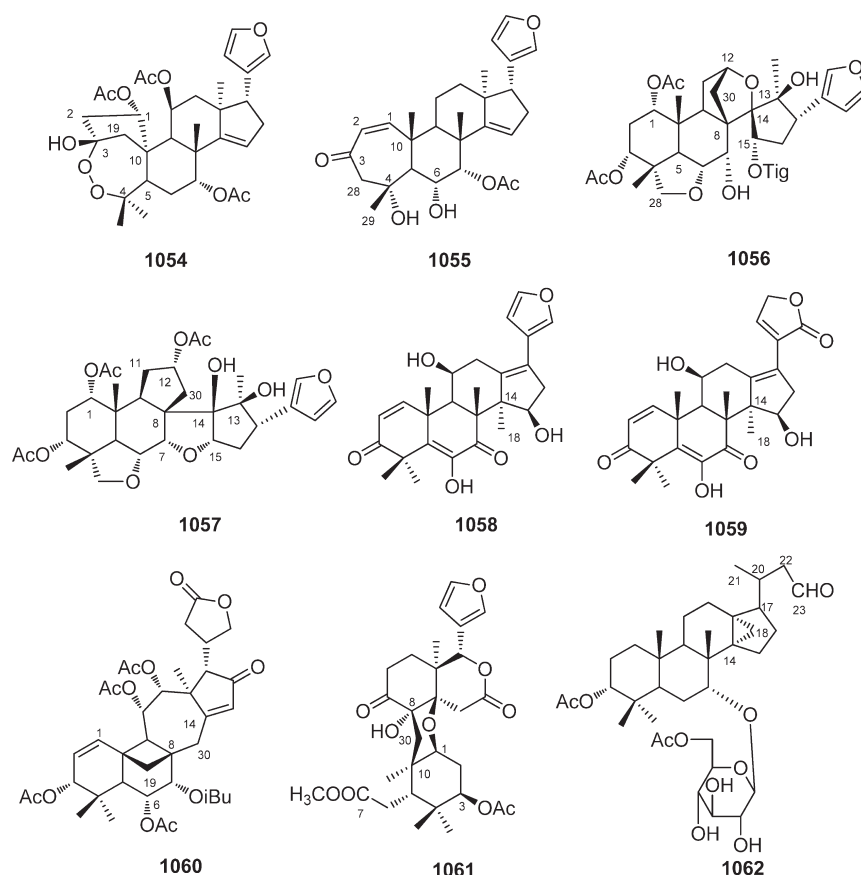


Figure 30. Structures of rearranged limonoids with other linkages 1054–1062.

different insects, but no data had been presented in the original paper. These limonoids were 7-acetyltrichilin A (**136**),²⁰⁰ 1 α ,3 α -diacetylvilasinin (**189**),²⁴⁵ toonacilin (**268**) and 6-acetoxytoonacilin (**269**),^{286,289} 21-(*R,S*)-hydroxytoonacilide (**279**) and 23-(*R,S*)-hydroxytoonacilide (**280**),²⁸⁸ salannin (**332**),⁸⁵³ 3-deacetylsalannin (**333**) and salannol (**336**),²⁴⁵ 2',3'-dehydrosalannol (**338**),³⁴⁹ munronins A–E (**498–500**, **1151**, **1116**),⁵⁰⁶ methyl 3 β -isobutyroxy-1-oxomeliac-8(30)-enate (**702**),⁶⁶⁶ salannolactam-(23) (**1154**), and salannolactam-(21) (**1155**).⁷⁶⁶ In addition, azadirachtol (**295**) was reported to exhibit higher antifeedant activity than azadirachtin (**292**), but supporting data was lacking for this claim.³²³ Negatively, nimbinin (**60**), 17-*epiazadiradione* (**77**), and nimbin (**391**) were inactive against *Reticulitermes speratus* and the PC₉₅ values were beyond the bioassay limits.¹⁰³

As for structure–activity relationship of the insect antifeedant activity, Govindachari et al. pointed out that the C-seco limonoids were the most effective compounds while the intact limonoids were the least effective.⁸⁶⁹ Similarly, antifeedant activity tests showed that azadirachtin-class C-seco limonoids were the most potent ones, followed by the 12 α -OH compounds of the trichilin-class and azedarachins containing a 14,15-epoxide combined with either a C-19/29 acetal bridge or a C-11/19 acetal bridge.^{85,209,341} Suresh et al. concluded that the most active among the fifty-six limonoids were the C-ring modified limonoids of the azadirachtin-class followed by the intact apo-euphol types having a 14,15-epoxide and either a C-19/28 lactol bridge or a cyclohexenone A ring.⁸⁷⁰ Another supporting example is provided by azedarachins and trichilins showing the most antifeedant activity against the larvae of *Spodoptera eridania* at a

concentration of 200–400 ppm, followed by nimbolidins at 500 ppm and trichilins at 1000 ppm.²³⁹

Ley et al. pointed out that the potent antifeedant activity of the derivatives of azadirachtin (**292**) with C-7 β -OH were significantly less active than its α -epimer.⁸⁷¹ Mordue et al. proposed that the C-7, C-11, C-22, and C-23 positions of the carbon ring were key positions for bioactivity where substitution significantly influences the potency of **292**.⁸⁷² Furthermore, it was possible to draw some general conclusions that hydrogenation of the C-22/23 enol ether double bond did not significantly diminish activity of either the azadirachtin or 11-deoxy series, and that both the bulky substituents at C-22 and increasingly larger groups at C-23 caused a considerable drop in antifeedancy.^{873,874} For example, both **292** and 22,23-dihydro-23 β -methoxyazadirachtin (**303**) were potent antifeedant against *S. littoralis* and *Heliothis virescens*, whereas the latter, which had greater steric bulk at C-23, had weaker activity.³⁰⁵ The nature of the substituents at C-1 and C-3 of the decalin ring of azadirachtins affected the antifeedancy of the compounds, as did the additional substituents to C-22/23.⁸⁷⁵ In addition, Yamasaki et al. suggested that the hydroxyl groups on **292** were essential for maximum activity and that the molecule must also have a lipophilic region.⁸⁷⁶ Methylation of the hydroxyl substituents on the azadirachtins molecule resulted in a decrease in antifeedant activity, as did the addition of bulky groups to the dihydrofuran ring.⁸⁷⁷ On the basis of the antifeedant potency of several limonoids from *Azadirachta indica*, it could be suggested that the furan ring, the α,β -unsaturated ketone, and the hydroxyl group each played an important role in determining the activity.¹⁰³

Table 29. Structures and Sources of Pentanortriterpenoids 1063–1114, Hexanortriterpenoids 1115–1118, Hepanortriterpenoids 1119–1126, Octanortriterpenoids 1127–1129, and Enneanortriterpenoids 1130–1131

no.	compounds	substitution groups and others	sources
1063	2-oxo-deacetyl salannin		<i>Azadirachta indica</i> ⁴¹¹
1064	voamatin C	R = palmityl	<i>Astrotrichilia voamatata</i> ⁷⁵⁴
1065	voamatin D	R = Cin	<i>A. voamatata</i> ⁷⁵⁴
1066	11 β -azadirachtin H	R ₁ = Tig; R ₂ = OH; R ₃ = H; R ₄ = COOCH ₃	<i>Azadirachta indica</i> ^{312,319,755} <i>A. excelsa</i> ³²⁴
1067	marrangin (azadirachtin L)	R ₁ = Tig; R ₂ = H; R ₃ = OAc; R ₄ = COOCH ₃	<i>A. excelsa</i> ^{322,324,746}
1068	11 α -hydroxy-12-norazadirachtin (11- <i>epi</i> -azadirachtin H, 11 α -azadirachtin H)	R ₁ = Tig; R ₂ = H; R ₃ = OH; R ₄ = COOCH ₃	<i>A. indica</i> ^{343,747,748,756} <i>A. excelsa</i> ³²⁴
1069	azadirachtin I	R ₁ = Tig; R ₂ = OH; R ₃ = H; R ₄ = CH ₃	<i>A. indica</i> ^{312,317,319}
1070	11- <i>epi</i> -azadirachtin I	R ₁ = Tig; R ₂ = H; R ₃ = OH; R ₄ = CH ₃	<i>A. indica</i> ⁷⁴⁹
1071	azadirachtin M	R ₁ = Tig; R ₂ = H; R ₃ = OH; R ₄ = CH ₂ OH	<i>A. indica</i> ³⁴³ <i>A. excelsa</i> ³²⁴
1072	azadirachtin P	R ₁ = <i>i</i> Val; R ₂ = H; R ₃ = OH; R ₄ = COOCH ₃	<i>A. excelsa</i> ³²⁴
1073	moluccensin M		<i>Xylocarpus moluccensis</i> ⁵⁶⁸
1074	chuktabularin A	R ₁ = R ₃ = Ac; R ₂ = H	<i>Chukrasia tabularis</i> ^{750,752}
1075	chuktabularin K	R ₁ = R ₃ = Ac; R ₂ = OAc	<i>C. tabularis</i> ⁷⁵²
1076	chuktabularin S	R ₁ = R ₂ = H; R ₃ = Ac	<i>C. tabularis</i> ⁷⁵²
1077	chuktabularin T	R ₁ = Ac; R ₂ = R ₃ = H	<i>C. tabularis</i> ⁷⁵²
1078	chuktabularin C	R ₁ = R ₃ = Ac; R ₂ = R ₄ = R ₅ = H	<i>C. tabularis</i> ^{750,752}
1079	chuktabularin L	R ₁ = R ₂ = R ₅ = H; R ₃ = Ac; R ₄ = OAc	<i>C. tabularis</i> ⁷⁵²
1080	chuktabularin M	R ₁ = R ₃ = Ac; R ₂ = R ₅ = H; R ₄ = OAc	<i>C. tabularis</i> ⁷⁵²
1081	chuktabularin N	R ₁ = Ac; R ₂ = R ₅ = H; R ₃ = propanoyl; R ₄ = OAc	<i>C. tabularis</i> ⁷⁵²
1082	chuktabularin O	R ₁ = Ac; R ₂ = R ₅ = H; R ₃ = <i>i</i> Bu; R ₄ = OAc	<i>C. tabularis</i> ⁷⁵²
1083	chuktabularin P	R ₁ = R ₃ = Ac; R ₂ = OH; R ₄ = R ₅ = H	<i>C. tabularis</i> ⁷⁵²
1084	chuktabularin Q	R ₁ = R ₃ = Ac; R ₂ = OAc; R ₄ = R ₅ = H	<i>C. tabularis</i> ⁷⁵²
1085	chuktabularin R	R ₁ = R ₂ = R ₄ = R ₅ = H; R ₃ = Ac	<i>C. tabularis</i> ⁷⁵²
1086	chukvelutin A	R ₁ = R ₄ = H; R ₂ = OAc; R ₃ = Ac; R ₅ = CH ₃	<i>C. tabularis</i> ⁷⁵¹
1087	chukvelutin B	R ₁ = R ₃ = Ac; R ₂ = OAc; R ₄ = H; R ₅ = CH ₃	<i>C. tabularis</i> ⁷⁵¹
1088	chukvelutin C	R ₁ = R ₂ = R ₃ = R ₄ = Ac; R ₅ = CH ₃	<i>C. tabularis</i> ⁷⁵¹
1089	chuktabularin D	R ₁ = R ₂ = R ₃ = R ₄ = Ac; R ₅ = H	<i>C. tabularis</i> ^{750,752}
1090	chuktabularin E	R ₁ = R ₅ = H; R ₂ = R ₃ = R ₄ = Ac	<i>C. tabularis</i> ⁷⁵²
1091	chuktabularin F	R ₁ = R ₂ = R ₃ = Ac; R ₄ = propanoyl; R ₅ = H	<i>C. tabularis</i> ⁷⁵²
1092	chuktabularin G	R ₁ = R ₂ = R ₃ = Ac; R ₄ = <i>i</i> Bu; R ₅ = H	<i>C. tabularis</i> ⁷⁵²
1093	chuktabularin H	R ₁ = R ₂ = R ₅ = H; R ₃ = R ₄ = Ac	<i>C. tabularis</i> ⁷⁵²
1094	chuktabularin I	R ₁ = R ₂ = Ac; R ₃ = R ₄ = R ₅ = H	<i>C. tabularis</i> ⁷⁵²
1095	chuktabularin J	R ₁ = R ₃ = R ₄ = R ₅ = H; R ₂ = Ac	<i>C. tabularis</i> ⁷⁵²
1096	chuktabularin B		<i>C. tabularis</i> ^{750,752}
1097	chuktabrin A		<i>C. tabularis</i> ⁶⁹⁷
1098	21,24,25,26,27-pentanor-15,22-oxo-7 α ,23-dihydroxy-apotirucalla(eupha)-1-en-3-one		<i>Trichilia estipulata</i> ⁷⁵⁷
1099	nimbinene	R = Ac	<i>Azadirachta indica</i> ⁷⁵⁸
1100	6-deacetylnimbinene	R = H	<i>A. indica</i> ⁷⁵⁸
1101	nimbandiol	R = H	<i>A. indica</i> ^{103,104,270,758}
1102	6-acetylnimbandiol	R = Ac	<i>A. indica</i> ^{316,758}
1103	5 α ,6 β ,8 α -trihydroxy-28-norisotoonafolin	R ₁ = O; R ₂ = H	<i>Toona ciliata</i> ^{161,290,291}
1104	5 α ,6 β ,8 α ,12 α -tetrahydroxy-28-norisotoonafolin	R ₁ = O; R ₂ = OH	<i>T. ciliata</i> ¹⁶¹
1105	toonaciliatin A	R ₁ = O; R ₂ = OH, $\Delta^{1,2}$	<i>T. ciliata</i> ²⁹⁰
1106	toonaciliatin F	R ₁ = R ₂ = OH	<i>T. ciliata</i> ²⁹⁰
1107	toonaciliatin G	R ₁ = OH; R ₂ = H	<i>T. ciliata</i> ²⁹⁰
1108	toonaciliatin H	R ₁ = Ac; R ₂ = OH	<i>T. ciliata</i> ²⁹¹
1109	toonaciliatin I	R ₁ = Ac; R ₂ = O	<i>T. ciliata</i> ²⁹¹
1110	toonaciliatin J	R ₁ = R ₂ = OH	<i>T. ciliata</i> ²⁹¹
1111	trijugin C	R ₁ = R ₂ = H	<i>Trichilia connaroides</i> ^{573,651,759}

Table 29. Continued

no.	compounds	substitution groups and others	sources
1112	trijugin D	$R_1 = \text{Ac}; R_2 = \text{H}$	<i>T. connaroides</i> ⁵⁷³
1113	trijugin E	$R_1 = \text{Ac}; R_2 = \text{OH}$	<i>T. connaroides</i> ⁵⁷³
1114	trijugin F		<i>T. connaroides</i> ⁵⁷³
1115	carapolide A		<i>Carapa procera</i> ⁵⁸¹
1116	munronin E		<i>Munronia henryi</i> ⁵⁰⁶
1117	nimolicinoic acid		<i>Azadirachta indica</i> ⁷²
1118	ceramicine A		<i>Chisocheton ceramicus</i> ^{262,412}
1119	entilin A	$R_1 = R_2 = \text{H}$	<i>Entandrophragma utile</i> ^{491,760}
1120	entilin B	$R_1 = \text{H}; R_2 = \text{Ac}$	<i>E. utile</i> ^{491,760}
1121	entilin C	$R_1 = \text{CH}_3; R_2 = \text{H}$	<i>E. utile</i> ⁷⁶¹
1122	entilin D		<i>E. utile</i> ^{491,762}
1123	munronin F		<i>Munronia henryi</i> ⁵⁰⁶
1124	turrapubescic acid A	$R = \text{Ac}$	<i>Turraea pubescens</i> ¹²⁶
1125	turrapubescic acid B	$R = \text{iBu}$	<i>T. pubescens</i> ¹²⁶
1126	turrapubescic acid C	$R = \text{Piv}$	<i>T. pubescens</i> ¹²⁶
1127	azadironol		<i>Azadirachta indica</i> ¹²⁸
1128	desfurano-6 α -hydroxyazadiradione	$R = \text{OH}$	<i>A. indica</i> ¹²⁰
1129	desfurano-azadiradione	$R = \text{H}$	<i>A. indica</i> ^{70,753}
1130	7 α -acetoxy-4,4,8-trimethyl-5 α -(13 α Me)-17-oxa-androsta-1,14-dien-3,16-dione (13 α -nimolactone)	$R = \alpha\text{-CH}_3$	<i>A. indica</i> ^{70,107,753}
1131	7 α -acetoxy-4,4,8-trimethyl-5 α -17-oxa-androsta-1,14-dien-3,16-dione (13 β -nimolactone)	$R = \beta\text{-CH}_3$	<i>A. indica</i> ^{70,107,753}

When trichilin-class limonoids are tested against *Spodoptera eridania*, there is a remarkably clear-cut structure activity relationship in which the 12 α -OH function was the most potent, followed by 12 β -OH, 12-desoxy, and 12 α -acetoxy groups, in order of decreasing potency.^{194,224} Similar results indicated that the 12-OH functionality could be necessary for maximum activity in trichilin-class limonoids, and it appeared from the variable activities of meliatoxins A₁ and A₂ that even the epoxide function on ring D had an important role to play.⁸⁷⁸ Zhou et al. also concluded that isomerization of the D-ring epoxide to a 15-keto and acetylation of the 12- and 29-OH groups of trichilin-class limonoids reduced the antifeedant activity, but the side-chain change at C-29 did not influence their activity.²²⁵ The highly oxygenated 1-O-acetylkhayanolide A (**1003**) was the most active antifeedant among the six limonoids from *Khaya senegalensis*. This finding was in agreement with the observation that the role played by increasing oxygenation in limonoids is to increase their biological activity.⁵⁵⁰ The introduction of the O-acetyl group of xylogranatin F (**1156**) at C-3 enhanced the antifeedant rate significantly (16 to 25%).⁶³⁸ Hydrogenation of the furan ring, replacement of the acetoxy group with methoxyl group, and saponification of the methyl ester at C-11 all increased the antifeedant activity of salannin (**332**) against *Leptinotarsa decemlineata*. Modification of the tigloyl group also changed this activity.⁸⁷⁹

5.1.2. Insects Growth Regulatory Activity. Besides the well-known antifeedant activity, azadirachtin (**292**) also showed strong insect growth regulating activity against many insects. Since **292** did not reduce feeding in *Pieris brassicae* pupae, the growth retardation and deformities were the direct effect of **292** and not due to lack of food.⁸⁸⁹ Nutritional analyses revealed that the insect growth inhibitory and antifeedant effects were independent of each other and relative to the level of treatment with **292**.⁸⁸⁴ Furthermore, 48 h feeding of **292** on foliage treated at

5–10 ppm appeared to be sufficient for growth disruption of *Spodoptera litura* at early instars age, and no juvenilizing effect was observed.⁸⁹⁰ Injection of **292** at higher concentration caused metabolic defects including weight reduction and metamorphosis inhibition in last larval instars of *Epilachna varivestis*.⁸⁹¹ In addition, prolonged development, wing deformities, unplastification of wing lobes, development of wingless adults, and larval mortality were the characteristic features of **292** on various stages of *Dysdercus koenigii*.⁸⁹²

The insect growth regulating activity of azadirachtin (**292**) focused its effects mainly on the molt of insects. Feeding on azadirachtin-sprayed creeping bentgrass caused molting disorders and death of early instar *Agrotis ipsilon* and slowed feeding and stunted the growth of late instars.⁸⁹³ **292** caused significant reduction in feeding activity at 2.5 g/L, prolonged the period for molting to nymphal stage, and caused 60% reduction in moltability.⁸⁹⁴ Gaaboub et al. investigated the molting inhibition of **292** against *Musca autumnalis*, which involved delayed lethal action, adult emergence, and pupae or adults size.⁸⁹⁵ The ED₅₀ values for molting inhibition by injected **292** were in the range of 10–25 ng/larvae for fourth-instar larvae of ten insect species of *Triatoma*, *Rhodnius* and *Panstrongylus*.⁸⁹⁶ In addition, **292** inhibited cold-induced supernumerary molt of last-instar *Galleria mellonella* and induced disturbances in larval and pupal ecdysis as well as in the metamorphic process, thus resulting in the formation of various intermediates.⁸⁹⁷ Feeding inhibition is an indirect effect on *Rhodnius prolixus* due to an interference of **292** with the endocrine system rather than through the inhibition of chemoreceptors.⁸⁸⁷ Although injection **292** elicited feeding inhibition, molt inhibition against *Locusta migratoria* was due to interference with the endocrine system rather than to the altered feeding behavior.⁸⁹⁸

Azadirachtin (**292**) inhibited the release of ecdysone from blowfly larval and pupal brain-ring gland complexes (BRGC)

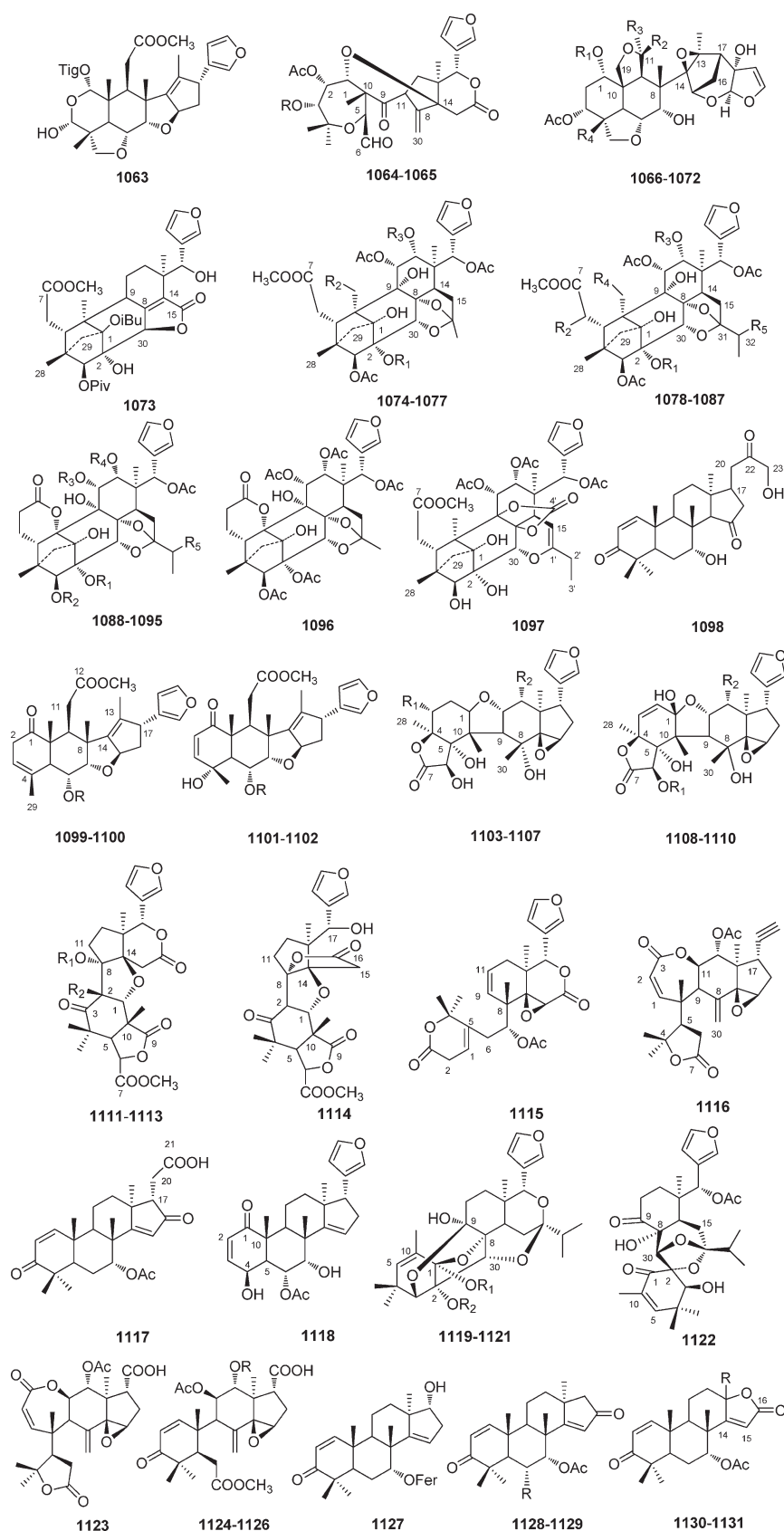


Figure 31. Structures of pentanortriterpenoids 1063–1114, hexanortriterpenoids 1115–1118, and hepanortriterpenoids 1119–1126, octanortriterpenoids 1127–1129, and enneanortriterpenoids 1130–1131.

Table 30. Structures and Sources of Simple Degraded Limonoids 1132–1149

no.	compounds	substitution groups and others	sources
1132	melazolid A	$R_1 = \text{OH}; R_2 = \text{H}$	<i>Melia azedarach</i> ⁴⁵²
1133	3-teracrylmelazolide A	$R_1 = \text{OH}; R_2 = \text{teracryl}$	<i>M. azedarach</i> ⁴⁵²
1134	3-teracrylmelazolide B	$R_1 = \text{H}; R_2 = \text{teracryl}$	<i>M. azedarach</i> ⁴⁵²
1135	dysodensiol A	$R = \beta\text{-OH}$	<i>Dysoxylum densiflorum</i> ⁷⁶⁴
1136	dysodensiol B	$R = \alpha\text{-OH}$	<i>D. densiflorum</i> ⁷⁶⁴
1137	dysodensiol C	$R = \text{O}$	<i>D. densiflorum</i> ⁷⁶⁴
1138	azedaralide		<i>Melia azedarach</i> ²³⁰
1139	trichiconnarin A		<i>Trichilia connaroides</i> ⁵⁷³
1140	trichiconnarin B		<i>T. connaroides</i> ⁵⁷³
1141	fraxinellonone	$R_1 = \text{O}; R_2 = \text{H}$	<i>Melia azedarach</i> ^{206,230}
1142	fraxinellone	$R_1 = R_2 = \text{H}$	<i>M. azedarach</i> ^{1,230,240,251,452}
1143	9 α -acetoxyfraxinellone	$R_1 = \alpha\text{-OAc}; R_2 = \text{H}$	<i>M. azedarach</i> ²⁰⁶
1144	9 α -hydroxy-12 α -acetoxyfraxinellone	$R_1 = \alpha\text{-OH}; R_2 = \text{OAc}$	<i>M. azedarach</i> ²¹⁸
1145	9 α -hydroxyfraxinellone	$R_1 = \alpha\text{-OH}; R_2 = \text{H}$	<i>M. azedarach</i> ^{218,452}
1146	9 β -hydroxyfraxinellone	$R_1 = \beta\text{-OH}; R_2 = \text{H}$	<i>M. azedarach</i> ⁴⁵²
1147	12 α -acetoxyfraxinellone	$R_1 = \text{H}; R_2 = \text{OAc}$	<i>M. azedarach</i> ²³⁰
1148	12 α -hydroxyfraxinellone	$R_1 = \text{H}; R_2 = \text{OH}$	<i>M. azedarach</i> ²¹⁸
1149	30-hydroxyfraxinellone		<i>M. azedarach</i> ⁴⁵²

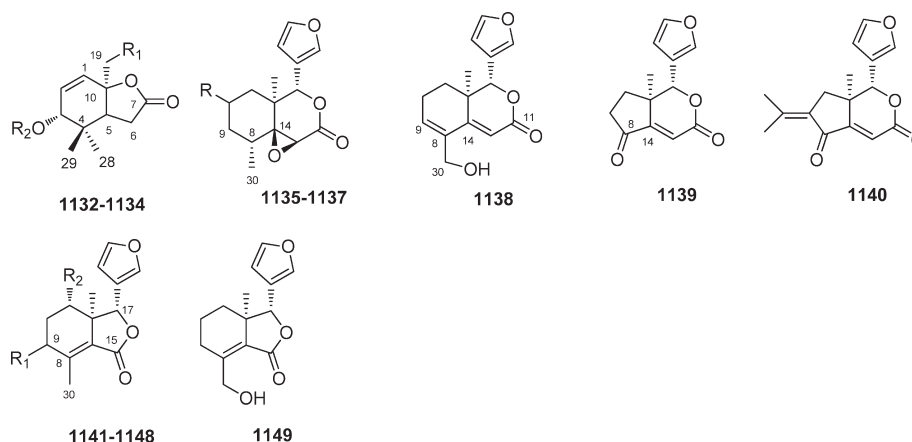


Figure 32. Structures of simple degraded limonoids 1132–1149.

Table 31. Structures and Sources of N-Containing Limonoids 1150–1159

no.	compounds	substitution groups and others	sources
1150	turraparvin D		<i>Turraea parvifolia</i> ¹²⁵
1151	munronin D	$R = \text{H}$	<i>Munronia henryi</i> ⁵⁰⁶
1152	munroniamide	$R = \text{CO}(\text{CH}_2)_2\text{NHNH}_2$	<i>M. henryi</i> ⁷⁶⁵
1153	turrapubesin B		<i>Turraea pubescens</i> ²⁸⁷
1154	salannolactam-(23)	$R_1 = \text{H}; R_2 = \text{O}$	<i>Azadirachta indica</i> ⁷⁶⁶
1155	salannolactam-(21)	$R_1 = \text{O}; R_2 = \text{H}$	<i>A. indica</i> ⁷⁶⁶
1156	xylogranatin F	$R = \text{H}; \Delta^{14,15}$	<i>Xylocarpus granatum</i> ⁶³⁸
1157	xylogranatin G	$R = \text{Ac}; \Delta^{14,15}$	<i>X. granatum</i> ⁶³⁸
1158	xylogranatin H	$R = \text{H}$	<i>X. granatum</i> ⁶³⁸
1159	granatoine		<i>X. granatum</i> ⁷²⁶

without affecting its biosynthesis.⁸⁹⁹ The induction of a super-numerary larval molt with moderate doses of the ecdysteroid agonist (RH-2485) and the synergistic potentiation of this effect by **292** were observed.⁹⁰⁰ Depending on the timing of injection

with **292**, the ecdysteroid levels of *Locusta migratoria* could be drastically reduced, or delayed, or extended, or unaffected.⁹⁰¹ Josephraj Kumar et al. found that when applied at ED₅₀ doses, **292** significantly depleted the content and altered the profile of

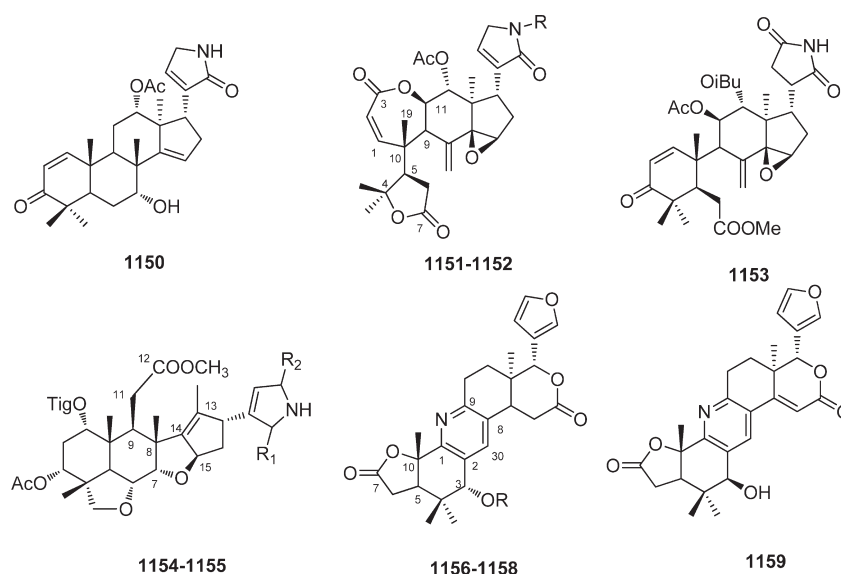
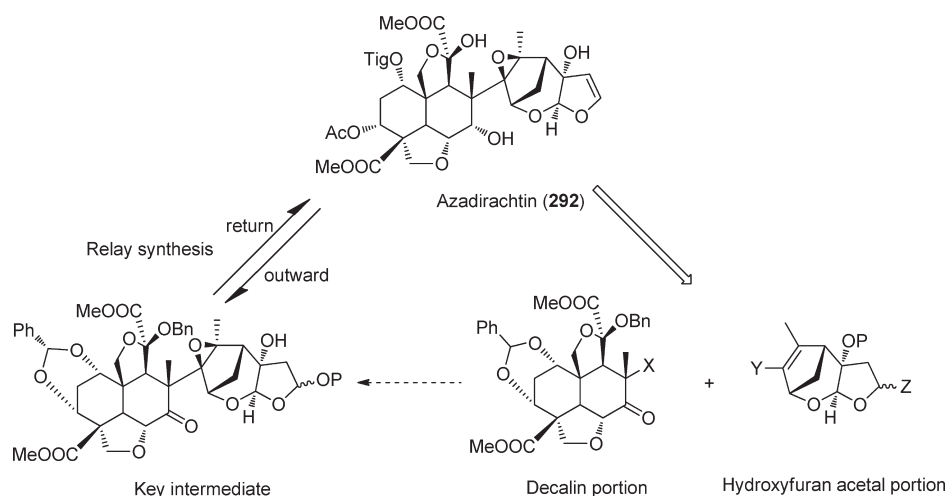


Figure 33. Structures of N-containing limonoids 1150–1159.

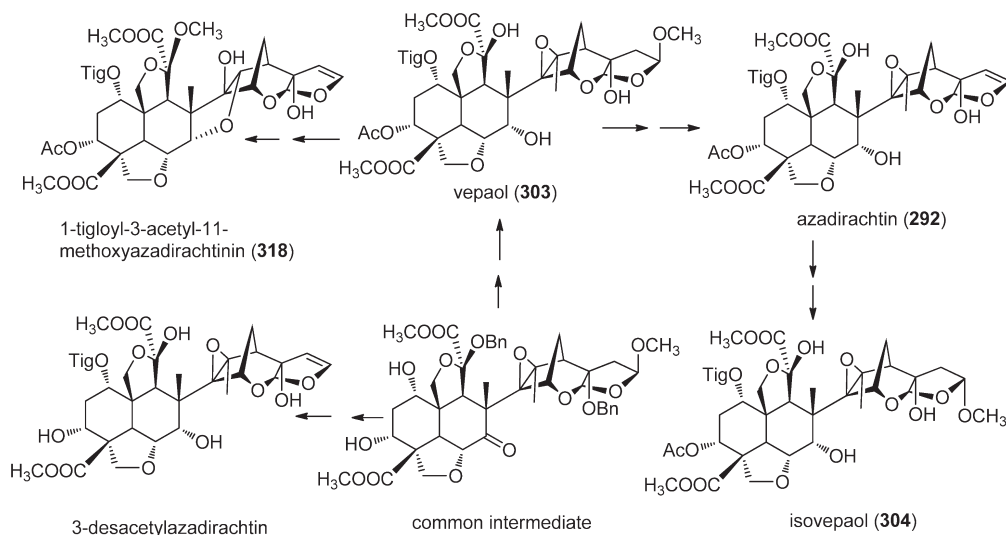
Scheme 1. Strategy for the Synthesis of Azadirachtin (292)



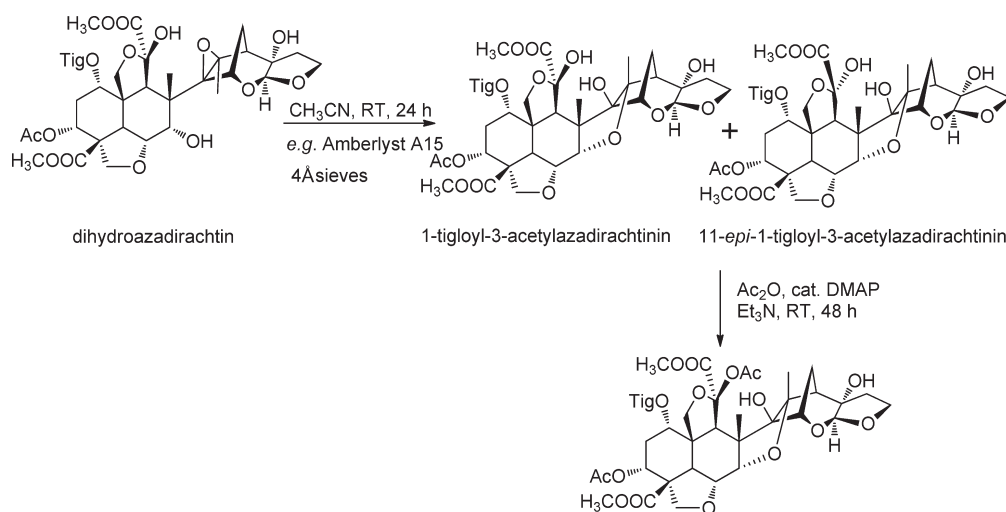
ecdysteroids at crucial stages. This involved modification of the ecdysteroid titer and then in turn led to changes in lysosomal enzyme activity causing overt morphological abnormalities during the metamorphic molt.⁹⁰² It seemed likely that pupation in azadirachtin-treated *Manduca sexta* was inhibited by a disturbed ecdysteroid regulation shortly before pupal ecdysis, and **292** was able to inhibit development even when individuals performed a complete molt after the treatment.⁹⁰³ In addition, low doses of **292** injected into newly molted last-instar larvae of *Oncopeltus fasciatus* prolonged the intermolt stage, apparently due to a delayed ecdysteroid peak.⁹⁰⁴ In preventing normal development of final-instar larvae of *Heliothis virescens*, **292** apparently reduced molting hormone titers by reducing prothoracicotropic hormone (PTTH) titers and the receptivity of prothoracic glands to produce ecdysone *via* stimulation by PTTH.⁹⁰⁵ Remold et al. suggested that **292** might influence the release of trophic hormones from the corpus cardiacum leading to alterations in timing and titer of morphogenetic hormone pools.⁹⁰⁶ The strong effect of

292 on larval-pupal and pupal-adult of *Epilachna varivestis* was interpreted as an interference with molting hormone pools.⁹⁰⁷ It was reported that **292** induced disturbances in larval and pupal ecdysis, decreased cold-induced elevation of juvenile hormone titers in the larval body, and might have an effect on the prothoracicotropic function of the brain.⁸⁹⁷ A brain factor, possibly the prothoracicotropic hormone that stimulates ecdysteroid production on the prothoracic glands, might act directly or indirectly on both the midgut cell organization and the intestinal microenvironment, interfering in the trypanosome survival and infection of the vector *Rhodnius prolixus*.⁹⁰⁸ Remold established a precise correlation between administered dose, resulting effects, and retention of **292**, and concluded that azadirachtin shifted and decreased the ecdysterone, juvenile hormone, and vitellogenin peaks concomitantly.⁹⁰⁹ The LC₅₀ values of **292** against ecdysone 20-monooxygenase activity ranged from 10^{−4} M for *Drosophila melanogaster* to 4 × 10^{−4} M for *Manduca sexta*.⁹¹⁰

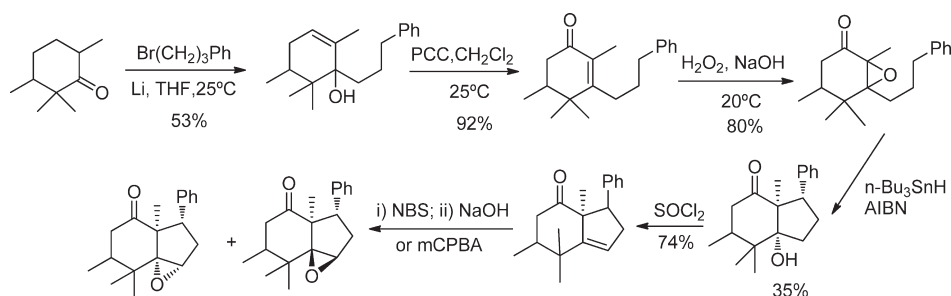
Scheme 2. Synthesis of Azadirachtin and Azadirachtinin Skeleton from a Common Intermediate



Scheme 3. Chemical Conversion from Azadirachtin Skeleton to Azadirachtinin Skeleton



Scheme 4. Strategy of Synthesis of 12-Oxo-14,15-epoxy Havanensin Derivatives



Exposure to **292** reduced the fertility and fecundity of adult *Myzus persicae*, *Nasonovia ribisnigri*, *Chaetosiphon fragaefolii* in a linear, concentration-dependent manner.⁹¹¹ Injection of **292** into newly hatched adults of *Oncopeltus fasciatus* affected the longevity, fecundity, and hatchability of eggs from treated parents, and there were marked differences between males and

females.⁹¹² Most of the *Locusta migratoria* treated with **292** had no oviposition, and radioimmunoassay showed quantitatively that only traces of ecdysteroids were present in their ovaries.⁹¹³ In addition, feeding adult *Epilachna varivestis* with **292** for first five days after molting decreased its reproduction, increased mortality, and delayed the onset of the oviposition.⁹¹⁴ Moreover, **292**

Scheme 5. Synthesis of Fraxinellone (1142) Using Stereoselective Oshima-Utimoto Reaction

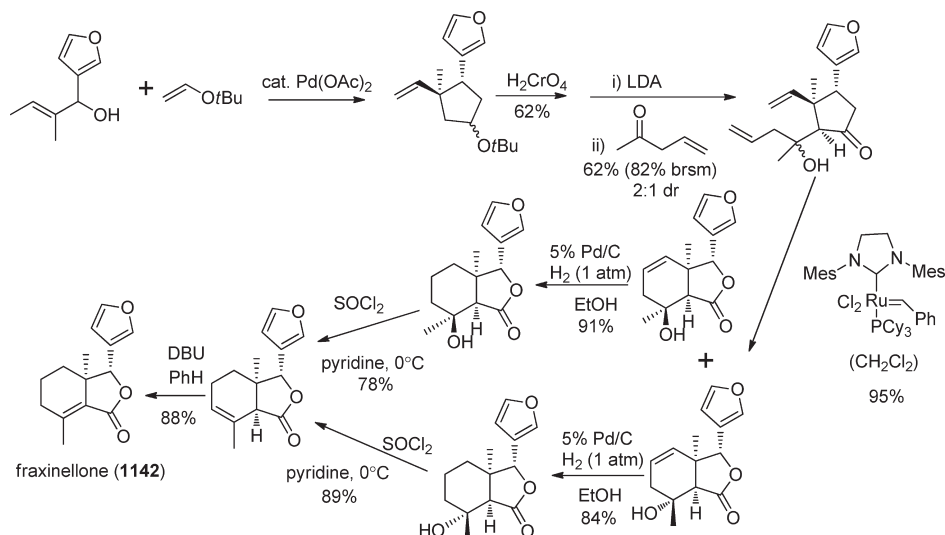


Table 32. Antifeedancy of Azadirachtin (292) against Insects

insects	antifeedancy
<i>Epilachna varivest</i>	EC ₅₀ = 13 ppm; ³²² EC ₁₀₀ = 120 ppm ³²²
<i>E. paenulata</i>	ED ₅₀ = 0.72 μg/cm ² , LD ₅₀ = 1.24 μg/cm ² (96 h) ⁸⁸⁰
<i>Helicoverpa armigera</i>	EC ₅₀ = 0.26 ppm (for neonates), 0.4 ppm (for 3rd instar larvae) ⁴⁹⁴
<i>Locusta migratoria</i>	MIC = 25 ppm ⁸⁸¹
<i>L. migratoria</i>	ED ₅₀ = 3 ppm ⁸⁸²
<i>Ostrinia nubilalis</i>	PC ₅₀ = 3.5 ppm (for neonate larvae), 24 ppm (for 3rd-instar larvae) ⁸⁸³
<i>Peridroma saucia</i>	EC ₅₀ = 0.26 ppm ⁸⁸⁴
<i>Pieris rapae</i>	AR = 100 (1000 ppm) ⁵⁰⁷
<i>Phyllotreta striolata</i>	MIC = 10 ppm ⁸⁸⁵
<i>Reticulitermes speratus</i>	PC ₉₅ = 65.293 ⁸⁸⁶
<i>Rhodnius prolixus</i>	ED ₅₀ = 25.0 μg/mL ^{887,888}
<i>Schistocerca gregaria</i>	ED ₅₀ = 0.001 ppm ⁸⁸²
<i>Spodoptera littoralis</i>	AI = 98.8 ± 1.11 (1 ppm), 100.0 ± 0.00 (10 ppm); ⁷⁹² 99 ± 1.1 (1 ppm) ³⁰⁵

delayed the release of one or more factors from the head that regulate oogenesis in *Aedes aegypti*.⁹¹⁵ Ovarian development was severely reduced in azadirachtin-injected females, and the vitellogenesis was rescuable by juvenile hormone treatment.⁹¹⁶ Both 20-hydroxyecdysone and **292** caused inhibition of vitellogenesis and ultrastructural damages in corpus allatum cells. Interestingly, some ultrastructural modifications were specific to each molecule, suggesting that they would act via different mechanisms.⁹¹⁷ The vitellogenesis inhibition produced by **292** in *Labidura riparia* consisted of direct cytotoxic effects as well as a generalized disruption of endocrine and neuroendocrine functions.⁹¹⁸ Spermiogenesis of *Mamestra brassicae* occurred in Grace's medium when the testis sheath was also present, but even in the presence of both ruptured testis and 20-hydroxyecdysone, 3 ppm of **292** caused degenerated spermatocysts.⁹¹⁹ Nisbet et al. reported that **292** bound preferentially to sites on the organelles associated with maturing *Schistocerca gregaria* sperm tails, and that **292** at concentrations of 10⁻⁴ M and above caused a time-dependent reduction in the motility of eupyrene sperm bundles liberated from the accessory glands of mature male *S. gregaria*.⁹²⁰ Subrahmanyam et al. pointed out that **292** delayed

the synthesis and release of neurosecretion from the A-type median neurosecretory cells of *S. gregaria*, thereby affecting the ovarian development.⁹²¹

Administration of a physiological dose of **292** into female *Locusta migratoria* by injection led neither to starvation (though food consumption was reduced) nor to a qualitative change in the neurosecretory proteins of the corpus cardiacum.⁹²² However, the neurosecretory system was accompanied by an unusually high accumulation of paraldehyde fuchsin (PAF)-stainable neurosecretory material in the brain fibers and in the storage lobes of the corpus cardiacum.⁹²³ The morphological and biochemical effects induced by **292** suggested a widespread blockade of factors presumably located in the central nervous system.⁹²⁴ **292** stimulated a specific deterrent neuron in the lepidopterous species tested and inhibited the firing of neurons with signal phagostimulants in another test.⁹²⁵

Experiments in vivo and in vitro proposed by Mordue et al. demonstrated that treatment with **292** resulted in a significant growth reduction in the rate of passage of food through the gut, and in gut motility of *Locusta migratoria*.⁹²⁶ Furthermore, azadirachtin (**292**) directly or indirectly inhibited the reduction

Table 33. Antifeedancy of Meliaceous Limonoids

compounds	insects and antifeedancy
azadirone (1)	<i>Leptinotarsa decemlineata</i> , AI = 11.6 ± 6.3 (100 ppm), 22.4 ± 7.4 (300 ppm), 26.9 ± 5.1 (500 ppm) ²⁷³
azadiradione (12)	<i>Reticulitermes speratus</i> , PC ₉₅ = 827.5 µg/disk; ¹⁰³ <i>Heliothis virescens</i> , EC ₅₀ = 560 ppm ¹⁰¹
7-deacetylazadiradione (13)	<i>H. virescens</i> , EC ₅₀ = 1600 ppm ¹⁰¹
17β-hydroxyazadiradione (18)	<i>Reticulitermes speratus</i> , PC ₉₅ = 235.6 µg/disk ¹⁰³
7-deacetyl-17β-hydroxyazadiradione (19)	<i>Heliothis virescens</i> , EC ₅₀ = 240 ppm ¹⁰¹
nilotin (129)	<i>Leptinotarsa decemlineata</i> , ED ₅₀ = 7 µg/mL ¹⁹¹
12α-hydroxyamoorastatin (166)	<i>Epilachna paenulata</i> , ED ₅₀ = 0.80 µg/cm ² (in choice assay); LD ₅₀ = 0.76 µg/cm ² (in no-choice assay) ⁸⁸⁰
chuanliansu (167)	<i>Helicoverpa armigera</i> , EC ₅₀ = 26.8 ppm; FI ₅₀ = 56.6 ppm (for third-instar larvae) ⁸⁶⁵ <i>Epilachna paenulata</i> , ED ₅₀ = 3.69 µg/cm ²⁸⁸⁰
1β,2β;21,23-diepoxy-7α-hydroxy-24,25,26,27-tetranor-apotirucalla-14,20,22-trien-3-one (246)	<i>Leptinotarsa decemlineata</i> , AI = 10.8 ± 4.5 (100 ppm), 21.4 ± 2.6 (300 ppm), 24.9 ± 3.7 (500 ppm) ²⁷³
3-tigloylazadirachtol (296)	<i>Epilachna varivestis</i> , EC ₅₀ = 30 ppm; ³²² EC ₁₀₀ = 150 ppm ³²² <i>Schistocerca gregaria</i> , ED ₅₀ = 80 µg/l ⁸⁷² <i>Locusta migratoria</i> , ED ₅₀ = 12 mg/L ⁸⁷²
1-tigloyl-3-acetylazadirachtol (297)	<i>Epilachna varivestis</i> , EC ₅₀ = 6 ppm; ³²² EC ₁₀₀ = 50 ppm ³²²
salannin (332)	<i>Spodoptera frugiperda</i> , ED ₅₀ = 13 µg/cm ² ; ³⁶² <i>Reticulitermes speratus</i> , PC ₉₅ = 203.3 µg/disk ¹⁰³
3-deacetylsalannin (333)	<i>R. speratus</i> , PC ₉₅ = 1373.1 µg/disk ¹⁰³
nimbolide (345)	<i>Epilachna varivestis</i> , EC ₅₀ = 90 ppm; ³²² EC ₁₀₀ > 500 ppm ³²²
volkensin (369)	<i>Spodoptera frugiperda</i> , ED ₅₀ = 3.5 µg/cm ²³⁶²
6-deacetylnimbin (392)	<i>Reticulitermes speratus</i> , PC ₉₅ = 1581.2 µg/disk ¹⁰³
gedunin (416)	<i>R. speratus</i> , PC ₉₅ = 218.4 µg/disk ¹⁰³
7-deacetylgedunin (421)	<i>R. speratus</i> , PC ₉₅ = 113.7 µg/disk ¹⁰³
prieurianin (458)	<i>Helicoverpa armigera</i> , EC ₅₀ = 18.8 ppm (for neonates), EC ₅₀ = 92.2 ppm (for 3rd instar larvae) ⁴⁹⁴
epoxyyprieurianin (464)	<i>H. armigera</i> , EC ₅₀ = 3.2 ppm (for neonates), EC ₅₀ = 55.7 ppm (for 3rd instar larvae) ⁴⁹⁴
dysoxylumin A (465)	<i>Pieris rapae</i> , AR = 73.8 (1000 ppm) ⁵⁰⁷
dysoxylumin B (466)	<i>P. rapae</i> , AR = 77.4 (1000 ppm) ⁵⁰⁷
dysoxylumin C (467)	<i>P. rapae</i> , AR = 74.9 (1000 ppm) ⁵⁰⁷
dysoxylumolide B (501)	<i>P. rapae</i> , AR = 28.3 (1000 ppm) ⁵⁰⁷
dysoxylumic acid D (502)	<i>P. rapae</i> , AR = 29.5 (1000 ppm) ⁵⁰⁷
dysoxylumic acid A (503)	<i>P. rapae</i> , AR = 78.7 (1000 ppm) ⁵⁰⁷
dysoxylumic acid B (504)	<i>P. rapae</i> , AR = 64.1 (1000 ppm) ⁵⁰⁷
dysoxylumic acid C (506)	<i>P. rapae</i> , AR = 59.4 (1000 ppm) ⁵⁰⁷
dysoxylumolide A (512)	<i>P. rapae</i> , AR = 27.9 (1000 ppm) ⁵⁰⁷
dysoxylumolide C (554)	<i>P. rapae</i> , AR = 22.4 (1000 ppm) ⁵⁰⁷
methyl angolensate (568)	<i>Spodoptera frugiperda</i> , AI = 66.4 ± 10.63 (1000 ppm) ⁵⁵⁶
swietenolide (638)	<i>S. frugiperda</i> , AI = 94.1 ± 2.90 (1000 ppm) ⁴⁴⁵
6-acetylswietenolide (645)	<i>S. frugiperda</i> , AI = 72.2 ± 19.60 (1000 ppm) ⁴⁴⁵
diacetylswietenolide (647)	<i>S. frugiperda</i> , AI = 72.0 ± 9.38 (1000 ppm) ⁴⁴⁵
xylocarpin (799)	<i>S. frugiperda</i> , AI = 77.8 ± 6.90 (1000 ppm) ⁵⁵⁶
swietemahonin F (805)	<i>S. frugiperda</i> , AI = 70.2 ± 8.90 (1000 ppm) ⁴⁴⁵
ruageanin A (808)	<i>S. frugiperda</i> , AI = 72.6 ± 19.60 (1000 ppm) ⁵⁵⁶
ruageanin B (809)	<i>S. frugiperda</i> , AI = 86.3 ± 6.41 (1000 ppm) ⁵⁵⁶
khayanolide A (1002)	<i>S. littoralis</i> , EC ₅₀ = 11.18 mg/kg ⁶⁷⁸
khayanolide B (1004)	<i>S. littoralis</i> , EC ₅₀ = 2.19 mg/kg ⁶⁷⁸
1-O-acetylkhayanolide B (1005)	<i>S. littoralis</i> , EC ₅₀ = 2.66 mg/kg ⁶⁷⁸
marrangin (1067)	<i>Epilachna varivestis</i> , EC ₅₀ = 6 ppm; ³²² EC ₁₀₀ = 50 ppm ³²²
nimbandiol (1101)	<i>Reticulitermes speratus</i> , PC ₉₅ = 245.4 µg/disk ¹⁰³
munroniamide (1152)	<i>Pieris brassicae</i> , AR = 27.6 (1000 ppm) ⁷⁶⁵

of trypsin by the enzyme-secreting cells of the midgut wall and consequently resulted in the increased costs and reduced rate of

growth.⁹²⁷ When *Spodoptera litura* larvae were fed a diet of castor leaves treated with **292**, gut enzyme-acid phosphatases, alkaline

Table 34. MAC Values (ppm) of Antifeedancy of Meliaceous Limonoids

compounds	insects	MAC values
trichilin B (137)	<i>Spodoptera exigua</i> ; ^{207,220,341} <i>S. littoralis</i> ²¹⁴	200
12-O-acetyltrichilin B (138)	<i>S. exigua</i> ^{220,341}	400
1,12-diacetyltrichilin B (139)	<i>S. exigua</i> ^{207,220,341}	
trichilin D (141)	<i>S. exigua</i> ^{207,220}	
aphanastatin (142)	<i>S. exigua</i> and <i>S. eridania</i> ³⁴¹	200
trichilin F (143)	<i>S. littoralis</i> ²²³	300
trichilin G (144)	<i>S. littoralis</i> ²²³	
trichilin H (145)	<i>S. exigua</i> ; ^{207,220,227,341} <i>S. eridania</i> ²²⁴	400
1-acetyltrichilin H (146)	<i>S. littoralis</i> ²²⁵	
trichilin I (151)	<i>S. exigua</i> ; ^{220,227,341} <i>S. eridania</i> ²²⁴	
trichilin J (153)	<i>S. exigua</i> ; ^{220,227,341} <i>S. eridania</i> ²²⁴	
trichilin K (154)	<i>S. eridani</i> ²²⁴	
trichilin L (155)	<i>S. eridani</i> ²²⁴	
sendanin (156)	<i>S. littoralis</i> ²¹⁴	
azedarachin A (158)	<i>S. exigua</i> ; ^{207,227,341} <i>S. eridania</i> ^{224,341}	200
12-O-acetylazedarachin A (159)	<i>S. exigua</i> ; ^{207,341} <i>S. eridania</i> ³⁴¹	
	<i>S. littoralis</i> ²¹⁴	400
azedarachin B (160)	<i>S. littoralis</i> ^{214,225}	200
12-O-acetylazedarachin B (161)	<i>S. eridani</i> ; ²²⁴ <i>S. exigua</i> ^{207,227}	400
azedarachin C (162)	<i>S. exigua</i> ^{228,341}	
meliatoxin A ₂ (163)	<i>S. litura</i> ⁸⁷⁸	300
	<i>S. exigua</i> ; ^{207,341} <i>S. eridania</i> ³⁴¹	400
12 α -hydroxyamoorastatin (166)	<i>S. littoralis</i> ²¹⁴	150
toosendanin (167)	<i>S. littoralis</i> ²¹²	200
	<i>S. littoralis</i> ²¹⁴	300
12 α -hydroxyamoorastatone (173)	<i>S. littoralis</i> ²²⁵	250
isochuanliansu (179)	<i>S. littoralis</i> ²¹⁴	400
	<i>S. littoralis</i> ²²⁵	300
neoazedarachins A, B, D (180–182)	<i>S. littoralis</i> ²²⁵	400
1-cinnamoyltrichilin (192)	<i>S. littoralis</i> ²¹²	1000
trichilin B (195)	<i>S. eridania</i> ²³⁹	
trichilin C (196)	<i>S. eridania</i> ²³⁹	
trichilin D (197)	<i>S. littoralis</i> ^{212,247}	
trichilin E (198)	<i>S. littoralis</i> ^{212,247}	
melicarpinin A (327)	<i>S. exigua</i> ; ³⁴¹ <i>S. littoralis</i> ²¹⁴	50
melicarpinin B (328)	<i>S. exigua</i> ³⁴⁰	150
	<i>S. exigua</i> and <i>S. eridania</i> ³⁴¹	50
melicarpinin C (329)	<i>S. exigua</i> and <i>S. eridania</i> ; ³⁴¹ <i>S. littoralis</i> ²¹⁴	50
melicarpinin D (330)	<i>S. exigua</i> and <i>S. eridania</i> ; ³⁴¹ <i>S. littoralis</i> ²¹⁴	
melicarpinin E (331)	<i>S. eridania</i> ³⁴²	
salannin (332)	<i>S. exigua</i> ; ³⁴¹ <i>S. eridania</i> ^{84,239,341,342,363}	1000
3-deacetylsalannin (333)	<i>S. eridania</i> ³⁴²	
nimbolinin A (355)	<i>S. littoralis</i> ²¹²	
1-deacetylnimbolinin A (356)	<i>S. littoralis</i> ²⁴⁷	
nimbolinin B (358)	<i>S. exigua</i> ; ³⁴¹ <i>S. eridania</i> ^{341,342}	
	<i>S. littoralis</i> ²⁴⁷	
nimbolinin C (363)	<i>S. littoralis</i> ²¹²	
nimbolinin D (364)	<i>S. littoralis</i> ²¹²	
ohchinolide C (386)	<i>S. eridania</i> ⁸⁴	
3-O-acetylochinolal (399)	<i>S. eridania</i> ⁸⁴	
nimbolidin B (407)	<i>S. eridania</i> ^{247,342}	1000
	<i>S. eridania</i> ³⁶³	500
nimbolidins C-E (410–412)	<i>S. eridania</i> ³⁶³	500
nimbolidin F (413)	<i>S. eridania</i> ⁸⁴	

Table 34. Continued

compounds	insects	MAC values
Trs A-C (462, 479, 463)	<i>Ajrotis segetum</i> Denis ⁴⁹³	200
methyl angolensate (568)	<i>Spodoptera littoralis</i> ^{547–549,551}	500
methyl 6-hydroxyangolensate (569)	<i>S. littoralis</i> ^{547–549}	
methyl 6-acetoxangolensate (570)	<i>S. littoralis</i> ^{547,549}	
sandoricin (573) and 6-hydroxysandoricin (574)	<i>S. frugiperda</i> ⁵³²	25
	<i>Ostrinia nubilalis</i> ⁵³²	200
khayanoside (598)	<i>Spodoptera littoralis</i> ⁵⁷⁴	1000
proceranolide butanoate (635)	<i>Agrotis segetum</i> ⁶⁴⁸	100
khayanone (668)	<i>Spodoptera littoralis</i> ⁶⁵⁸	300
angolensins A-C (672, 766, and 673)	<i>S. littoralis</i> ⁵⁴⁵	1000
8 β ,14 α -dihydroxyswietenolide (674)	<i>S. littoralis</i> ⁵¹⁰	500
khayalactol (774)	<i>S. littoralis</i> ⁵⁴⁷	300
seneganolide (777)	<i>S. littoralis</i> ^{547,549,551}	
2-hydroxyseneganolide (778)	<i>S. littoralis</i> ^{559,658}	200
2-hydroxyswietenahonolide (797)	<i>S. littoralis</i> ⁶³⁰	500
swietenahonin G (806)	<i>S. littoralis</i> ⁶³⁰	300
6-O-acetylswietenahonin G (807)	<i>S. littoralis</i> ⁶³⁰	500
xylocensin L (829)	<i>Picea brassicae</i> ⁶³⁵	1000
tabulalide D (857)	<i>Spodoptera littoralis</i> ⁷⁰⁶	500
swietenialides A–E (921–923, 889, 895)	<i>S. littoralis</i> ⁶⁶⁴	1000
xylocensins P, Q (949, 950)	<i>Mythimna separata</i> ⁷⁰⁰	500
tabulalin (973)	<i>Spodoptera littoralis</i> ⁷⁰⁶	
tabulalides A, B, E (995, 996, and 978)	<i>S. littoralis</i> ⁷⁰⁶	1000
khayanolide A (1002)	<i>S. littoralis</i> ^{547–549}	300
1-O-acetylkhayanolide A (1003)	<i>S. littoralis</i> ^{559,658}	100
khayanolide B (1004)	<i>S. littoralis</i> ^{547–549}	1000
1-O-acetylkhayanolide B (1005)	<i>S. littoralis</i> ⁵⁴⁷	300
khayanolide D (1006)	<i>S. littoralis</i> ⁵⁵⁹	200
	<i>S. littoralis</i> ⁵⁷⁴	1000
khayanolide E (1007)	<i>S. littoralis</i> ⁵⁷⁴	100
khayanolide C (1013)	<i>S. littoralis</i> ⁵⁴⁹	500
spirosendan (1056)	<i>S. littoralis</i> ²⁴⁷	1000
azedararide (1138)	<i>S. littoralis</i> ²³⁰	500
fraxinellone (1142)	<i>S. littoralis</i> ²³⁰	
12 α -acetoxyfraxinellone (1147)	<i>S. littoralis</i> ²³⁰	

phosphatases, adenosine triphosphatases, and lactate dehydrogenase decreased.⁹²⁸

Using *Drosophila melanogaster* as model system, the insect cellular cytoskeletal β -actin was found to be the probable target of azadirachtin (292).^{929,930} Azadirachtin (292), salannin (332), nimbin (391), and 6-deacetylnimbin (392) inhibited the ecdysone 20-monooxygenase (E-20-M) activity against *Aedes aegypti*, *Drosophila melanogaster*, and *Manduca sexta* in a dose-dependent fashion. Based on the dose response as well as the 50% inhibition (I_{50}) value, 332 was found to be the most effective whereas 391 was the least effective.⁹³¹ The effects of 17 β -hydroxyazadiradione (18), 292, 332, 3-deacetylnimbin (333), gedunin (416), and 7-deacetylgedunin (421) on enzyme lactate dehydrogenase (LDH) activity of *Cnaphalocrocis medinalis* larvae were investigated with clear dose–response dependency manner. Among these compounds, 292 is most potent in all experiments with EC_{50} values at least 0.043, 0.057, and 0.063 ppm for third, fourth and fifth instars, respectively.^{932,933} Azadirachtin B (296) was 2.5-fold less active than azadirachtin (292) as an insect growth

inhibitor but comparably effective in ecdysis inhibition.^{316,843} Surprisingly, salannin (332) was comparable to 292 in growth-regulatory activity against *Spodoptera litura*, *Pericallia ricini*, and *Oxya fuscovittata*.⁹³⁴

Nimocinolide (26) and isonimocinolide (29) affected fecundity in *Musca domestica* at doses of 100–500 ppm and showed mutagenic properties in *Aedes aegypti* producing intermediates.⁸⁰ Nutritional analyses revealed that both growth inhibition and reduced consumption of cedrelone (81) were a consequence of postingestive malaise rather than a peripherally mediated antifeedant effect.⁹³⁵ The feeding experiments showed the ED_{50} values of sendanin (156) for growth inhibition against *Pectinophora gossypiella*, *Heliothis zea*, *H. virescens*, and *Spodoptera frugiperda* ranged from 9 to 60 ppm, with *P. gossypiella* being the most sensitive and *Heliothis* complex the least.¹⁹⁸ When incorporated into artificial diets of neonates at 50 ppm, humilinalides A–D (793, 794, 695, and 697) caused larval mortality, as well as growth reduction and increased the development time of survivors in a concentration-dependent manner. In addition, 695 at

Table 35. Insects Growth Regulatory Activity of Meliaceous Limonoids

compounds	insects and efficacy
hirtin (94)	<i>Peridroma saucia</i> , EC ₅₀ = 13 ppm ¹⁷⁰
toosendanin (167)	<i>Spodoptera frugiperda</i> , LC ₅₀ = 7.0 ppm ⁴¹³
azadirachtin (292)	<i>Heliothis zea</i> and <i>H. virescens</i> , ED ₅₀ = 0.7 ppm; <i>Spodoptera frugiperda</i> , <i>Pectinophora gossypiella</i> , ED ₅₀ = 0.4 ppm ⁹³⁶ <i>Rhodnius prolixus</i> , ED ₅₀ = 0.04 µg/mL ⁸⁸⁸ <i>Helicoverpa armigera</i> , EC ₅₀ = 0.26 ppm; <i>Spodoptera litura</i> , EC ₅₀ = 0.21 ppm ⁴⁴²
azadirachtin B (296)	<i>Rhodnius prolixus</i> , ED ₅₀ = 0.015 µg/mL ⁸⁸⁸
salannin (332)	<i>Helicoverpa armigera</i> , EC ₅₀ = 74.5 ppm, ⁴⁴² EC ₅₀ = 86.5 ppm, EC ₉₅ = 187.4 ppm ³⁶⁶ <i>Spodoptera litura</i> , EC ₅₀ = 72.0 ppm ⁴⁴² <i>S. litura</i> , EC ₅₀ = 87.7 ppm, EC ₉₅ = 197.3 ppm and FI ₅₀ = 2.8 µg/cm ²³⁶⁶
salannol (336)	<i>S. litura</i> , EC ₅₀ = 77.4 ppm, EC ₉₅ = 220.8 ppm, and FI ₅₀ = 2.3 µg/cm ²³⁶⁶ <i>Helicoverpa armigera</i> , EC ₅₀ = 79.7 ppm, EC ₉₅ = 219.7 ppm ³⁶⁶
salannol acetate (337)	<i>H. armigera</i> , EC ₅₀ = 64.2 ppm, EC ₉₅ = 166.9 ppm ³⁶⁶ <i>Spodoptera litura</i> , EC ₅₀ = 65.6 ppm, EC ₉₅ = 169.1 ppm, and FI ₅₀ = 2.0 µg/cm ²³⁶⁶
gedunin (416)	<i>Spodoptera litura</i> , EC ₅₀ = 40.4 ppm ⁴⁴² <i>S. frugiperda</i> , LC ₅₀ = 39.0 ppm ⁴¹³ <i>Helicoverpa armigera</i> , EC ₅₀ = 50.8 ppm ⁴⁴²
6β-hydroxygedunin (420)	<i>H. armigera</i> , EC ₅₀ = 24.2 ppm; <i>Spodoptera litura</i> , EC ₅₀ = 21.5 ppm ⁴⁴²
photogedunin (433)	<i>S. frugiperda</i> , LC ₅₀ = 10.0 ppm ⁴¹³
prieurianin (458)	<i>Drosophila melanogaster</i> , ED ₅₀ = 10 ^{−5} M ⁴⁹⁸
rohitukin (480)	<i>D. melanogaster</i> , ED ₅₀ = 1.25 × 10 ^{−4} M ⁴⁹⁸
khayalactol (774)	<i>Spodoptera littoralis</i> , EC ₅₀ = 11.48 mg/kg ⁶⁷⁸
khayanolide A (1002)	<i>S. littoralis</i> , EC ₅₀ = 14.65 mg/kg ⁶⁷⁸
khayanolide B (1004)	<i>S. littoralis</i> , EC ₅₀ = 6.96 mg/kg ⁶⁷⁸
1-O-acetylkhayanolide B (1005)	<i>S. littoralis</i> , EC ₅₀ = 16.75 mg/kg ⁶⁷⁸
nimbinene (1099)	<i>S. litura</i> , EC ₅₀ = 404.5 ppm; <i>Helicoverpa armigera</i> , EC ₅₀ = 394.1 ppm ⁴⁴²

5 ppm also reduced growth and survivorship of *Ostrinia nubilalis*.⁶⁶⁵

The EC₅₀ values of 7-deacetyl-17β-hydroxyazadiradione (19), azadiradione (12), and nimbecinol (13) against *Heliothis virescens* were 240, 560, and 1600 ppm, respectively, which suggested that the insect growth regulating activity was reduced by a hydroxyl group at C-7 but increased by a hydroxyl group at C-17.¹⁰¹ Siddiqui et al. proposed that the seneciolyloxy substituent at C-7 in 7-O-deacetyl-23-O-methyl-7α-O-seneciolylnimbinolide (28) resulted in a significant increase of insect growth regulating activity against *Aedes aegypti*.¹¹⁹

5.1.3. Insecticidal Activity. The insecticidal activities of azadirachtin-like compounds were listed in detail by Govindachari et al. in 1998.⁹³⁷ We now summarize the insecticidal efficacy of limonoids in Table 36. The LC₅₀ values of 292 against the second-instar nymphs of nine species of aphids ranged from 2.4 ppm for *Myzus persicae* on pepper to 635.0 ppm for *Chaetosiphon fragaefolii* on strawberry.⁹³⁸ Contact and dipping LC₅₀ values of 292 against larvae of *Hyalomma dromedarii* were >20.3 µg/cm² and >2.5 g/L, respectively.⁸⁹⁴ Arnason et al. proved that 292 was an effective botanical insecticide for control of *Ostrinia nubilalis* at 10 ppm.⁸⁸³ In addition, 292 was efficacious against *Haematobia irritans*, *Stomoxys calcitrans*, and *Musca domestica* and also had potential for *H. irritans* control.⁹³⁹ It was announced that 292 in ppm concentrations inhibited proliferation and monolayer formation of *Spodoptera frugiperda* (Sf9) insect cells in monolayer culture.^{831,940} However, Cohen et al. stated that 292 was not cytotoxic against Sf9 cell lines.⁹⁴¹ The evidence presented by Salehzadeh et al. suggested that in insect cells 292 acted similarly to the antimitotic plant metabolite colchicine, namely, by interfering with the polymerization of tubulin.⁹⁴²

Swietenin C (679), humilinolide E (698), methyl-2-hydroxy-3β-isobutyroxy-1-oxomeliac-8(30)-enate (699), and humilin B (812) reduced survivorships at various stages against *Ostrinia nubilalis*, while 6α-acetoxygedunin (418) reduced growth at the test concentration of 50 ppm.⁴³⁴ Khayasin (652) exhibited marked insecticidal activity against the fifth larvae of *Brontispa longissima* at a concentration of 10 mg/L.⁵⁵⁸ Among khayasin T (655), febrifugin (694), cipadesin (703), ruageanin A (808), cipadesin A (815), and febrifugin A (716), the last showed the highest insecticidal activity at 50.0 mg/kg against *Spodoptera frugiperda*, comparable to that of the positive control-gedunin (416).⁶⁵⁶ Moluccensins H and I (964 and 965) showed moderate insecticidal activity against the fifth instar larvae of *Brontispa longissima* at a concentration of 100 mg/L, whereas moluccensins J–L (966, 969, 970) exhibited no activity.⁵⁶⁸ Preliminary studies showed that the limonoids and triterpenoids in *Cedrela fissilis* and *C. fruticosa* were promising in controlling leaf-cutting ants *Atta sexdens rubropilosa*,⁶⁷¹ and subsequent research revealed that the toxicity for the ants seemed not to be related only to the presence of the limonoids.¹¹³ Neither 53 nor 20,21,22,23-tetrahydro-23-oxoazadirone (56) showed insecticidal activity against *Peridroma saucia*.¹³¹ In addition, meliacinol (456) did not show insecticidal activity against *Aedes aegypti* at up to 100 ppm.⁹³

Quantitative molecular calculations of the structure–activity relationship indicated that the insecticidal activity of azadirachtins was directly proportional to the polarity of ring A, the steric requirements of the substituents at C-7, and the rotations around the single bond between C-8 and C-14.⁹⁴³ The potent larvicidal activity of gedunin (416) indicated that the epoxidation and expansion of ring D had a favorable effect on this activity, as was

Table 36. Insecticidal Efficacy of Meliaceous Limonoids

compounds	insects and efficacy
nimocinol (7)	<i>Aedes aegypti</i> , LC ₅₀ = 21 ppm ⁹³
6 α -O-acetyl-7-deacetylnimocinol (8)	<i>A. aegypti</i> , LC ₅₀ = 83 ppm ⁹³
23-O-methylnimocinolide (27)	<i>A. aegypti</i> , LC ₅₀ = 53 ppm ¹¹⁹
7-O-deacetyl-23-O-methyl-7 α -O-seneciolylnimocinolide (28)	<i>A. aegypti</i> , LC ₅₀ = 2.14 ppm ¹¹⁹
22,23-dihydronimocinol (33)	<i>Anopheles stephensi</i> , LC ₅₀ = 60 ppm ¹²⁰
1 α ,7 α ,11 β -triaceoxy-4 α -carbomethoxy-12 α -(2-methylpropanoxy)-14 β ,15 β -epoxyhavanensin (123)	<i>A. gambiae</i> , LD ₅₀ = 4.0 ppm ¹⁸⁸
1 α ,11 β -diaceoxy-4 α -carbomethoxy-7 α -hydroxy-12 α -(2-methylpropanoxy)-15-oxohavanensin (130)	<i>A. gambiae</i> , LD ₅₀ = 3.6 ppm ¹⁸⁸
1 α -acetyl-3 α -propionylvilasinin (187)	<i>A. gambiae</i> , LD ₅₀ = 7.1 ppm ¹⁸⁸
melietetraolene (245)	<i>A. stephensi</i> , LC ₅₀ = 16 ppm ²⁷²
azadirachtin (292)	<i>A. gambiae</i> , LD ₅₀ = 57.1 ppm ¹⁸⁸ <i>Plutella xylostella</i> , LD ₅₀ = 7.04 (24 h); 4.12 (48 h); 1.28 (72 h); 0.87 (96 h) $\mu\text{g/g}$ ³²⁴ <i>Spodoptera littoralis</i> , LC ₅₀ = 0.32 ppm, EC ₅₀ = 0.11 ppm ³³⁸
azadirachtol (295)	<i>Plutella xylostella</i> , LD ₅₀ = 4.88 (24 h); 3.28 (48 h); 2.35 (72 h); 1.78 (96 h) $\mu\text{g/g}$ ³²⁴
azadirachtin B (296)	<i>P. xylostella</i> , LD ₅₀ = 4.85 (24 h); 2.26 (48 h); 1.56 (72 h); 1.06 (96 h) $\mu\text{g/g}$ ³²⁴
azadirachtin O (301)	<i>P. xylostella</i> , LD ₅₀ = 3.92 (24 h); 1.92 (48 h); 1.19 (72 h); 0.79 (96 h) $\mu\text{g/g}$ ³²⁴
azadirachtin Q (302)	<i>P. xylostella</i> , LD ₅₀ = 5.95 (24 h); 1.89 (48 h); 1.40 (72 h); 1.10 (96 h) $\mu\text{g/g}$ ³²⁴
1,3-dicinnamoyl-11-hydroxymeliacarpin (313)	<i>Spodoptera littoralis</i> , LC ₅₀ = 2.36 ppm, EC ₅₀ = 0.57 ppm ³³⁸
1-cinnamoyl-3-acetyl-11-hydroxymeliacarpin (314)	<i>S. littoralis</i> , LC ₅₀ = 0.48 ppm ³³⁸
1-cinnamoyl-3-methacrylyl-11-hydroxymeliacarpin (315)	<i>S. littoralis</i> , LC ₅₀ = 1.19 ppm, EC ₅₀ = 0.57 ppm ³³⁸
7 α ,12 α -diacetoxy-11 β -hydroxyneoteceanin (621)	<i>Anopheles gambiae</i> , LD ₅₀ = 7.83 ppm ⁵⁷⁹
11 β ,12 α -diacetoxyneoteceanin (622)	<i>A. gambiae</i> , LD ₅₀ = 7.07 ppm ⁵⁷⁹
11 β ,12 α -diacetoxy-14 β ,15 β -epoxyneoteceanin (623)	<i>A. gambiae</i> , LD ₅₀ = 7.05 ppm ⁵⁷⁹
azadirachtin L (1067)	<i>Plutella xylostella</i> , LD ₅₀ = 10.27 (24 h); 7.89 (48 h); 5.39 (72 h); 1.92 (96 h) $\mu\text{g/g}$ ³²⁴
11 α -azadirachtin H (1068)	<i>P. xylostella</i> , LD ₅₀ = 5.75 (24 h); 4.20 (48 h); 1.38 (72 h); 0.75 (96 h) $\mu\text{g/g}$ ³²⁴
azadirachtin M (1071)	<i>P. xylostella</i> , LD ₅₀ = 8.46 (24 h); 4.84 (48 h); 4.23 (72 h); 1.30 (96 h) $\mu\text{g/g}$ ³²⁴
azadirachtin P (1072)	<i>P. xylostella</i> , LD ₅₀ = 2.19 (24 h); 1.73 (48 h); 1.19 (72 h); 0.79 (96 h) $\mu\text{g/g}$ ³²⁴
desfurano-6 α -hydroxyazadiradione (1128)	<i>Anopheles stephensi</i> , LC ₅₀ = 43 ppm ¹²⁰

also the case for the C=C bond in the ring A in nimbocinol (13) and nimolicinol (451).⁹⁴⁴

5.1.4. Antiphytopathogen Activity. Interestingly, pure azadiradione (12), epoxyazadiradione (60), salannin (332), and nimbin (391) did not have appreciable antifungal activity. However, when these limonoids were mixed and bioassayed, they showed antifungal activity against *Drechslera oryzae*, *Alternaria tenuis*, and *Fusarium oxysporum* f. sp. *vasinfectum*, indicating possible additive/synergistic effects.¹⁰⁵ Among azadiradione (12), cedrelone (81), and several derivatives of 81, the most effective in reducing rust pustule emergence was 81 itself, which gave emergence reductions of 98.4% and 93.4% at concentrations of 1 $\mu\text{g}/\text{cm}^2$ and 10 $\mu\text{g}/\text{cm}^2$, respectively.⁹⁴⁵ The results obtained by Kraus et al. showed that nimbolide (345) inhibited *Bacillus subtilis* even at a concentration of 0.5 $\mu\text{g}/\text{spot}$.³²² Nimbin (391) inhibited the growth of potato virus X *in vitro* by <50% at a concentration of 1000 ppm.⁹⁴⁶ Ten limonoids from *Khaya ivorensis* were tested antifungal activity against *Botrytis cinerea*, and among these 1,3,7-trideacetylkhivorin (438) and 568 showed the highest activity, while 7-deacetylgedunin (421) had the lowest activity.⁴⁴⁷ With the exception of *Penicillium expansum*, 3 α ,7 α -dideacetylkhivorin (440) showed stronger antimicrobial activity than methyl 6-hydroxyangolensate (569) against all of the fungi tested (*Aspergillus niger*, *Monilinia fructicola*, *Botrytis cinerea*, *Geotrichum candidum*, *Colletotrichum acutatum*, *Penicillium expansum*, *P. italicum*, *Glomerella cingulata*, and *Phytophthora citrophthora*).⁴⁴⁷ Among the microbial species tested

(*Bacillus subtilis*, *Aspergillus fumigatus*, *A. niger*, and *Alternaria alternata*), methyl angolensate (568) exhibited the maximum zone of inhibition (17.3 mm) against *A. niger*.⁹⁴⁷ mexicanolide (626), 2 α ,3 β -dihydroxy-3-deoxymexicanolide (628), 3 β -hydroxy-3-deoxymexicanolide (629), 6-acetyl-3-tigloylswitenolide (646), and 6-acetylswietenine (687) effectively reduced the number of rust pustules on detached groundnut leaves.⁶⁰³ 2-Acetoxyseneganolide (725) at concentrations of 1000 and 1500 ppm showed inhibitions against *B. cinerea* growth of 61.50% and 68.33%, respectively, which differ only insignificantly from the inhibitions yielded by methyl 6-hydroxyangolensate (569) at 1500 ppm (65.33%) and seneganolide A (723) at 1000 ppm (60.83%).⁴⁷² 1,2-Dihydro-6 α -acetoxyazadirone (239) showed strong inhibitory properties against the pathogenic fungi *Curvularia verruciformis*, *Drechslera oryzae*, and *Alternaria solani*, but no related data were presented in the original paper.²⁶⁷ 6-Acetoxy-7 α -hydroxy-3-oxo-14 β ,15 β -epoxymeliac-1,5-diene (69) exhibited strong antibacterial activity against *Bacillus anti-macis*, *B. pumilus*, and *B. subtilis*, but no data were provided in the original paper.¹⁴²

5.1.5. Others. Cherry found that 292 did not cause mortality, antifeeding responses, or change the growth rate of *Melanotus communis* wireworms; however, azadirachtin-treated soil was repellent to the wireworms.⁹⁴⁸ 7-Deacetoxy-7-oxogedunin (423) acted as an inhibitor of photophosphorylation in spinach thylakoids since it inhibited ATP synthesis and phosphorylating electron flows by 88 and 83%, respectively, at a concentration

Table 37. Cytotoxic Activity of Meliaceous Limonoids against Tumor Cell Lines

compounds	cells	activity
dysobinin (11)	KB	IC ₅₀ = 3.17 $\mu\text{g/mL}$ ⁹⁷
	NCI-H187	IC ₅₀ = 1.67 $\mu\text{g/mL}$ ⁹⁷
	MCF7	IC ₅₀ = 2.15 $\mu\text{g/mL}$ ⁹⁷
azadiradione (12)	KB	IC ₅₀ = 9.38 $\mu\text{g/mL}$ ⁹⁷
	NCI-H187	IC ₅₀ = 6.44 $\mu\text{g/mL}$ ⁹⁷
	MCF7	IC ₅₀ = 7.13 $\mu\text{g/mL}$ ⁹⁷
mahonin (17)	NCI-H187	IC ₅₀ = 15.61 $\mu\text{g/mL}$ ⁹⁷
	MCF7	IC ₅₀ = 18.42 $\mu\text{g/mL}$ ⁹⁷
epoxyazadiradione (nimbinin) (60)	GPK	ED ₅₀ = 7.13 $\mu\text{g/mL}$ ⁵⁰⁰
	KB	IC ₅₀ = 12.87 $\mu\text{g/mL}$ ⁹⁷
	NCI-H187	IC ₅₀ = 7.54 $\mu\text{g/mL}$ ⁹⁷
	MCF7	IC ₅₀ = 4.68 $\mu\text{g/mL}$ ⁹⁷
	N1 $\times 10^{-115}$	IC ₅₀ = 23 μM ⁹⁴¹
	143B.TK	IC ₅₀ = 24 μM ⁹⁴¹
anthothecol (84)	P388	ED ₅₀ = 1.2 $\mu\text{g/mL}$ ²¹⁰
1,12-diacetylrichilin B (139)	P388	IC ₅₀ = 0.46 $\mu\text{g/mL}$ ²²¹
trichilin D (141)	P388	IC ₅₀ = 0.055 $\mu\text{g/mL}$ ²²¹
trichilin H (145)	P388	IC ₅₀ = 0.16 $\mu\text{g/mL}$ ²²¹
	KB	IC ₅₀ = 0.11 $\mu\text{g/mL}$ ²¹¹
1-acetylrichilin H (146)	P388	IC ₅₀ = 0.47 $\mu\text{g/mL}$ ²²¹
1-acetyl-2-deacetylrichilin H (147)	P388	IC ₅₀ = 0.66 $\mu\text{g/mL}$ ²²¹
3-deacetylrichilin H (148)	P388	IC ₅₀ = 0.045 $\mu\text{g/mL}$ ²²¹
1-acetyl-3-deacetylrichilin H (149)	P388	IC ₅₀ = 0.40 $\mu\text{g/mL}$ ²²¹
12-O-deacetylrichilin H (150)	HeLa S3	IC ₅₀ = 0.48 μM ²²⁶
12-deacetylrichilin I (152)	P388	IC ₅₀ = 0.011 $\mu\text{g/mL}$ ²²¹
sendanin (156)	P388	IC ₅₀ = 0.078 $\mu\text{g/mL}$ ²⁰⁵ ED ₅₀ = 0.01 $\mu\text{g/mL}$ ²¹⁰
	N1 $\times 10^{-115}$	IC ₅₀ = 133 μM ⁹⁴¹
	143B.TK	IC ₅₀ = 89 μM ⁹⁴¹
29-deacetylsendanin (157)	Hepa1c1c7	GI ₅₀ = 0.238 $\mu\text{g/mL}$ ²⁰²
	HepG2	GI ₅₀ = 0.805 $\mu\text{g/mL}$ ²⁰²
	P388	IC ₅₀ = 0.026 $\mu\text{g/mL}$ ²⁰⁵
29-isobutylsendanin (161)	P388	IC ₅₀ = 0.034 $\mu\text{g/mL}$ ²⁰⁵
12 α -hydroxyamoorastatin (166)	P388	ED ₅₀ = 0.002 $\mu\text{g/mL}$ ²¹⁰ IC ₅₀ = 0.090 $\mu\text{g/mL}$ ²⁰⁵
toosendanin (167)	KB	IC ₅₀ = 3.82 $\mu\text{g/mL}$ ²¹¹
	PC3	IC ₅₀ = 1.2×10^{-7} M (120 h) ⁹⁶⁰
	BEL7404	IC ₅₀ = 2.6×10^{-8} M (96 h) ⁹⁶⁰
	SH-SY5Y	IC ₅₀ = 1.5×10^{-7} M (96 h) ⁹⁶⁰
	U251	IC ₅₀ = 3.3×10^{-8} M (96 h) ⁹⁶⁰
	HL-60	IC ₅₀ = 6.1×10^{-9} M (96 h) ⁹⁶⁰
	U937	IC ₅₀ = 5.4×10^{-9} M (72 h) ⁹⁶⁰
amoorastatone (172)	P388	ED ₅₀ = 30 $\mu\text{g/mL}$ ²¹⁰
meliatoxin B ₁ (177)	P388	IC ₅₀ = 5.4 $\mu\text{g/mL}$ ²²¹
	KB	IC ₅₀ >10 $\mu\text{g/mL}$ ²¹¹
toosendanin (185)	KB	IC ₅₀ >10 $\mu\text{g/mL}$ ²¹¹
meliavolkina (200)	A-549	ED ₅₀ = 0.57 $\mu\text{g/mL}$ ²⁴⁸
	MCF-7	ED ₅₀ = 0.26 $\mu\text{g/mL}$ ²⁴⁸
	HT-29	ED ₅₀ = 0.12 $\mu\text{g/mL}$ ²⁴⁸
malleastrone A (227)	A2780	IC ₅₀ = 0.49 μM ²⁴²
	MDA-MB-435	IC ₅₀ = 0.41 μM ²⁴²
	HT-29	IC ₅₀ = 0.24 μM ²⁴²
	H552-T1	IC ₅₀ = 0.24 μM ²⁴²
	U937	IC ₅₀ = 0.20 μM ²⁴²
malleastrone B (228)	A2780	IC ₅₀ = 0.63 μM ²⁴²
	MDA-MB-435	IC ₅₀ = 0.34 μM ²⁴²

Table 37. Continued

compounds	cells	activity
	HT-29	IC ₅₀ = 0.22 μ M ²⁴²
	H552-T1	IC ₅₀ = 0.23 μ M ²⁴²
	U937	IC ₅₀ = 0.19 μ M ²⁴²
malleastrone C (229)	A2780	IC ₅₀ = 18 μ M ²⁴²
turrapubesin A (290)	P388	IC ₅₀ = 12.14 μ M ²⁸⁷
1-tigloyl-3-acetyl-11-methoxymeliacarpinin (318)	P388	IC ₅₀ = 3.2 μ g/mL ²⁰⁵
1-tigloyl-3,20-diacetyl-11-methoxymeliacarpinin (321)	P388	IC ₅₀ = 100 μ g/mL ³⁴⁵
3-tigloyl-1,20-diacetyl-11-methoxymeliacarpinin (322)	P388	IC ₅₀ = 48 μ g/mL ³⁴⁵
1-cinnamoyl-3-hydroxy-11-methoxymeliacarpinin (323)	P388	IC ₅₀ = 1.5 μ g/mL ³⁴⁵
1-deoxy-3-methacrylyl-11-methoxymeliacarpinin (324)	P388	IC ₅₀ = 47 μ g/mL ³⁴⁵
1-cinnamoyl-3-acetyl-11-methoxymeliacarpinin (327)	P388	IC ₅₀ = 10.5 μ g/mL ³⁴⁵
1-acetyl-3-tigloyl-11-methoxymeliacarpinin (329)	P388	IC ₅₀ = 3.3 μ g/mL ²⁰⁵
nimbolide (345)	GPK	ED ₅₀ = 10.14 μ g/mL ⁵⁰⁰
	N1 $\times 10^{-115}$	IC ₅₀ = 1.5 μ g/mL; ⁹⁶¹ 5.2 μ M ⁹⁴¹
	143B.TK	IC ₅₀ = 4.3 μ M ⁹⁴¹
	BC-1	ED ₅₀ = 0.39 μ g/mL; ³⁷³ 3.1 μ g/mL ³⁶⁹
	COL-2	ED ₅₀ = 0.41 μ g/mL; ³⁷³ 4.2 μ g/mL ³⁶⁹
	HT-1080	ED ₅₀ = 0.31 μ g/mL ³⁷³
	LU-1	ED ₅₀ = 0.42 μ g/mL; ³⁷³ 3.3 μ g/mL ³⁶⁹
	MEL-2	ED ₅₀ = 0.53 μ g/mL ³⁷³
	KB	ED ₅₀ = 0.25 μ g/mL; ³⁷³ 1.7 μ g/mL ³⁶⁹
	P388	ED ₅₀ = 0.065 μ g/mL ³⁷³
	LNCaP	ED ₅₀ = 0.9 μ g/mL ³⁶⁹
28-deoxonimbolide (346)	BC-1	ED ₅₀ = 1.34 μ g/mL; ³⁷³ 3.2 μ g/mL ³⁶⁹
	COL-2	ED ₅₀ = 1.81 μ g/mL; ³⁷³ 9.0 μ g/mL ³⁶⁹
	HT-1080	ED ₅₀ = 1.04 μ g/mL ³⁷³
	LU-1	ED ₅₀ = 0.84 μ g/mL; ³⁷³ 8.5 μ g/mL ³⁶⁹
	MEL-2	ED ₅₀ = 2.05 μ g/mL ³⁷³
	KB	ED ₅₀ = 1.30 μ g/mL; ³⁷³ 4.1 μ g/mL ³⁶⁹
	P388	ED ₅₀ = 0.66 μ g/mL ³⁷³
	LNCaP	ED ₅₀ = 1.9 μ g/mL ³⁶⁹
12-O-methylvolkensin (370)	KB	IC ₅₀ = 8.72 μ g/mL ²¹¹
1-O-deacetylchinchinide A (372)	HeLa S3	IC ₅₀ = 2.40 μ M ³⁸⁷
1-O-deacetyl-1-O-tigloylochinchinide A (373)	HeLa S3	IC ₅₀ = 29.7 μ M ³⁸⁷
ohchinchinide B (374)	HeLa S3	IC ₅₀ = 40.5 μ M ³⁸⁷
1-O-deacetylchinchinide B (375)	HeLa S3	IC ₅₀ = 0.10 μ M ³⁸⁷
1-O-deacetyl-1-O-tigloylochinchinide B (376)	HeLa S3	IC ₅₀ = 33.8 μ M ³⁸⁷
1-O-deacetyl-1-O-benzoylochinchinide B (377)	HeLa S3	IC ₅₀ = 33.0 μ M ³⁸⁷
chisonimbolin C (380)	HeLa	IC ₅₀ = 13 μ M ³⁹⁰
chisonimbolin D (381)	HeLa	IC ₅₀ = 32 μ M ³⁹⁰
15-O-deacetyl-15-O-methylnimbolindin A (406)	HeLa S3	IC ₅₀ = 37.4 μ M ²²⁶
15-O-deacetylnimbolindin B (408)	HeLa S3	IC ₅₀ = 0.10 μ M ²²⁶
15-O-deacetyl-15-O-methylnimbolindin B (409)	HeLa S3	IC ₅₀ = 28.3 μ M ²²⁶
walsogyne A (414)	P388	IC ₅₀ = 5 μ g/mL ⁴¹²
gedunin (416)	CaCo-2	IC ₅₀ = 16.83 μ M ⁴⁹
	GPK	ED ₅₀ = 275.10 μ g/mL ⁵⁰⁰
	P388	IC ₅₀ = 3.3 μ g/mL ⁴³³
7-deacetylgedunin (421)	CHAGO	IC ₅₀ = 16.00 μ M ⁴⁴⁸
	Hep-G2	IC ₅₀ = 10.26 μ M ⁴⁴⁸
	P388	IC ₅₀ = 4.5 μ g/mL ⁴³³
7-deacetoxy-7-oxogedunin (423)	Hep-G2	IC ₅₀ = 16.17 μ M ⁴⁴⁸
7-deacetoxy-7 α ,11 β -dihydroxygedunin (424)	P388	IC ₅₀ = 7.8 μ g/mL ⁴³³
11 α -hydroxygedunin (426)	P388	IC ₅₀ = 71 μ g/mL ⁴³³
11 β -hydroxygedunin (427)	P388	IC ₅₀ = 5.4 μ g/mL ⁴³³
11-oxogedunin (429)	P388	IC ₅₀ = 3.0 μ g/mL ⁴³³

Table 37. Continued

compounds	cells	activity
3 α ,7 α -diacetylkhivirin (440)	Caco-2	IC ₅₀ = 35 ppm ⁴⁷³
	SiHa	IC ₅₀ = 54 ppm ⁴⁷³
	MCF-7	IC ₅₀ = 69 ppm ⁴⁷³
humilinolide C (695)	A-549	ED ₅₀ = 37.7 μ g/mL ⁶⁶⁵
	MCF-7	ED ₅₀ = 94.1 μ g/mL ⁶⁶⁵
humilinolide D (697)	A-549	ED ₅₀ = 60.6 μ g/mL ⁶⁶⁵
	MCF-7	ED ₅₀ = 65.0 μ g/mL ⁶⁶⁵
	HT-29	ED ₅₀ = 53.6 μ g/mL ⁶⁶⁵
erythrocarpine B (714)	P388	IC ₅₀ = 6.0 μ g/mL ⁶⁶⁷
erythrocarpine C (715)	P388	IC ₅₀ = 9.9 μ g/mL ⁶⁶⁷
erythrocarpine A (727)	P388	IC ₅₀ = 2.0 μ g/mL ⁶⁶⁷
xylogranatin B (762)	P388	IC ₅₀ = 8.9 μ M ⁶³⁷
	A549	IC ₅₀ = 11.3 μ M ⁶³⁷
xylogranatin C (763)	P388	IC ₅₀ = 6.3 μ M ⁶³⁷
xylogranatin D (764)	P388	IC ₅₀ = 14.6 μ M ⁶³⁷
xyloccensin M (771)	HCT-8	IC ₅₀ = 14.77 μ M ⁶⁷⁷
	Bel-7402	IC ₅₀ = 12.81 μ M ⁶⁷⁷
	BGC-283	IC ₅₀ = 8.90 μ M ⁶⁷⁷
	A549	IC ₅₀ = 18.55 μ M ⁶⁷⁷
	A2780	IC ₅₀ = 16.60 μ M ⁶⁷⁷
	HCT-8	IC ₅₀ = 7.75 μ M ⁶⁷⁷
	Bel-7402	IC ₅₀ = 8.22 μ M ⁶⁷⁷
xylocarpin J (776)	BGC-283	IC ₅₀ = 8.38 μ M ⁶⁷⁷
	A549	IC ₅₀ = 5.35 μ M ⁶⁷⁷
	A2780	IC ₅₀ = 4.77 μ M ⁶⁷⁷
	A-549	ED ₅₀ = 64.4 μ g/mL ⁶⁶⁵
	MCF-7	ED ₅₀ = 79.5 μ g/mL ⁶⁶⁵
humilinolide A (793)	HT-29	ED ₅₀ = 59.6 μ g/mL ⁶⁶⁵
	HT-29	ED ₅₀ = 81.1 μ g/mL ⁶⁶⁵
humilinolide B (794)	HT-29	ED ₅₀ = 81.1 μ g/mL ⁶⁶⁵
granaxylocarpin A (819)	P388	IC ₅₀ = 9.3 μ M ⁶³²
xyloxmexicanin A (821)	KT	IC ₅₀ = 4.59 μ M ⁶⁷⁵
granaxylocarpin B (822)	P388	IC ₅₀ = 4.9 μ M ⁶³²
xylogranatin C (823)	CHAGO	IC ₅₀ = 9.16 μ M ⁴⁴⁸
erythrocarpine D (827)	P388	IC ₅₀ = 10.0 μ g/mL ⁶⁶⁷
erythrocarpine E (828)	P388	IC ₅₀ = 16.0 μ g/mL ⁶⁶⁷
xylogranatin A (832)	A549	IC ₅₀ = 15.7 μ M ⁶³⁷
xyloccensin Y (988)	HCT-8	IC ₅₀ = 10.43 μ M ⁶⁷⁷
	Bel-7402	IC ₅₀ = 13.55 μ M ⁶⁷⁷
	BGC-283	IC ₅₀ = 9.87 μ M ⁶⁷⁷
	A549	IC ₅₀ = 16.23 μ M ⁶⁷⁷
	A2780	IC ₅₀ = 11.64 μ M ⁶⁷⁷
	P388	IC ₅₀ = 15 μ g/mL ⁴¹²
ceramicine A (1118)	P388	IC ₅₀ = 15 μ g/mL ⁴¹²

of 300 μ M.⁴³⁵ The epimeric mixture of photogedunin (433)⁴⁶² and cedrelanolid I (599)⁵⁷¹ partially inhibited photophosphorylation, H⁺ uptake, and noncyclic electron flow, and then 599 interfered with monocot preemergence properties, mainly energy metabolism of the seeds at the level of respiration.⁵⁷¹ In addition, an epimeric mixture of photogedunin inhibited seed germination, seedling growth, and root and hypocotyl/coleoptyle growth in all species assayed.⁹⁴⁹ Humilinolides A (793) and C (695) inhibited the radicle growth of *Echinochloa crus-galli* with IC₅₀ values of 99.06 μ g/mL and 163.0 μ g/mL, respectively. In addition, *Amaranthus hypochondriacus* was less sensitive to 793 and 695 with IC₅₀ values of 199.0 μ g/mL and 215.8 μ g/mL, respectively, in contrast to no

inhibition of humilinolides B (794) and D (697) at the tested concentration.⁶²⁹

5.2. Biological Activities in Medicinal Use

5.2.1. Antineoplastic Activity. Most limonoids showed their antineoplastic activity as cytotoxicity with the IC₅₀ values listed in Table 37. The cytotoxicity of ten limonoids from *Turrea pubescens* was evaluated. Of these limonoids, isoazadironolide (38) and turrapubesin E (276) exhibited moderate activities against the P388 cell line, with the IC₅₀ values of 16.0 and 12.3 μ M, respectively, and none of them were active against the A549 cells.¹²⁶ Among the eight human cancer cell lines M14,

Table 38. Inactive Meliaceae Limonoids against Tumor Cell Lines

compounds	cell lines
mahonin (17)	KB ⁹⁷
6 α -acetoxyepoxyazadiradione (62)	KB, NCI-H187, MCF7 ⁹⁷
toonacilaton A (73), perforin A (535), and methyl 3 β -acetoxy-1-oxomelic-14(15)-enate (741)	SMMC-7721, HL-60, A549, SK-BR-3, PANC-1 ¹⁴⁵
3-deoxymethylnimbidate (339), 2,3-dihydronimbolide (347)	ASK ³⁶⁹
ohchinolide A (371), 1- <i>O</i> -detigloyl-1- <i>O</i> -benzoylohchinolal (397), 1- <i>O</i> -detigloyl-1- <i>O</i> -cinnamoylohchinolal (398), ohchinolal (556)	HeLa S3 ³⁸⁷
chisonimbolins A–G (378–384)	HeLa, SMMC-7721 ³⁹⁰
7-deacetoxy-7 α ,11 α -dihydroxygedunin (425)	P388 ⁴³³
rohitukin (480)	P388 ²¹⁰
gaudichaudysolin A (492)	HL-60, RPMI8226, NCI-H226, HCT116, MCF7 ⁵⁰²
cipadonoids B–G (567, 1046–1050)	P388 ⁵⁴⁴
methyl angolensate (568), mexicanolide (626), proceranolide (632), xylocensins K (788), O (948), P (949)	CHAGO, SW-620, KATO-3, BT-474, Hep-G2 ⁴⁴⁸
methyl 2 β ,3 β -diacetoxy-3-deoxoangolensate (577), cineracipadesins A–F (816, 580–583, 1040)	P-388 ⁵⁶³
humilinolide C (695)	HT-29 ⁶⁶⁵
xylomexicanin B (750)	HeLa, HEC-1, SHIN3, HOC-2, HAC-2, HLE, U251-SP, T-98,MM1-CB, HMV-1, KT ⁶⁷⁵
xylogranatin S (765)	HeLa, HLE, MDA-MB-231, SW-620 ⁶⁷⁶
humilinolide B (794)	A549, MCF-7 ⁶⁶⁵
granaxylcarpins A and B (819 and 840)	A549 ⁶³²
xylomexicanin A (821)	HeLa, HEC-1, SHIN3, HOC-2, HAC-2, HLE, U251-SP, T-98,MM1-CB, HMV-1 ⁶⁷⁵
xylocarpanoid A (825)	MDAMB-21, SW-620 ⁶³⁴
granaxylcarpins C–E (830, 984, and 981)	P388, A549 ⁶³²
moluccensins H–J (963, 967, and 968)	BT474, CHAGO, Hep-G2, KATO-3, SW-620 ⁷²³
trichiliton A (997)	HL-60, SMMC-7721, A-549, SK-BR-3 ⁶⁵¹
cipatrijugins A–D (1023–1026), cipadesin A (1051)	A549, K562 ⁷³⁵
trichilins A and B (1036 and 1043)	HL-60, BEL7402, Hela, MCF-7 ⁷³¹
cipadonoid F (1049)	HT29, HCT116, SW480, MDA-MB-231, MDA-MB-468, MCF-7, SMMC-7721, BEL-7402, MKN28, MKN45, SGF-7901, KB, RH30, SK-OV-3, Hela, HL-60, K562, K562/A02 ⁵⁴⁴

NCI-H23, SF-539, PC-3, SW620, KM12, UO-31, and ACHN, the most sensitive cells according to the dose–response profiles to 29-deacetylSENDANIN (157) were SF-539 and PC-3 which had GI₅₀ (growth inhibition of 50%) values of less than 0.010 $\mu\text{g}/\text{mL}$.²⁰³ 12 α -Hydroxyamoorastatin (166), 12 α -acetoxyamoorastatin (167), and 12 α -hydroxyamoorastatone (173) were all significantly cytotoxic to the human tumor cell lines of A-549, SK-OV-3, SK-MEL-2, XF-498, and HCT-15. Of these compounds, 167 was the most active with ED₅₀ values from 0.7 to 40 ng/mL .²¹³ In the human glioblastoma cell lines of G-28, G-112, and G-60, azadirachtin (292) induced a significant suppression of the binucleation index of 11, 8, and 24% respectively.⁹⁵⁰ In comparison with azadirachtin (292), nimbolide (345) was found to be a more potent antiproliferative and apoptosis-inducing agent and offered promise as a candidate agent in multitargeted prevention and treatment of cancer.^{951,952} The cellular and molecular mechanism by which 292 and 345 act against the HeLa cell line was investigated, and it was concluded that both compounds simultaneously arrest the cell cycle and target multiple molecules involved in mitochondrial apoptosis, and thus offer immense potential as anticancer therapeutic drugs.⁹⁵³ Treatment with nimbolide (345) resulted in dose and time-dependent inhibition of growth of BeWo cells,^{954,955} HL-60, U937, THP-1 and B16,⁹⁵⁶ suggesting that 345 has immense potential in cancer prevention and therapy based on

its antiproliferative and apoptosis inducing effects. The nimbolide-induced growth inhibition and cell cycle arrest of HT-29 were not associated with cellular differentiation, but instead with the time-dependent up-regulation of p21, cyclin D2, Chk2.⁹⁵⁷ Methyl angolensate (568) inhibited growth of T-cell leukemia and chronic myelogenous leukemia cells in a time- and dose-dependent manner, which involved the induction of apoptosis by triggering the intrinsic pathway.⁹⁵⁸

Nimbinol B (366) was moderately active in the brine shrimp lethality test, and it was significantly cytotoxic against HT-29 with an ED₅₀ value of $<10^{-3}$ $\mu\text{g}/\text{mL}$.³⁸⁴ Volkensinin (1057) showed weak bioactivity in BST with an LC₅₀ value of 57 $\mu\text{g}/\text{mL}$, and it was generally but weakly cytotoxic against six human tumor cell lines, giving ED₅₀ values of 27.90, 28.35, 33.56, 29.56, 8.43, and 28.51 $\mu\text{g}/\text{mL}$ against A-498, PC-3, PACA-2, A-549, MCF-7, and HT-29, respectively.⁷⁴⁴ Gedunin (416) showed anticancer activity via inhibition of the 90 kDa heat shock protein (Hsp90) folding machinery and caused the degradation of Hsp90-dependent client proteins similarly to other Hsp90 inhibitors.⁹⁵⁹ Nymanin 1 (522) showed reproducible, significant, and selective activity against the DNA repair-deficient RS322YK yeast strain, whereas Tr-B (479) exhibited moderate but selective activity, suggesting that they might have cytotoxic activity mediated by a DNA-damaging mechanism.¹⁹²

Aphanastatin (142), together with amoorastatin (165) and 12 α -hydroxyamoorastatin (166), was reported as showing

significant antineoplastic activity, but no data were provided.¹⁹⁷ On the negative side, many limonoids were found to be inactive against specific tumor cell lines. These results are listed in Table 38 in detail.

The presence of both a C-19/28 lactol and a C-14/15-epoxide group was found to be especially important for pronounced inhibition of the P-388 lymphocytic leukemia system in vitro cell line, and substitution of an A-ring α,β -unsaturated ketone (3-oxo-1-ene) for the lactol led to diminished activity, while reduction of the olefin caused complete loss of activity.⁸⁴⁵ Most trichilin-class limonoids with a C-14/15-epoxide and a C-19/28 acetal bridge exhibited strong cytotoxicity against P388 cells.^{196,205,213,221,226,433} Similarly, trichilin H (**145**) and toosendanin (**167**), which have C-14/15 epoxide moieties, showed highly cytotoxicity against KB cell, whereas toosendanin (**185**) and meliatoxin B₁ (**177**), possessing C-15 keto structure, did not show any significant level of cytotoxicity.²¹¹ The ED₅₀ values of 12 α -hydroxyamoorastatin (**166**) (0.002 μ g/mL) and amoorastatinone (**172**) (30 μ g/mL) further supported the supposition that the C-14 β /15 β epoxy was a definite requirement for growth inhibition of P388 cell lines.²¹⁰ The cytotoxic activity against P388 cells of the five melicarpin derivatives (**321**–**324** and **327**) with a C-3 acetate was decreased, and with a C-20 acetate it was almost zero.³⁴⁵ The more pronounced cell growth inhibitory activity of the structurally simpler amoorastatin (**165**) as compared to aphanastatin (**142**) suggested that the 1 α -acetoxy, 2 α ,12 α -dihydroxy, and 28-methylbutyryl groups of **142** were unnecessary and indeed might even lessen inhibition of neoplastic (P388) cell growth.²²⁹ In addition, the α,β -unsaturated enone moiety or its equivalent conjugated system in the A-ring, the C-7 acetoxy/chloroacetoxy or keto group on the B-ring, and the furan moiety were the structural requirements for the high activity of azadirone (**1**), which was a potent cytotoxic agent with good in vitro and in vivo activity.⁸³

5.2.2. Antimicrobial Activity. Among the five limonoids dysobinin (**11**), azadiradione (**12**), mahonin (**17**), epoxyazadiradione (**60**), and 6 α -acetoxyepoxyazadiradione (**62**), only **12** exhibited a strong antibacterial effect against *Mycobacterium tuberculosis*, giving a MIC of 6.25 μ g/mL.⁹⁷ 6-Acetoxy-11 α -hydroxy-7-oxo-14 β ,15 β -epoxymeliacin-1,5-diene-3-O- α -L-rhamnopyranoside (**104**) had more positive antibacterial activity than streptomycin at the concentrations tested against *Vibrio cholerae*, *Klebsiella pneumoniae*, *Salmonella typhimurium*, and *Escherichia coli*.¹⁷⁶ 1-Cinnamoyltrichilin (**192**), trichilin B (**195**), and 12-ethoxynimbolin C (**385**) exhibited significant antibacterial activity against *Porphyromonas gingivalis* ATCC 33 277, with MIC values of 15.6, 31.5, and 31.3 μ g/mL, respectively.¹⁸⁶ No mutagenicity of nimbolide (**345**) was detected by Ames' test using both TA98 and TA100 tested strains. However, at 0.875 mg/disk it exhibited antibacterial activity against the three strains *Staphylococcus aureus*, *S. coagulase* (+), and *S. coagulase* (-) out of a total of 3/17 strains.⁹⁶² The results obtained by Kraus et al. showed that **345** inhibited *Pseudomonas stutzeri* even at a concentration of 0.5 μ g/spot.³²² 3 α ,7 α -Dideacetylkhivorin (**440**) showed stronger antimicrobial activity than methyl 6-hydroxyangolensate (**569**) against *Rhizopus stolonifer*.⁴⁴⁷ Methyl angolensate (**568**) displayed growth inhibition against *Proteus vulgaris* with an inhibition zone of 14.1 mm, followed by *Klebsiella pneumoniae* with 13.5 mm, *Staphylococcus aureus* with 13.3 mm, *Escherichia coli* with 12.8 mm, and *Salmonella typhimurium* with 12.0 mm.⁹⁴⁷ As swietenolide (**638**) and 2-hydroxy-3-O-tigloylswietenolide (**642**) have the same skeleton, and show

promising antibacterial activity against all the eight tested multiple-drug-resistant (MDR) bacterial strains tested, this limonoid skeleton may be useful as a template for the synthesis of more potent structural analogs.⁶⁴⁹ 2-Hydroxy-3-O-isobutyrylproceranolid (**636**) and 2-hydroxyfissinolid (**649**) exhibited antimicrobial activity against *Micrococcus luteus* ATCC 9341 with MIC values of 50 and 12.5 μ g/mL, respectively.⁴⁵⁸ Moluccensins H–J (**963**, **967**, and **970**) were tested for antibacterial properties against *Staphylococcus aureus*, *S. hominis*, *S. epidermidis*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, and *Salmonella typhimurium*, but only **967** displayed weak activity against *S. hominis* and *E. faecalis* with a MIC at 256 μ g/mL.⁷²³ 6-Acetoxy-7 α -hydroxy-3-oxo-14 β ,15 β -epoxymeliac-1,5-diene (**69**) exhibited strong antibacterial activity against *Salmonella paratyphi* and *Vibrio cholerae* but no data were provided in the original paper.¹⁴²

Neither xylocensin I (**769**) nor xylocensin J (**770**) was active in a broad screening effort which included assays for antimicrobial, antiviral, anthelmintic, and antikinase responses.⁶²⁶ The six limonoids grandifolide A (**775**), anthothecanolide (**779**), 3-O-acetyl anthothecanolide (**780**), 6S-hydroxykhalaceton (**999**), khayanolide A (**1002**), and deacetylkhayanolide E (**1008**), were all inactive in an antimicrobial assay against *Escherichia coli*, *Staphylococcus aureus*, *S. epidermidis*, and *Candida albicans* with MIC values of greater than 50 μ g/mL.⁶⁷⁹

The antiviral activity of limonoids was also investigated. 29-DeacetylSENDANIN (**157**) showed antiviral activity by inhibiting the replication of HSV-1, reducing the synthesis of HSV-1 TK, and leading to the formation of defective nucleocapsids.⁹⁶³ Dysoxylins A–D (**205**–**208**) showed anti-RSV (respiratory syncytial virus) activities with the EC₅₀ values in the range of 1.0–4.0 μ g/mL in cytopathic effect inhibition and plaque reduction assays.²⁵⁵ 1-Cinnamoyl-3,11-dihydroxymeliacarpin (**312**) displayed a potent antiviral action affecting both DNA and RNA viruses by the same mechanism of action, and also comprised an additional biological property consisting of altering the NF- κ B pathway, which suggested an eventual role as an anti-inflammatory agent.³³⁷ In addition, **312** showed IC₅₀ values of 6 μ M and 20 μ M for vesicular stomatitis (VSV) and herpes simplex (HSV-1) viruses, respectively.³³⁶ **312** exerted its antiviral action on the endocytic and exocytic pathways of VSV by pre- and post-treatment, respectively.⁹⁶⁴ In addition to its antiviral effect, **312** would be acting as an immunomodulating candidate, which would be responsible for the improvement of murine HSK already reported.⁹⁶⁵ The delay on glycoprotein transport caused by **312** would account for the strong inhibition on virus multiplication without interfering with the bioactivity of cellular glycoproteins.⁹⁶⁶ Besides, for 6-O-acetyl-2-hydroxyswietenine (**688**), 2-hydroxyswietenine (**689**), 2-hydroxyswietenmahonolide (**797**), swietenmahonin G (**806**), and 6-O-acetylswietenmahonin G (**807**), their antiviral activity against HIV-1 replication was tested by their inhibition of virus-induced cytopathicity in MT-4 cells, and none of them showed activity at 100 μ g/mL.⁶³⁰

5.2.3. Antiprotozoal Activity. Omar et al. reviewed the traditionally used antimalarials from *Azadirachta indica*, *Lansium domesticum*, and *Cedrela odorata*, and presented the improvement of the activity in vivo of gedunin (**416**).⁹⁶⁷ Gedunin (**416**) has been proved to be the most active limonoid according to miscellaneous antimalarial tests up to now. It had IC₅₀ values against *Plasmodium falciparum* of 3.1 and 0.14 μ M using [³H]-hypoxanthine and 48 h culture assays, respectively.⁹⁶⁸ Its antimalarial activity was qualitatively assessed in vitro with an IC₅₀ of

$\sim 1 \mu\text{M}$ after 48 h exposure ($0.3 \mu\text{M}$ after 96 h), which is roughly equivalent to quinine.⁴²⁹ Among the 27 limonoids tested, **416** showed the most potent activity against *P. falciparum* with an IC_{50} value of $0.72 \mu\text{g/mL}$, but it did not inhibit *P. berghei* in a 4-day test in mice at doses of 90 mg/kg/day .⁵⁰⁰ The five limonoids, gedunin (**416**), 1-deacetylkhivorin (**435**), 7-deacetylkhivorin (**437**), methyl angolensate (**568**), and 6-acetylswietenolide (**645**) showed antimalarial activity with IC_{50} values between 1.25 and $9.63 \mu\text{g/mL}$, among which the most active, **416**, had an additive effect with chloroquine.⁴³⁶ When orally administered at 50 mg/kg/d for 4 days, **416** suppressed the parasitemia level by 44%, and synergism with the cytochrome P450 inhibitor dillapiol or addition of a stable methoxy group at the C-7 position increased its antimalarial activity.⁹⁶⁹

Among the four limonoids nimocinol (**7**), meldonin (**243**), isomeldonin (**244**), and nimbandiol (**1101**), **243** was the most active with IC_{50} value of $5.23 \mu\text{g/mL}$ against a chloroquine-resistant *Plasmodium falciparum* strain.²⁷⁰ All limonoids of dysobinin (**11**), azadiradione (**12**), mahonin (**17**), epoxyazadiradione (**60**), and 6α -acetoxyepoxyazadiradione (**62**) had an inhibitory effect against *P. falciparum* with IC_{50} values ranging from 2.06 to $6.31 \mu\text{g/mL}$.⁹⁷ Azadiradione (**12**), domesticulides B–D (**562**, **589**, and **590**), methyl angolensate (**568**), methyl 6-acetoxyangolensate (**570**), dukunolide C (**616**), and 6-acetoxymexicanolide (**631**) showed antimalarial activities against *P. falciparum* with IC_{50} values of 2.4 – $9.7 \mu\text{g/mL}$, and among these **589** was the most active.¹⁰⁰ Anthotechol (**84**) showed potent antimalarial activity against *P. falciparum* with IC_{50} values of 1.4 and $0.17 \mu\text{M}$ as measured by two different assays.⁹⁶⁸ Ceramicine B (**222**) had potent in vitro antiplasmodial activity against *P. falciparum* 3D7 with an IC_{50} value of $0.23 \mu\text{g/mL}$, while ceramicines C and D (**223** and **224**) exhibited moderate activity with IC_{50} values of $2.38 \mu\text{g/mL}$ and $2.15 \mu\text{g/mL}$, respectively.²⁶² Trichirubine A (**226**) had significant antimalarial activity against *P. falciparum* with an IC_{50} value of $0.3 \mu\text{g/mL}$.²⁶³ A single dose of **292** was sufficient to give the insect host-*Rhodnius prolixus*, a permanent resistance against its reinfection with *Trypanosoma cruzi* and to block the ecdysis for a long time.⁹⁷⁰ Fifth-instar larvae of *Rhodnius prolixus*, *Triatoma infestans*, and *Dipetalogaster maximus* infected with different clone/strains of *Trypanosoma cruzi* displayed drastic inhibition of trypanosome development when treated with **292**, which might act directly on gut physiology and/or indirectly through the neurosecretory system.⁹⁷¹ Jones et al. demonstrated blockage of the development of the motile male malarial gamete by azadirachtin (**292**), and changes in the hemiacetal group at C-11 in the molecule resulted in a loss of activity.⁹⁷² In addition, **292** disrupted formation of organized microtubule arrays during microgametogenesis of *P. berghei* and specifically disrupted the patterning of microtubules into more complex structures, such as mitotic spindles and axonemes.⁹⁷³ Nimbolide (**345**) inhibited *P. falciparum* in culture with moderate potency, giving an EC_{50} of 0.95 mg/mL .⁹⁷⁴ 7-Deacetylgedunin (**421**) and 7-deacetoxy-7-oxogedunin (**423**) exhibited good antiprotozoal activity against *Trypanosoma brucei rhodesiense*, *T. cruzi*, *Plasmodium falciparum*, and *Leishmania donovani*, suggesting a lack of specificity for a protozoal target.⁴⁴³ Among mexicanolide (**626**), febrifugin (**694**), cipadesin (**703**), and cipadesin A (**815**), the last, with an IC_{50} value of $136.1 \mu\text{M}$, showed more appreciable trypanocidal activity against *Trypanosoma cruzi*.⁶⁴³ Fissinolide (**648**) was slightly active against chloroquine resistant strains of *P. falciparum* (IC_{50} $48 \pm 3 \mu\text{M}$) and promastigotes of *Leishmania major*

(IC_{50} $69 \pm 13 \mu\text{M}$), and 2,6-dihydroxyfissinolide (**668**) had an IC_{50} of $0.12 \pm 0.08 \text{ mM}$ against *P. falciparum* and an IC_{50} of greater than 0.20 mM against *L. major*.⁶⁰¹ Walsuronoids A and B (**1054** and **1058**) showed 40% inhibition of *P. falciparum* at a concentration of $40 \mu\text{M}$.⁷³⁹

The in vitro trypanocidal activity of six mexicanolide- and gedunin-class limonoids on trypomastigote forms of *Trypanosoma cruzi* was less than the activity of oleanane- and tirucallane-type triterpenes.¹³² Ceramicines B–D (**222**–**224**), which contain a tetrahydrofuran ring, showed potent antiplasmodial activity, whereas ceramicine A (**1118**) without the tetrahydrofuran ring exhibited relatively weak activity.²⁶² From the data obtained with the modified furan moieties of gedunin (**416**), it seemed that this section of the molecule was less important for antimalarial activity than the α,β -unsaturated ketone in ring A and the 7-acetate function in ring B.⁴³² A comparison of the activities of methyl angolensate (**568**) and methyl 6-hydroxyangolensate (**569**) suggested that the addition of a hydroxyl group at C-6 decreased the antimalarial activity considerably.¹⁰⁰

5.2.4. Others. Dysobinin (**11**) showed general CNS-depressant action and mild anti-inflammatory activity.⁶⁶ All of azadiradione (**12**), 7-acetyl-16,17-dehydro-16-hydroxyneotrichilenone (**23**), epoxyazadiradione (**60**), 17-*epi*-17-hydroxyazadiradione (**78**), 7-deacetylgedunin (**421**), and nimolicinol (**451**) exhibited marked anti-inflammatory activity (ID_{50} values 0.09 – 0.26 mg/ear) against TPA-induced inflammation.⁷⁰ 6α -Acetoxyepoxyazadiradione (**62**), gedunin (**416**), 6α -acetoxygedunin (**418**), 7-deacetoxy-7-oxogedunin (**423**), andirobin (**556**), and methyl angolensate (**568**) of *Carapa guianensis* oil were responsible for the antiedematogenic and analgesic effects which were dependent on blockade of signaling mechanisms triggered by histamine, bradykinin, and PAF.⁹⁷⁵ In addition, these limonoids inhibited zymosan-induced arthritis in mice via the impairment of TNF- α , IL-1 β , and CXCL8/IL-8 generation, as well as the NF- κ B signaling pathway.⁹⁷⁶ Isochuanliansu (**179**) and 1-O-tigloyl-1-O-debenzoylohlchinal (**344**) were the active constituents contributing to the anti-inflammatory and analgesic effects of the fruit of *Melia toosendan*.²³⁵ The data provided by Thoh et al. suggested that azadirachtin (**292**) modulated cell surface TNFRs thereby decreasing TNF-induced biological responses, which might be beneficial for anti-inflammatory therapy.⁹⁷⁷ Among the eleven limonoids isolated from *Swietenia macrophylla*, 6-O-acetylswietenmahonin G (**807**) showed the most effective anti-inflammatory activity ($\text{IC}_{50} = 27.6 \pm 1.7 \mu\text{M}$) against fMLP-induced superoxide anion generation.⁶⁵³

Toosendanin (**167**), which itself was not able to form ion channels in lipid bilayers, increased Ca^{2+} conductance related to the intrinsic channel activity.⁹⁷⁸ **167** not only had different effects on various subtypes of calcium channels,⁹⁷⁹ but also had an inhibitory effect on the inward rectifier potassium channel in an excised inside-out patch of the neuron under a symmetrical 150 mM K^{+} condition.⁹⁸⁰ It inhibited the activity of small-conductance calcium-activated potassium channels by significant concentration-dependent reduction of the open probability and open frequency, and these effects were partially reversible.⁹⁸¹ Moreover, **167** did not selectively affect acetylcholine release, but probably acted on a common mechanism responsible for transmitter release at different synapses by interfering with the proteins involved in fusion and resulting in diffusion of the vesicular contents into the cytoplasm and blockage of normal exocytosis.⁹⁸²

Salannin (**332**) showed a significant protective activity on aspirin induced gastric lesions at oral doses of 10, 20, and 50 mg/kg. At 0.5 and 0.25% concentrations, **332** also showed spermicidal activity against human spermatozoa.⁹⁸³ $H^+ K^+$ -ATPase activity in vitro was significantly inhibited by gedunin (**416**) and photogedunin (**433**) with IC_{50} values of 58.86 and 66.54 $\mu\text{g/mL}$, respectively, confirming their antisecretory activity as compared to the IC_{50} value of omeprazole (30.24 $\mu\text{g/mL}$).⁴²⁷ Methyl angolensate (**568**) produced its antiulcer activity by inhibition of gastric acid secretion,⁹⁸⁴ exerted significant spasmolytic activity through concentration dependent inhibition of smooth muscle and reduced the propulsive action of the gastrointestinal tract in mice,⁹⁸⁵ reduced spontaneous motor activity in mice, prolonged the duration of pentobarbital sleeping time, and attenuated amphetamine-induced stereotype behavior in rats.⁹⁸⁶

Among the limonoids tested (swietenolide (**638**), 3-acetyls-wietenolide (**643**), swietenine (**677**), swietemahonin A (**800**), and swietemahonin E (**804**)), when the final concentration of PAF and sample were 7.5×10^{-8} M and 100 $\mu\text{g/mL}$, respectively, **800** showed the strongest anti-PAF activity with an inhibition of 97.4% against rabbit platelet aggregation.⁶⁵² In another test, **800** showed an IC_{50} value of 40.3 $\mu\text{g/mL}$ against PAF-induced aggregation of rabbit platelets in vitro, comparable to that of swietemahonin D (**803**).⁹⁸⁷

Penido et al. demonstrated that in mice the inhibition of allergic eosinophilia by 6 α -acetoxyepoxyazadiradione (**62**), gedunin (**416**), 6 α -acetyoxygedunin (**418**), 7-deacetoxy-7-oxogedunin (**423**), andirobin (**556**), and methyl angolensate (**568**) was correlated with the inhibition of CCL11/eotaxin and IL-5 generation through impairment of the NF- κ B signaling pathway.⁹⁸⁸ 29-Deacetylsendanin (**157**) was found to promote slightly the drug metabolizing enzyme activities and decreased serum transaminase activities, which were elevated by CCl_4 intoxication.²⁰⁴ TS3 (**221**) increased chloride conductance in epithelial cells to an extent comparable to genistein, a known cystic fibrosis transmembrane conductance regulator.²⁶¹ In a similar bioassay, rubralins A and B (**262** and **263**) showed moderate inhibitory activity with IC_{50} values of 30–50 μM .²⁸¹ Rubrins A–G (**518**–**524**), with the hemi ortho ester A-ring moiety which is crucial to potency, showed potent inhibitory activity in the LFA-1:ICAM-1 mediated cell adhesion assay with IC_{50} values of 10–25 nM.⁵⁰⁴ Oral administration of swietenine (**677**) at 25 and 50 mg/kg body weight per day to diabetic rats was found to possess significant dose dependent hypoglycemic and hypolipidemic activity in type 2 diabetic rats.⁶⁶² The contractile response induced by humilinolide A (**793**) could be mediated by estrogens, probably by occupancy of some receptors in myometrial plasma membranes to induce uterotonic response, which might be estrogen-dependent.⁶⁸⁴ Owing to the low DPPH free radical scavenging activity of swietephragmins H and I (**945** and **946**), the IC_{50} values could not be determined in the study proposed by Tan et al.⁷¹⁷ In comparison with pentoxifylline as a standard, the antisickling activity of methyl 1 α , 2 β , 3 α , 6, 8 α , 14 β -hexahydroxy-[4,2,1^{10,30},1^{1,4}]tricyclomeliac-7-oate (**1014**) was much higher at any concentration and incubation condition without altering significantly the corpuscular indices.⁷²⁸

AUTHOR INFORMATION

Corresponding Author

*Phone: 86-871-5223177. Fax: 86-871-5150227. E-mail: xdluo@mail.kib.ac.cn.

BIOGRAPHIES



Qin-Gang Tan was born in Sichuan, China, in 1977. He received his B.Sc. degree from Southwest Forestry College in 2000, M.S. degree from Yunnan University of Traditional Chinese Medicine in 2006, and Ph.D. degree from State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences in 2009. Now he is a lecturer in Natural Products Chemistry Department at Guilin Medical University. His research interests include the structure and biological significance of secondary metabolites in the Traditional Chinese Medicine and ethnopharmacol system.



Xiao-Dong Luo (born 1970) is a professor of natural products chemistry at State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences. He received his B.Sc. degree in Applied Chemistry from East China University of Sciences and Technology (1991), and Ph.D. degree in Phytochemistry from Kunming Institute of Botany, CAS (1999). He worked as an assistant engineer in Yunnan Baiyao Pharmaceutical Corporation (1991), Postdoctoral research fellow (2001) in Lehman College, City University of New York, and a visiting scientist (2005) in Chemistry Department, Oxford University. He is interesting in discovery and development of natural bioactive compounds. During his research career, he has published over 90 scientific papers in international journals. Besides, his group developed a market neem pesticide and finished pre-clinical trials of a new natural medicine in China.

ACKNOWLEDGMENT

The research related to this review was supported by Natural Science Foundation of China (30000213, 30370160, 30670214),

the National Basic Research Program of China (973 Program 2009CB522300), and the Chinese Academy of Sciences (XiBuZhiGuang Project). The authors thank Dr. Yan-Ping Zhang for the courtesy of photographs, Dr. Da-Gang Wu, Dr. Edward J. Kennelly, and Dr. Yi-Wei Li for their advice and polishing on this review, and Dr. Xiang-Hai Cai, Dr. Shu-Hua Qi, Dr. Hua-Ping Zhang et al. for their related phytochemical research.

REFERENCES

- (1) da Silva, M. F. das G. F.; Gottlieb, O. R. *Biochem. Syst. Ecol.* **1987**, *15*, 85.
- (2) Editorial Committee of Flora of China. *Flora Reipublicae Popul-aris Sinicae*; Science Press: Beijing, 1997; Vol. 43.
- (3) Ascher, K. R. S. *Arch. Insect Biochem. Physiol.* **1993**, *22*, 433.
- (4) Liang, G. M.; Chen, W.; Liu, T. X. *Crop Prot.* **2003**, *22*, 333.
- (5) <http://www.neem4organicfarming.com/index2.htm>; accessed December 2009.
- (6) Wang, Y. B.; Wen, Y. X. *J. Tradit. Chin. Med.* **1959**, *262*, 46.
- (7) Connolly, J. D. *Annu. Proc. Phytochem. Soc.* **1983**, *22*, 175.
- (8) Banerji, B.; Nigam, S. K. *Fitoterapia* **1984**, *55*, 3.
- (9) Taylor, D. A. H. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Eds.; Springer: Vienna, 1984; Vol. 45.
- (10) Mackinnon, S.; Chauret, D.; Wang, M.; Mata, R.; Pereda-Miranda, R.; Jimenez, A.; Bernard, C. B.; Krishnamurthy, H. G.; Poveda, L. J.; Sanchez-Vindas, P. E.; Arnason, J. T.; Durst, T. *ACS Symp. Ser.* **1997**, *658*, 49.
- (11) Mulholland, D. A.; Parel, B.; Coombes, P. H. *Curr. Org. Chem.* **2000**, *4*, 1011.
- (12) Connolly, J. D.; Overton, K. H.; Polonsky, J. *Progr. Phytochem.* **1970**, *2*, 385.
- (13) Dreyer, D. L. *Fortschr. Chem. Org. Naturst.* **1968**, *26*, 190.
- (14) Moss, G. P. *Planta Med.* **1966**, *Suppl.*, 86.
- (15) Taylor, D. A. H. In *Annual Proceedings of the Phytochemical Society of Europe*; Waterman, P. G., Grundon, M. F., Eds.; Academic Press: London, 1983; Vol. 22.
- (16) Jain, D. C.; Tripathi, A. K. *Phytother. Res.* **1993**, *7*, 327.
- (17) Champagne, D. E.; Koul, O.; Isman, M. B.; Scudder, G. G. E.; Towers, G. H. N. *Phytochemistry* **1992**, *31*, 377.
- (18) Roy, A.; Saraf, S. *Biol. Pharm. Bull.* **2006**, *29*, 191.
- (19) Sundaram, K. M. S. *J. Environ. Sci. Health, Part B* **1996**, *31*, 913.
- (20) Kraus, W.; Bokel, M.; Schwinger, M.; Vogler, B.; Soellner, R.; Wendisch, D.; Steffens, R.; Wachendorff, U. *Proc. Phytochem. Soc. Eur.* **1993**, *34*, 18.
- (21) Ley, S. V.; Denholm, A. A.; Wood, A. *Nat. Prod. Rep.* **1993**, *10*, 109.
- (22) Hansen Dale, J.; Cuomo, J.; Khan, M.; Gallagher Rex, T.; Ellenberger William, P. In *Natural and Engineered Pest Management Agents*; American Chemical Society: Washington, DC, 1993; Vol. 551.
- (23) Ley, S. V. *Pure Appl. Chem.* **2005**, *77*, 1115.
- (24) Devakumar, C.; Kumar, R. *Curr. Sci.* **2008**, *95*, 573.
- (25) Mordue, A. J.; Blackwell, A. J. *Insect Physiol.* **1993**, *39*, 903.
- (26) Simmonds, M. S. J.; Blaney, W. M. *Entomol. Exp. Appl.* **1996**, *80*, 23.
- (27) Karnavar, G. K. *Proc.—Indian Acad. Sci., Anim. Sci.* **1987**, *96*, 341.
- (28) Subrahmanyam, B. *Proc.—Indian Acad. Sci., Anim. Sci.* **1990**, *99*, 277.
- (29) Lowery, D. T.; Isman, M. B. *ACS Symp. Ser.* **1994**, *557*, 78.
- (30) Mordue, A. J.; Nisbet, A. J. *Ann. Soc. Entomol. Brasil* **2000**, *29*, 615.
- (31) Mordue (Luntz), A. J. In *Neem: Today and in the New Millennium*; Koul, O., Wahab, S., Eds.; Kluwer Academic: Netherlands, 2004.
- (32) Rembold, H. *Adv. Invertebr. Reprod.* **1984**, *3*, 481.
- (33) Schmutterer, H. *J. Insect Physiol.* **1988**, *34*, 713.
- (34) Champagne, D. E.; Isman, M. B.; Towers, G. H. N. *ACS Symp. Ser.* **1989**, *387*, 95.
- (35) Rembold, H. *ACS Symp. Ser.* **1989**, *387*, 150.
- (36) Jacobson, M. *ACS Symp. Ser.* **1986**, *296*, 220.
- (37) Mahato, S. B.; Sahu, N. P.; Podder, G. *Sci. Cult* **1987**, *53*, 29.
- (38) Ley, S. V. *Ciba Found. Symp.* **1990**, *154*, 80.
- (39) Schmutterer, H. *Annu. Rev. Entomol.* **1990**, *35*, 271.
- (40) Akhila, A.; Rani, K. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Eds.; Springer: Vienna, 1999; Vol. 78.
- (41) Biswas, K.; Chattopadhyay, I.; Banerjee, R. K.; Bandyopadhyay, U. *Curr. Sci.* **2002**, *82*, 1336.
- (42) van der Nat, J. M.; van der Sluis, W. G.; de Silva, K. T.; Labadie, R. P. *J. Ethnopharmacol.* **1991**, *35*, 1.
- (43) Govindachari, T. R. *Curr. Sci.* **1992**, *63*, 117.
- (44) Kataria, H. C. *Orient. J. Chem.* **1994**, *10*, 178.
- (45) Vishnukanta, A. C. R. *Pharmacogn. Rev.* **2008**, *2*, 173.
- (46) Nakatani, M. *Insect Antifeeding Limonoids from the Chinaberry Tree Melia Azedarach Linn. And Related Compounds*; CRC Press: New York, 1999; p 1.
- (47) Nakatani, M. In *Bioact. Compd. Nat. Sources*; Tringali, C., Ed.; Taylor & Francis Ltd.: London, 2001.
- (48) Govindachari, T. R. *J. Indian Chem. Soc.* **1968**, *45*, 1063.
- (49) Uddin, S. J.; Nahar, L.; Shilpi, J. A.; Shoeb, M.; Borkowski, T.; Gibbons, S.; Middleton, M.; Byres, M.; Sarker, S. D. *Phytother. Res.* **2007**, *21*, 757.
- (50) Narender, T.; Khaliq, T.; Shweta; Reddy, K. P.; Sharma, R. K. *Nat. Prod. Commun.* **2007**, *2*, 203.
- (51) Butterworth, J. H.; Morgan, E. D. *J. Chem. Soc., Chem. Commun.* **1968**, *1*, 23.
- (52) Broughton, H. B.; Ley, S. V.; Slawin, A. M. Z.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1986**, *1*, 46.
- (53) Ren, Y. L.; Tang, Q. R.; Di, Y. T.; He, H. P.; Zhang, Z.; Li, S. L.; Hao, X. J. *Helv. Chim. Acta* **2007**, *90*, 764.
- (54) Yuan, X. H.; Li, B. G.; Xu, C. X.; Zhou, M.; Qi, H. Y.; Zhang, G. L. *Chem. Pharm. Bull.* **2007**, *55*, 902.
- (55) Taylor, A. R. H.; Taylor, D. A. H. *Phytochemistry* **1983**, *22*, 2870.
- (56) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Chem. Pharm. Bull.* **1990**, *38*, 894.
- (57) Lavie, D.; Jain, M. K. *Chem. Commun. (London)* **1967**, *6*, 278.
- (58) Lavie, D.; Levy, E. C.; Jain, M. K. *Tetrahedron* **1971**, *27*, 3927.
- (59) Ali, M.; Qadry, J. S. *Curr. Sci.* **1988**, *57*, 550.
- (60) Halsall, T. G.; Troke, J. A. *J. Chem. Soc., Perkin Trans. 1* **1975**, *18*, 1758.
- (61) Suresh, G.; Narasimhan, N. S.; Palani, N. *Phytochemistry* **1997**, *45*, 807.
- (62) Suresh, G.; Narasimhan, N. S.; Masilamani, S.; Partho, P. D.; Gopalakrishnan, G. *Phytoparasitica* **1997**, *25*, 33.
- (63) Kabaleeswaran, V.; Malathi, R.; Rajan, S. S.; Suresh, G.; Narashiman, N. S. *Acta Crystallogr., Sect. C* **2000**, *S6*, 82.
- (64) Siddiqui, S.; Siddiqui, B. S.; Faizi, S.; Mahmood, T. *Phytochemistry* **1984**, *23*, 2899.
- (65) Gopalakrishnan, G.; Singh, N. D. P.; Kasinath, V. *Molecules* **2002**, *7*, 112.
- (66) Singh, S.; Garg, H. S.; Khanna, N. M. *Phytochemistry* **1976**, *15*, 2001.
- (67) Sarkhel, S.; Jain, G. K.; Singh, S.; Subramanya, H. S.; Maulika, P. R. *Acta Crystallogr., Sect. C* **2000**, *S6*, e253.
- (68) Kraus, W.; Cramer, R.; Sawitzki, G. *Phytochemistry* **1981**, *20*, 117.
- (69) Saikia, B.; Katakya, J. C. S.; Mathur, R. K.; Baruah, J. N. *Indian J. Chem., Sect. B* **1978**, *16*, 1042.
- (70) Akihisa, T.; Noto, T.; Takahashi, A.; Fujita, Y.; Banno, N.; Tokuda, H.; Koike, K.; Suzuki, T.; Yasukawa, K.; Kimura, Y. *J. Oleo Sci.* **2009**, *S8*, 581.
- (71) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Chem. Pharm. Bull.* **1990**, *38*, 1495.
- (72) Siddiqui, S.; Mahmood, T.; Faizi, S.; Siddiqui, B. S. *J. Chem. Soc., Perkin Trans. 1* **1987**, *7*, 1429.
- (73) Narayanan, C. R.; Pachapurkar, R. V.; Sawant, B. M. *Tetrahedron Lett.* **1967**, *37*, 3563.

- (74) Chan, W. R.; Gibbs, J. A.; Taylor, D. R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1047.
- (75) Mulholland, D. A.; Osborne, R.; Roberts, S. L.; Taylor, D. A. H. *Phytochemistry* **1994**, *37*, 1417.
- (76) Nakatani, M.; Okamura, H.; Iwagawa, T.; Huang, R. C.; Zhou, J. B.; Yagi, F.; Tadera, K. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1995**, *37*, 289.
- (77) Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., C* **1968**, *14*, 1828.
- (78) Narayanan, C. R.; Pachapurkar, R. V.; Sawant, B. M.; Wadia, M. S. *Indian J. Chem.* **1969**, *7*, 187.
- (79) Siddiqui, S.; Siddiqui, B. S.; Ghiasuddin, Faizi, S. *Phytochemistry* **1991**, *30*, 1615.
- (80) Siddiqui, S.; Faizi, S.; Mahmood, T.; Siddiqui, B. S. *J. Chem. Soc., Perkin Trans. 1* **1986**, *6*, 1021.
- (81) Siddiqui, S.; Faizi, S.; Siddiqui, B. S.; Ghiasuddin, J. *Nat. Prod.* **1992**, *55*, 303.
- (82) Siddiqui, S.; Faizi, S.; Siddiqui, B. S. *Z. Naturforsch., B* **1986**, *41*, 922.
- (83) Nanduri, S.; Thunuguntla, S. S. R.; Nyavanandi, V. K.; Kasu, S.; Kumar, P. M.; Ram, P. S.; Rajagopal, S.; Kumar, R. A.; Deevi, D. S.; Rajagopalan, R.; Venkateswarlu, A. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4111.
- (84) Zhou, J. B.; Minami, Y.; Yagi, F.; Tadera, K.; Nakatani, M. *Phytochemistry* **1997**, *46*, 911.
- (85) Nakatani, M. *Heterocycles* **1999**, *50*, 595.
- (86) Arenas, C.; Rodriguez-Hahn, L. *Phytochemistry* **1990**, *29*, 2953.
- (87) Bentley, M. D.; Gaul, F.; Rajab, M. S.; Hassanali, A. *J. Nat. Prod.* **1992**, *55*, 84.
- (88) Purushothaman, K. K.; Duraiswamy, K.; Connolly, J. D.; Rycroft, D. S. *Phytochemistry* **1985**, *24*, 2349.
- (89) Ekong, D. E. U.; Okogun, J. I.; Sondengam, B. L. *J. Chem. Soc., Perkin Trans. 1* **1975**, *21*, 2118.
- (90) Odero, O. J. H.; Ndung'u, M.; Hassanali, A. *J. Kenya Chem. Soc.* **2008**, *5*, 43.
- (91) Laphookhieo, S.; Maneerat, W.; Koysomboon, S.; Kiattansakul, R.; Chantrapromma, K.; Syers, J. K. *Can. J. Chem.* **2008**, *86*, 205.
- (92) Siddiqui, B. S.; Afshan, F.; Gulzar, T.; Hanif, M. *Phytochemistry* **2004**, *65*, 2363.
- (93) Siddiqui, B. S.; Afshan, F.; Ghiasuddin, Faizi, S.; Naqvi, S. N. H.; Tariq, R. M. *Phytochemistry* **2000**, *53*, 371.
- (94) Chatterjee, A.; Nayak, L.; Das, B.; Patra, A.; Dhara, K. P.; Mukherjee, K.; Banerji, J.; Shoolery, J. N. *Indian J. Chem., Sect. B* **1989**, *28*, 231.
- (95) Yadav, R. D.; Katakya, J. C. S.; Mathur, R. K. *Indian J. Chem., Sect. B* **1999**, *38*, 1359.
- (96) Sarmah, G. K.; Bhattacharyya, N. K.; Goswami, B. N.; Borthakur, N.; Baruah, P.; Katakya, J. C. S. *Chemistry (Rajkot, India)* **2003**, *1*, 42.
- (97) Maneerat, W.; Laphookhieo, S.; Koysomboon, S.; Chantrapromma, K. *Phytomedicine* **2008**, *15*, 1130.
- (98) de Paula, J. R.; Vieira, I. J. C.; da Silva, M. F. das G. F.; Fo, E. R.; Fernandes, J. B.; Vieira, P. C.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1997**, *44*, 1449.
- (99) Coombes, P. H.; Mulholland, D. A.; Randrianarivelosoa, M. *Phytochemistry* **2004**, *65*, 377.
- (100) Saewan, N.; Sutherland, J. D.; Chantrapromma, K. *Phytochemistry* **2006**, *67*, 2288.
- (101) Lee, S. M.; Olsen, J. I.; Schweizer, M. P.; Klocke, J. A. *Phytochemistry* **1988**, *27*, 2773.
- (102) Govindachari, T. R.; Sandhya, G.; Raj, S. P. G. *Indian J. Chem., Sect. B* **1992**, *31*, 295.
- (103) Ishida, M.; Serit, M.; Nakata, K.; Juneja, L. R.; Kim, M.; Takahashi, S. *Biosci. Biotechnol. Biochem.* **1992**, *56*, 1835.
- (104) Serit, M.; Ishida, M.; Nakata, K.; Kim, M.; Takahashi, S. *Nippon Noyaku Gakkaishi* **1992**, *17*, 267.
- (105) Govindachari, T. R.; Suresh, G.; Gopalakrishnan, G.; Banumathy, B.; Masilamani, S. *Phytoparasitica* **1998**, *26*, 109.
- (106) Govindachari, T. R.; Suresh, G.; Gopalakrishnan, G. *J. Liq. Chromatogr.* **1995**, *18*, 3465.
- (107) Kraus, W.; Koll-Weber, M.; Maile, R.; Wunder, T.; Vogler, B. *Pure Appl. Chem.* **1994**, *66*, 2347.
- (108) Siddiqui, S.; Waheed, T. N.; Luecke, J.; Voelter, W. *Z. Naturforsch., B* **1975**, *30*, 961.
- (109) Siddiqui, S.; Faizi, S. S.; Shaheen, B. *Z. Naturforsch., B* **1986**, *41*, 922.
- (110) Galkwad, B. R.; Mayelvaganan, T.; Vyas, B. A.; Bhat, S. V. *Phytochemistry* **1990**, *29*, 3963.
- (111) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Chem. Pharm. Bull.* **1989**, *37*, 1419.
- (112) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Chem. Pharm. Bull.* **1990**, *38*, 639.
- (113) Ambrozina, A. R. P.; Leite, A. C.; Bueno, F. C.; Vieira, P. C.; Fernandes, J. B.; Bueno, O. C.; da Silva, M. F. das G. F.; Pagnocca, F. C.; Hebling, M. J. A.; Bacci, M., Jr. *J. Braz. Chem. Soc.* **2006**, *17*, 542.
- (114) Kraus, W.; Cramer, R. *Tetrahedron Lett.* **1978**, *19*, 2395.
- (115) Hallur, G.; Sivramakrishnan, A.; Bhat, S. V. *J. Nat. Prod.* **2002**, *65*, 1177.
- (116) Siddiqui, S.; Fuchs, S.; Lucke, J.; Voelter, W. *Tetrahedron Lett.* **1978**, *19*, 611.
- (117) Connolly, J. D.; Labbe, C.; Rycroft, D. S.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, *12*, 2959.
- (118) Siddiqui, S.; Mahmood, T.; Siddiqui, B. S.; Faizi, S. *Heterocycles* **1987**, *26*, 1827.
- (119) Siddiqui, B. S.; Afshan, F.; Ghiasuddin, Faizi, S.; Naqvi, S. N.-u.-H.; Tariq, R. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, *16*, 2367.
- (120) Siddiqui, B. S.; Afshan, F.; Faizi, S.; Naeem-ul-Hassan Naqvi, S.; Tariq, R. M. *J. Nat. Prod.* **2002**, *65*, 1216.
- (121) Siddiqui, S.; Siddiqui, B. S.; Mahmood, T.; Faizi, S. *Heterocycles* **1989**, *29*, 87.
- (122) Siddiqui, S.; Faizi, S.; Mahmood, T.; Siddiqui, B. S. *Heterocycles* **1986**, *24*, 1319.
- (123) Siddiqui, B. S.; Ghiasuddin, Faizi, S.; Rasheed, M. *J. Nat. Prod.* **1999**, *62*, 1006.
- (124) Siddiqui, B. S.; Ali, S. T.; Rasheed, M.; Kardar, M. N. *Helv. Chim. Acta* **2003**, *86*, 2787.
- (125) Cheplogoi, P. K.; Mulholland, D. A. *Phytochemistry* **2003**, *62*, 1173.
- (126) Wang, X. N.; Yin, S.; Fan, C. Q.; Lin, L. P.; Ding, J.; Yue, J. M. *Tetrahedron* **2007**, *63*, 8234.
- (127) Siddiqui, B. S.; Rasheed, M. *Helv. Chim. Acta* **2001**, *84*, 1962.
- (128) Siddiqui, B. S.; Ghiasuddin, Faizi, S. *Phytochemistry* **1998**, *47*, 1631.
- (129) Cortez, D. A. G.; Fernandes, J. B.; Viera, P. C.; da Silva, M. F. das G. F.; Ferreira, A. G.; Cass, Q. B.; Pirani, J. R. *Phytochemistry* **1998**, *49*, 2493.
- (130) Kumar, C. S. S. R.; Srinivas, M.; Yakkundi, S. *Phytochemistry* **1996**, *43*, 451.
- (131) Gunning, P. J.; Jeffs, L. B.; Isman, M. B.; Towers, G. H. N. *Phytochemistry* **1994**, *36*, 1245.
- (132) Leite Ana, C.; Ambrozina Alessandra, R.; Fernandes Joao, B.; Vieira Paulo, C.; da Silva, M. F. das G. F.; de Albuquerque, S. *Planta Med.* **2008**, *74*, 1795.
- (133) Zhang, Y.; Tang, C. P.; Ke, C. Q.; Yao, S.; Ye, Y. *J. Nat. Prod.* **2010**, *73*, 664.
- (134) Connolly, J. D.; Handa, K. L.; McCrindle, R. *Tetrahedron Lett.* **1968**, *9*, 437.
- (135) Madhusudan, K. P.; Chaturvedi, R.; Garg, H. S.; Bhakuni, D. S. *Indian J. Chem., Sect. B* **1984**, *23*, 1082.
- (136) Siddiqui, S.; Mitra, C. J. *Sci. Ind. Res.* **1945**, *4*, 5.
- (137) Lavie, D.; Levy, E. C.; Zelnik, R. *Bioorg. Chem.* **1972**, *2*, 59.
- (138) Maneerat, W.; Fun, H. K.; Buatip, T.; Laphookhieo, S.; Chantrapromma, S. *Acta Crystallogr., Sect. E* **2007**, *63*, o3583.
- (139) Govindachari, T. R.; Malathi, R.; Gopalakrishnan, G.; Suresh, G.; Rajan, S. S. *Phytochemistry* **1999**, *52*, 1117.
- (140) Neto, J. O.; Agostinho, S. M. M.; da Silva, M. F. das G. F.; Vieira, P. C.; Fernandes, J. B.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1995**, *38*, 397.

- (141) Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1972**, 12, 1488.
- (142) Srivastava, S. K.; Gupta, H. O. *Indian J. Chem., Sect. B* **1985**, 24, 166.
- (143) Mulholland, D. A.; Monkhe, T. V.; Coombes, P. H.; Rajab, M. S. *Phytochemistry* **1998**, 49, 2585.
- (144) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G. *J. Nat. Prod.* **2000**, 63, 947.
- (145) Ning, J.; He, H. P.; Li, S. F.; Geng, Z. L.; Fang, X.; Di, Y. T.; Li, S. L.; Hao, X. J. *J. Asian Nat. Prod. Res.* **2010**, 12, 448.
- (146) Das, K.; Sinha, U. C.; Mayelvaganan, T.; Bhat, S. V.; Tavale, S. S. *Acta Crystallogr., Sect. C* **1991**, 47, 1426.
- (147) Parihar, D. B.; Dutt, S. J. *Indian Chem. Soc.* **1950**, 27, 77.
- (148) Grant, I. J.; Hamilton, J. A.; Hamor, T. A.; Hodges, R.; McGeachin, S. G.; Raphael, R. A.; Robertson, J. M.; Sim, G. A. *Proc. Chem. Soc., London* **1961**, Dec, 444.
- (149) Gofrinath, K. W.; Govindachari, T. R.; Parthasarathy, P. C.; Viswanathan, N.; Arigoni, D.; Wildmann, W. C. *Proc. Chem. Soc., London* **1961**, Dec, 446.
- (150) Hodges, R.; McGeachin, S. G.; Raphael, R. A. *J. Chem. Soc.* **1963**, 2515.
- (151) Aghoramurthy, K.; Dass, I.; Mukherjee, S. K.; Rao, M. M. *J. Sci. Ind. Res. (India)* **1962**, 21B, 95.
- (152) Chaudhuri, B.; Das, I. M.; Talukdar, A. N. *Indian J. Phys.* **1962**, 36, 602.
- (153) Grant, I. J.; Miss, J. A. H.; Hamor, T. A.; Robertson, J. M.; Sim, G. A. *J. Chem. Soc.* **1963**, 2506.
- (154) Agostinho, S. M. M.; Fatima, M.; da Silva, M. F. das G. F.; Fernandes, J. B.; Vieira, P. C.; Pinheiro, A. L.; Vilela, E. F. *Biochem. Syst. Ecol.* **1994**, 22, 323.
- (155) Gopalakrishnan, G.; Singh, N. D. P.; Kasinath, V.; Malathi, R.; Rajan, S. S. *Photochem. Photobiol.* **2000**, 72, 464.
- (156) Burke, B. A.; Chan, W. R.; Rawle, J. R.; Taylor, D. R. *Experientia* **1977**, 33, 578.
- (157) Devi, S. S.; Rajan, S. S.; Kumar, R. M.; Narasimhan, S. *Acta Crystallogr., Sect. E* **2007**, 63, o3963.
- (158) Chatterjee, A.; Chakraborty, T.; Chandrasekharan, S. *Phytochemistry* **1971**, 10, 2533.
- (159) Banerji, R.; Mitra, C. R. *Planta Med.* **1975**, 28, 52.
- (160) Modey, W. K.; Mulholland, D. A.; Raynor, M. W. *J. Chromatogr. Sci.* **1996**, 34, 320.
- (161) Neto, J. O.; da Silva, M. F. das G. F.; Fo, E. R.; Fernandes, J. B.; Vieira, P. C.; Pinheiro, A. L. *Phytochemistry* **1998**, 49, 1369.
- (162) Mulholland, D. A.; Taylor, D. A. H. *Phytochemistry* **1992**, 31, 4163.
- (163) Adesogan, E. K.; Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., C* **1970**, 2, 205.
- (164) Adesida, G. A.; Adesogan, E. K.; Okorie, D. A.; Taylor, D. A. H.; Styles, B. T. *Phytochemistry* **1971**, 10, 1845.
- (165) Matos, A. P.; Nebo, L.; Vieira, P. C.; Fernandes, J. B.; da Silva, M. F. das G. F.; Rodrigues, R. R. *Quim. Nova* **2009**, 32, 1553.
- (166) Bevan, C. W. L.; Rees, A. H.; Taylor, D. A. H. *J. Chem. Soc.* **1963**, 983.
- (167) Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H. *J. Chem. Soc.* **1963**, 980.
- (168) Bevan, C. W. L.; Ekong, D. E. U.; Taylor, D. A. H. *Nature (London, U. K.)* **1965**, 206, 1323.
- (169) Chan, W. R.; Taylor, D. R. *Chem. Commun. (London)* **1966**, 7, 206.
- (170) Xie, Y. S.; Isman, M. B.; Gunning, P.; MacKinnon, S.; Arnason, J. T.; Taylor, D. R.; Sanchez, P.; Hasbun, C.; Towers, G. H. N. *Biochem. Syst. Ecol.* **1994**, 22, 129.
- (171) Simmonds, M. S. J.; Stevenson, P. C.; Porter, E. A.; Veitch, N. C. *J. Nat. Prod.* **2001**, 64, 1117.
- (172) Cortez, D. A. G.; Vieira, P. C.; Fernandes, J. B.; da Silva, M. F. das G. F.; Ferreira, A. G. *Phytochemistry* **1992**, 31, 625.
- (173) Srivastava, S. D.; Srivastava, S. K. *J. Indian Chem. Soc.* **1996**, 73, 467.
- (174) Srivastava, S. D. *Planta Med.* **1987**, 53, 100.
- (175) Rusia, K.; Srivastava *Proc. Natl. Acad. Sci. India, Sect. A* **1988**, 58, 33.
- (176) Srivastava, S. D. *J. Nat. Prod.* **1986**, 49, 56.
- (177) Okorie, D. A.; Taylor, D. A. H. *Chem. Commun.* **1968**, 13, 737.
- (178) Connolly, J. D.; Handa, K. L.; McCrindle, R.; Overton, K. H. *J. Chem. Soc., C* **1968**, 2227.
- (179) Ochi, M.; Kotsuki, H.; Tokoroyama, T. *Chem. Lett.* **1978**, 6, 621.
- (180) Torto, B.; Bentley, M. D.; Cole, B. J. W.; Hassanali, A.; Huang, F. Y.; Gelbaum, L.; Vanderveer, D. G. *Phytochemistry* **1995**, 40, 239.
- (181) Chan, W. R.; Gibbs, J. A.; Taylor, D. R. *Chem. Commun.* **1967**, 14, 720.
- (182) Taylor, D. R. *Rev. Latinoam. Quim.* **1971**, 2, 87.
- (183) Adesogan, E. K.; Taylor, D. A. H. *Chem. Commun.* **1967**, 8, 379.
- (184) Taylor, D. A. H. *J. Chem. Soc., C* **1969**, 18, 2439.
- (185) Connolly, J. D.; Handa, K. L.; McCrindle, R.; Overton, K. H. *Chem. Commun. (London)* **1966**, 23, 867.
- (186) Zhang, Q.; Shi, Y.; Liu, X. T.; Liang, J. Y.; Ip, N. Y.; Min, Z. D. *Planta Med.* **2007**, 73, 1298.
- (187) Rogers, L. L.; Zeng, L.; Kozlowski, J. F.; Shimada, H.; Alali, F. Q.; Johnson, H. A.; McLaughlin, J. L. *J. Nat. Prod.* **1998**, 61, 64.
- (188) Ndung'u, M. W.; Kaoneka, B.; Hassanali, A.; Lwande, W.; Hooper, A. M.; Tayman, F.; Zerbe, O.; Torto, B. *J. Agric. Food Chem.* **2004**, 52, 5027.
- (189) Akinniyi, J. A.; Connolly, J. D.; Mulholland, D. A.; Rycroft, D. S.; Taylor, D. A. H. *Phytochemistry* **1986**, 25, 2187.
- (190) Torto, B.; Hassanali, A.; Nyandat, E.; Bentley, M. D. *Phytochemistry* **1996**, 42, 1235.
- (191) Bentley, M. D.; Adul, G. O.; Alford, A. R.; Huang, F. Y.; Gelbaum, L.; Hassanali, A. *J. Nat. Prod.* **1995**, 58, 748.
- (192) Gunatilaka, A. A. L.; da S. Bolzani, V.; Dagne, E.; Hofmann, G. A.; Johnson, R. K.; McCabe, F. L.; Mattern, M. R.; Kingston, D. G. I. *J. Nat. Prod.* **1998**, 61, 179.
- (193) Nakatani, M.; Nakanishi, K. *Kagoshima Daigaku Rigakubu Kiyo, Sugaku, Butsurigaku, Kagaku* **1992**, 25, 59.
- (194) Nakatani, M.; James, J. C.; Nakanishi, K. *J. Am. Chem. Soc.* **1981**, 103, 1228.
- (195) Oelrichs, P. B.; Hill, M. W.; Valley, P. J.; MacLeod, J. K.; Molinski, T. F. *Phytochemistry* **1983**, 22, 531.
- (196) Polonsky, J.; Varon, Z.; Arnoux, B.; Pascard, C.; Pettit, G. R.; Schmidt, J. H.; Lange, L. M. *J. Am. Chem. Soc.* **1978**, 100, 2575.
- (197) Arnoux, B.; Pascard, C. *Acta Crystallogr., Sect. B* **1980**, 36, 2709.
- (198) Kubo, I.; Klocke, J. A. *Experientia* **1982**, 38, 639.
- (199) Ochi, M.; Kotsuki, H.; Hirotsu, K.; Tokoroyama, T. *Tetrahedron Lett.* **1976**, 17, 2877.
- (200) Nakatani, M.; Iwashita, T.; Naoki, H.; Hase, T. *Phytochemistry* **1985**, 24, 195.
- (201) Ochi, M.; Kotsuki, H.; Ishida, H.; Tokoroyama, T. *Chem. Lett.* **1978**, 1, 99.
- (202) Kim, Y. H.; Hwang, B. Y.; Kim, S. E.; Kim, H. M.; Oh, G. T.; Ro, J. S.; Lee, K. S.; Lee, J. J. *Yakhak Hoechi* **1994**, 38, 6.
- (203) Kim, H. M.; Oh, G. T.; Han, S. B.; Hong, D. H.; Hwang, B. Y.; Kim, Y. H.; Lee, J. J. *Arch. Pharmacol. Res.* **1994**, 17, 100.
- (204) Kim, B.; Kim, H.; Choi, J. W.; Lee, C. K. *Saengyak Hakhoechi* **1996**, 27, 47.
- (205) Itokawa, H.; Qiao, Z. S.; Hirobe, C.; Takeya, K. *Chem. Pharm. Bull.* **1995**, 43, 1171.
- (206) Nakatani, M.; Huang, R. T.; Arikawa, S.; Yamauchi, K.; Okamura, H.; Iwagawa, T.; Naoki, H. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1993**, 35, 385.
- (207) Huang, R. C.; Okamura, H.; Iwagawa, T.; Nakatani, M. *Bull. Chem. Soc. Jpn.* **1994**, 67, 2468.
- (208) Carpinella, C.; Ferrayoli, C.; Valladares, G.; Defago, M.; Palacios, S. *Biosci. Biotechnol. Biochem.* **2002**, 66, 1731.
- (209) Huang, R. C.; Zhou, J. B.; Suenaga, H.; Takezaki, K.; Kenjiro, T.; Nakatani, M. *Biosci. Biotechnol. Biochem.* **1995**, 59, 1755.

- (210) Polonsky, J.; Varon, Z.; Marazano, C.; Arnoux, B.; Pettit, G. R.; Schmid, J. M.; Ochi, M.; Kotsuki, H. *Experientia* **1979**, *35*, 987.
- (211) Tada, K.; Takido, M.; Kitanaka, S. *Phytochemistry* **1999**, *51*, 787.
- (212) Nakatani, M.; Fukuman, Y.; Sakumoto, T.; Yamashita, N.; Okamura, H.; Iwagawa, T. *Heterocycles* **2000**, *53*, 689.
- (213) Ahn, J. W.; Choi, S. U.; Lee, C. O. *Phytochemistry* **1994**, *36*, 1493.
- (214) Zhou, J. B.; Minami, Y.; Yagi, F.; Tadera, K.; Nakatani, M. *Heterocycles* **1997**, *45*, 1781.
- (215) Chung, C. C.; Hsie, T. H.; Chen, S. F.; Liang, H. T. *Acta Pharmac. Sin.* **1975**, *33*, 35.
- (216) Shu, G. X.; Liang, X. T. *Acta Pharmac. Sin.* **1980**, *38*, 196.
- (217) Vardamides, J. C.; Dongo, E.; Nkengfack, A. E.; Fomum, Z. T.; Ngando, T. M.; Vogler, B.; Kraus, W. *Fitoterapia* **2001**, *72*, 386.
- (218) Fukuyama, Y.; Nakaoka, M.; Yamamoto, T.; Takahashi, H.; Minami, H. *Chem. Pharm. Bull.* **2006**, *54*, 1219.
- (219) Huang, R. C.; Okamura, H.; Iwagawa, T.; Suenaga, H.; Nakatani, M. *Kagoshima Daigaku Rigakubu Kiyo, Sugaku, Butsurigaku, Kagaku* **1994**, *27*, 45.
- (220) Nakatani, M.; Chun Huang, R.; Okamura, H.; Naoki, H.; Iwagawa, T. *Phytochemistry* **1994**, *36*, 39.
- (221) Takeya, K.; Qiao, Z. S.; Hirobe, C.; Itokawa, H. *Bioorg. Med. Chem.* **1996**, *4*, 1355.
- (222) Oelrichs, P. B.; Hill, M. W.; Vallely, P. J.; MacLeod, J. K.; Molinski, T. F. In *Plant Toxicology, Proceedings of the Australia–U.S.A. Poisonous Plants Symposium*; Seawright, A. A., Ed.; Queensland Poisonous Plants Committee: Yeerongpilly, Australia, 1985.
- (223) Nakatani, M.; Nakanishi, K. *Heterocycles* **1993**, *36*, 725.
- (224) Zhou, J. B.; Okamura, H.; Iwagawa, T.; Nakatani, M. *Phytochemistry* **1996**, *41*, 117.
- (225) Zhou, J. B.; Tadera, K.; Minami, Y.; Yagi, F.; Kurawaki, J.; Takezaki, K.; Nakatani, M. *Biosci. Biotechnol. Biochem.* **1998**, *62*, 496.
- (226) Zhou, H. L.; Hamazaki, A.; Fontana, J. D.; Takahashi, H.; Wandscheer, C. B.; Fukuyama, Y. *Chem. Pharm. Bull.* **2005**, *53*, 1362.
- (227) Nakatani, M.; Zhou, J. B.; Iwagawa, T.; Okamura, H. *Heterocycles* **1994**, *38*, 2407.
- (228) Huang, R. C.; Okamura, H.; Iwagawa, T.; Tadera, K.; Nakatani, M. *Phytochemistry* **1995**, *38*, 593.
- (229) Polonsky, J.; Varon, Z.; Arnoux, B.; Pascard, C.; Pettit, G. R.; Schmidt, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 7731.
- (230) Nakatani, M.; Huang, R. C.; Okamura, H.; Iwagawa, T.; Tadera, K. *Phytochemistry* **1998**, *49*, 1773.
- (231) Ahn, J. W.; Yoo, G. S.; Ho, Z.; Lee, S. H. *Bull. Korean Chem. Soc.* **1993**, *14*, 554.
- (232) Ahn, J. W.; Choe, S. W.; Lee, J. O.; Ji, O. P.; Yu, S. Y.; Han, J. S. KR Patent 9615969, 1996; *Chem. Abstr.* **2000**, *133*, 238153.
- (233) Zhou, C. Y.; Tang, H. Y.; Li, X.; Sang, Y. S. *Helv. Chim. Acta* **2009**, *92*, 1191.
- (234) Xie, J. X.; Yuan, A. X. *Acta Pharmacol. Sin.* **1985**, *20*, 188.
- (235) Xie, F.; Zhang, M.; Zhang, C. F.; Wang, Z. T.; Yu, B. Y.; Kou, J. P. *J. Ethnopharmacol.* **2008**, *117*, 463.
- (236) Podder, G.; Mahato, S. B. *Heterocycles* **1985**, *23*, 2321.
- (237) Nakatani, M.; Iwashita, T.; Mizukawa, K.; Hase, T. *Heterocycles* **1987**, *26*, 43.
- (238) Pachapurkar, R. V.; Kornule, P. M.; Narayanan, C. R. *Chem. Lett.* **1974**, *4*, 357.
- (239) Zhou, J. B.; Okamura, H.; Iwagawa, T.; Yumiko, N.; Nakayama, N.; Tadera, K.; Nakatani, M. *Heterocycles* **1995**, *41*, 2795.
- (240) Ekong, D. E. U.; Fakunle, C. O.; Fasina, A. K.; Okogun, J. I. *J. Chem. Soc., Chem. Commun.* **1969**, *20*, 1166.
- (241) Zhang, H. P.; Bao, G. H.; Wang, H. B.; Qin, G. W. *Nat. Prod. Res.* **2004**, *18*, 415.
- (242) Murphy, B. T.; Brodie, P.; Slebodnick, C.; Miller, J. S.; Birkinshaw, C.; Randriananjana, L. M.; Andriantsiferana, R.; Rasamison, V. E.; TenDyke, K.; Suh, E. M.; Kingston, D. G. I. *J. Nat. Prod.* **2008**, *71*, 325.
- (243) Cheplogoi, P. K.; Mulholland, D. A. *Biochem. Syst. Ecol.* **2003**, *31*, 799.
- (244) Coombes, P. H.; Mulholland, D. A.; Randrianarivelosia, M. *Biochem. Syst. Ecol.* **2008**, *36*, 74.
- (245) Kraus, W.; Cramer, R. *Liebigs Ann. Chem.* **1981**, *1*, 181.
- (246) Rajab, M. S.; Bentley, M. D. *J. Nat. Prod.* **1988**, *51*, 840.
- (247) Nakatani, M.; Shimokoro, M.; Zhou, J. B.; Okamura, H.; Iwagawa, T.; Tadera, K.; Nakayama, N.; Naoki, H. *Phytochemistry* **1999**, *52*, 709.
- (248) Zeng, L.; Gu, Z. M.; Fang, X. P.; Fanwick, P. E.; Chang, C. J.; Smith, D. L.; McLaughlin, J. L. *Tetrahedron* **1995**, *51*, 2477.
- (249) Mitra, C. R.; Garg, H. S.; Pandey, G. N. *Phytochemistry* **1971**, *10*, 857.
- (250) Mitra, C. R.; Garg, H. S.; Pandey, G. N. *Tetrahedron Lett.* **1970**, *11*, 2761.
- (251) Okogun, J. I.; Fakunle, C. O.; Ekong, D. E. U.; Connolly, J. D. *J. Chem. Soc., Perkin Trans. 1* **1975**, *14*, 1352.
- (252) Banerji, R.; Nigam, S. K. *Fitoterapia* **1981**, *52*, 3.
- (253) Purushothaman, K. K.; Duraiswamy, K.; Connolly, J. D. *Phytochemistry* **1984**, *23*, 135.
- (254) Srivastava, S. D.; Srivastava, S. K. *Fitoterapia* **1996**, *67*, 113.
- (255) Chen, J. L.; Kernan, M. R.; Jolad, S. D.; Stoddart, C. A.; Bogan, M.; Cooper, R. *J. Nat. Prod.* **2007**, *70*, 312.
- (256) Ragasa, C. Y.; Nacpil, Z. D.; Natividad, G. M.; Tada, M.; Coll, J. C.; Rideout, J. A. *Phytochemistry* **1997**, *46*, 555.
- (257) Bilton, J. N.; Broughton, H. B.; Jones, P. S.; Ley, S. V.; Rzepa, H. S.; Sheppard, R. N.; Slawin, A. M. Z.; Williams, D. J.; Lidert, Z.; Morgan, E. D. *Tetrahedron* **1987**, *43*, 2805.
- (258) Nguyen, K. P. P.; Nguyen, T. A. T.; Tran, T. T. *Tap Chi Hoa Hoc* **2004**, *42*, 227.
- (259) Cai, X. H.; Luo, X. D. *Chin. J. Chem.* **2007**, *25*, 986.
- (260) Siddiqui, S.; Ghiasuddin, S.; Bina, Faizi, S. *Pak. J. Sci. Ind. Res.* **1989**, *32*, 435.
- (261) deCarvalho, A. C. V.; Ndi, C. P.; Tsopmo, A.; Tane, P.; Ayafor, J.; Connolly, J. D.; Teem, J. L. *Mol. Med.* **2002**, *8*, 75.
- (262) Mohamad, K.; Hirasawa, Y.; Litaudon, M.; Awang, K.; Hadi, A. H. A.; Takeya, K.; Ekasari, W.; Widyawaruyanti, A.; Zaini, N. C.; Morita, H. *Bioorg. Med. Chem.* **2009**, *17*, 727.
- (263) Krief, S.; Martin, M. T.; Grellier, P.; Kasenene, J.; Sevenet, T. *Antimicrob. Agents Chemother.* **2004**, *48*, 3196.
- (264) Nanduri, S.; Banstola, K. P. *Indian J. Chem., Sect. B* **1995**, *34*, 1019.
- (265) El-Shamy, A. M.; El-Shabrawy, A. O.; Selim, M. A.; Motawe, H. M. *Fitoterapia* **1988**, *59*, 219.
- (266) Qi, S. H.; Wu, D. G.; Zhang, S.; Luo, X. D. *Z. Naturforsch., B* **2003**, *58*, 1128.
- (267) Bordoloi, M.; Saikia, B.; Mathur, R. K.; Goswami, B. N. *Phytochemistry* **1993**, *34*, 583.
- (268) Rajab, M. S.; Bentley, M. D.; Hassanali, A.; Chapya, A. *Phytochemistry* **1988**, *27*, 2353.
- (269) Pachapurkar, R. V.; Kornule, P. M. *Acta Cienc. Indica, Chem.* **1983**, *9*, 55.
- (270) Joshi, S. P.; Rojatkhar, S. R.; Nagasampagi, B. A. *J. Med. Arom. Plant Sci.* **1998**, *20*, 1000.
- (271) Pachapurkar, R. V.; Kornule, P. M. *Acta Cienc. Indica, Chem.* **1983**, *9*, 55.
- (272) Siddiqui, B. S.; Afshan, F.; Gulzar, T.; Sultana, R.; Naqvi, S. N. H.; Tariq, R. M. *Chem. Pharm. Bull.* **2003**, *51*, 415.
- (273) Rodriguez, B.; Caballero, C.; Ortego, F.; Castanera, P. *J. Nat. Prod.* **2003**, *66*, 452.
- (274) Mulholland, D. A.; Taylor, D. A. H. *Phytochemistry* **1980**, *19*, 2421.
- (275) Mulholland, D. A.; Naidoo, N. *Phytochemistry* **1999**, *51*, 927.
- (276) Ayafor, J. F.; Kimbu, S. F.; Ngadjui, B. T.; Akam, T. M.; Dongo, E.; Sondengam, B. L.; Connolly, J. D.; Rycroft, D. S. *Tetrahedron* **1994**, *50*, 9343.
- (277) Sondengam, B. L.; Kamga, C. S.; Connolly, J. D. *Tetrahedron Lett.* **1979**, *20*, 1357.
- (278) Kraus, W.; Kypke, K. *Tetrahedron Lett.* **1979**, *20*, 2715.

- (279) Chen, H. D.; Yang, S. P.; Liao, S. G.; Zhang, B.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2008**, *71*, 93.
- (280) Sondengam, B. L.; Kamga, C. S.; Kimbu, S. F.; Connolly, J. D. *Phytochemistry* **1981**, *20*, 173.
- (281) Musza, L.; Killar, L. M.; Speight, P.; Barrow, C. J.; Gillum, A. M.; Cooper, R. *Phytochemistry* **1995**, *39*, 621.
- (282) Lin, L. G.; Tang, C. P.; Ke, C. Q.; Zhang, Y.; Ye, Y. *J. Nat. Prod.* **2008**, *71*, 628.
- (283) MacLachlan, L. K.; Taylor, D. A. H. *Phytochemistry* **1982**, *21*, 1701.
- (284) Fraser, L. A.; Mulholland, D. A.; Nair, J. J. *Phytochemistry* **1994**, *35*, 455.
- (285) McFarland, K.; Mulholland, D. A.; Fraser, L.-A. *Phytochemistry* **2004**, *65*, 2031.
- (286) Kraus, W.; Grimminger, W.; Sawitzki, G. *Angew. Chem., Int. Ed.* **1978**, *17*, 452.
- (287) Wang, X. N.; Yin, S.; Fan, C. Q.; Wang, F. D.; Lin, L. P.; Ding, J.; Yue, J. M. *Org. Lett.* **2006**, *8*, 3845.
- (288) Kraus, W.; Grimminger, W. *Nouv. J. Chim.* **1980**, *4*, 651.
- (289) Kraus, W.; Grimminger, W.; Sawitzki, G. In *IUPAC International Symposium on Chemistry of Natural Products*, 11th; Marekov, N., Ognjanov, I., Orahovats, A., Eds.; Izd. BAN: Sofia, Bulg., 1978; Vol. 2.
- (290) Liao, S. G.; Yang, S. P.; Yuan, T.; Zhang, C. R.; Chen, H. D.; Wu, Y.; Xu, Y. K.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 1268.
- (291) Chen, H. D.; Yang, S. P.; Wu, Y.; Dong, L.; Yue, J. M. *J. Nat. Prod.* **2009**, *72*, 685.
- (292) Kraus, W.; Grimminger, W. *Liebigs Ann. Chem.* **1981**, *10*, 1838.
- (293) Butterworth, J. H.; Morgan, E. D. *J. Insect Physiol.* **1971**, *17*, 969.
- (294) Butterworth, J. H.; Morgan, E. D.; Percy, G. R. *J. Chem. Soc., Perkin Trans. I* **1972**, 2445.
- (295) Nakanishi, K. *Recent Adv. Phytochem.* **1975**, *9*, 283.
- (296) Zanno, P. R.; Miura, I.; Nakanishi, K. *J. Am. Chem. Soc.* **1975**, *97*, 1975.
- (297) Bilton, J. N.; Broughton, H. B.; Ley, S. V.; Lidert, Z.; Morgan, E. D.; Rzepa, H. S.; Sheppard, R. N. *J. Chem. Soc., Chem. Commun.* **1985**, *14*, 968.
- (298) Kraus, W.; Bokel, M.; Klenk, A.; Pohn, H. *Tetrahedron Lett.* **1985**, *26*, 6435.
- (299) Kraus, W.; Bokel, M.; Cramer, R.; Klenk, A.; Poehnl, H. *F.E.C. S. Int. Conf. Chem. Biotechnol. Biol. Act. Nat. Prod., [Proc.]*, 3rd **1987**, *4*, 446.
- (300) Kraus, W.; Bokel, M.; Bruhn, A.; Cramer, R.; Klaiber, I.; Klenk, A.; Nagl, G.; Pohnl, H.; Sadlo, H.; Vogler, B. *Tetrahedron* **1987**, *43*, 2817.
- (301) Turner, C. J.; Tempesta, M. S.; Taylor, R. B.; Zagorski, M. G.; Termini, J. S.; Schroeder, D. R.; Nakanishi, K. *Tetrahedron* **1987**, *43*, 2789.
- (302) Govindachari, T. R.; Gopalakrishnan, G.; Raghunathan, R.; Rajan, S. S. *Curr. Sci.* **1994**, *66*, 295.
- (303) Kabaleswaran, V.; Rajan, S. S.; Govindachari, T. R.; Gopalakrishnan, G. *Curr. Sci.* **1994**, *66*, 362.
- (304) Ley, S. V.; Lovell, H.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1992**, *18*, 1304.
- (305) Ley, S. V.; Anderson, J. C.; Blaney, W. M.; Lidert, Z.; Morgan, E. D.; Robinson, N. G.; Simmonds, M. S. J. *Tetrahedron Lett.* **1988**, *29*, 5433.
- (306) Taylor, D. A. H. *Tetrahedron* **1987**, *43*, 2779.
- (307) Klenk, A.; Bokel, M.; Kraus, W. *J. Chem. Soc., Chem. Commun.* **1986**, *7*, 523.
- (308) Kubo, I.; Matsumoto, T.; Matsumoto, A.; Shoolery, J. N. *Tetrahedron Lett.* **1984**, *25*, 4729.
- (309) Rembold, H.; Forster, H.; Sonnenbichler, J. *Z. Naturforsch., C* **1987**, *42*, 4.
- (310) Sidhu, O. P.; Behl, H. M. *Curr. Sci.* **1996**, *70*, 1084.
- (311) Rojatkhar, S. R.; Nagasampagi, B. A. *Phytochemistry* **1992**, *32*, 213.
- (312) Govindachari, T. R.; Sandhya, G.; Raj, S. P. G. *J. Nat. Prod.* **1992**, *55*, 596.
- (313) Kraus, W.; Gutzeit, H.; Bokel, M. *Tetrahedron Lett.* **1989**, *30*, 1797.
- (314) Morgan, E. D.; Thornton, M. D. *Phytochemistry* **1973**, *12*, 391.
- (315) Uebel, E. C.; Warthen, J. D., Jr.; Jacobson, M. J. *Liq. Chromatogr.* **1979**, *2*, 875.
- (316) Kubo, I.; Matsumoto, A.; Matsumoto, T.; Klocke, J. A. *Tetrahedron* **1986**, *42*, 489.
- (317) Jarvis, A. P.; Morgan, E. D.; Edwards, C. *Phytochem. Anal.* **1999**, *10*, 39.
- (318) Johnson, S.; Morgan, E. D. *J. Chromatogr., A* **1997**, *761*, 53.
- (319) Govindachari, T. R.; Sandhya, G.; Ganeshray, S. P. *Chromatographia* **1991**, *31*, 303.
- (320) Yamasaki, R. B.; Klocke, J. A.; Lee, S. M.; Stone, G. A.; Darlington, M. V. *J. Chromatogr., A* **1986**, *356*, 220.
- (321) Govindachari, T. R.; Gopalakrishnan, G.; Suresh, G. J. *Liq. Chromatogr. Relat. Technol.* **1996**, *19*, 1729.
- (322) Kraus, W.; Maile, R.; Vogler, B.; Wundrak, B. *J. Indian Chem. Soc.* **1997**, *74*, 870.
- (323) Malathi, R.; Rajan, S. S.; Gopalakrishnan, G.; Suresh, G. *Acta Crystallogr., Sect. C* **2002**, *58*, o708.
- (324) Kanokmedhakul, S.; Kanokmedhakul, K.; Prajuabsuk, T.; Panichajakul, S.; Panyamee, P.; Prabpai, S.; Kongsaree, P. *J. Nat. Prod.* **2005**, *68*, 1047.
- (325) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G. *Nat. Prod. Res. Dev.* **2001**, *13*, 9.
- (326) Govindachari, T. R.; Gopalakrishnan, G.; Suresh, G. J. *Liq. Chromatogr. Relat. Technol.* **1997**, *20*, 1633.
- (327) Kalinowski, H. O.; Krack, C.; Ermel, K.; Chriathamjaree, C. Z. *Naturforsch., B* **1997**, *52*, 1413.
- (328) Rojatkhar, S. R.; Nagasampagi, B. A. *Indian J. Chem., Sect. B* **1995**, *34*, 1016.
- (329) Govindachari, T. R.; Gopalakrishnan, G. *Phytochemistry* **1997**, *45*, 397.
- (330) Lee, S. M.; Klocke, J. A.; Balandrin, M. F. *Tetrahedron Lett.* **1987**, *28*, 3543.
- (331) Lee, S. M.; Klocke, J. A.; Barnby, M. A.; Yamasaki, R. B.; Balandrin, M. F. *ACS Symp. Ser.* **1991**, *449*, 293.
- (332) Klocke, J. A.; Lee, S. M.; Yamasaki, R. B. EP Patent 308044, 1989; *Chem. Abstr.* **1989**, *112*, 153732.
- (333) Wagner, H.; Fansworth, N. R. *Economic and Medicinal Plant Research*; Academic Press: London, UK, 1989; p57.
- (334) Rojatkhar, S. R.; Nagasampagi, B. A. *Phytochemistry* **1993**, *34*, 1663.
- (335) Ramji, N.; Venkatakrishnan, K.; Madyastha, K. M. *Phytochemistry* **1998**, *49*, 265.
- (336) Alche, L. E.; Ferek, G. A.; Meo, M.; Coto, C. E.; Maier, M. S. Z. *Naturforsch., C* **2003**, *58*, 215.
- (337) Barquero, A. A.; Michelini, F. M.; Alche, L. E. *Biochem. Biophys. Res. Commun.* **2006**, *344*, 955.
- (338) Bohnenstengel, F. I.; Wray, V.; Witte, L.; Srivastava, R. P.; Proksch, P. *Phytochemistry* **1999**, *50*, 977.
- (339) Nakatani, M.; Arikawa, S.; Okamura, H.; Iwagawa, T. *Heterocycles* **1994**, *38*, 327.
- (340) Nakatani, M.; Huang, R. C.; Okamura, H.; Iwagawa, T. *Chem. Lett.* **1993**, *22*, 2125.
- (341) Nakatani, M.; Huang, R. C.; Okamura, H.; Iwagawa, T.; Tadera, K.; Naoki, H. *Tetrahedron* **1995**, *51*, 11731.
- (342) Huang, R. C.; Tadera, K.; Yagi, F.; Minami, Y.; Okamura, H.; Iwagawa, T.; Nakatani, M. *Phytochemistry* **1996**, *43*, 581.
- (343) Luo, X. D.; Ma, Y. B.; Wu, S. H.; Wu, D. G. *J. Nat. Prod.* **1999**, *62*, 1022.
- (344) Tan, Q. G.; Li, X. N.; Chen, H.; Feng, T.; Cai, X. H.; Luo, X. D. *J. Nat. Prod.* **2010**, *73*, 693.
- (345) Takeya, K.; Qiao, Z. S.; Hirobe, C.; Itokawa, H. *Phytochemistry* **1996**, *42*, 709.
- (346) Fukuyama, Y.; Ogawa, M.; Takahashi, H.; Minami, H. *Chem. Pharm. Bull.* **2000**, *48*, 301.
- (347) Kabaleswaran, V.; Rajan, S. S.; Gopalakrishnan, G.; Govindachari, T. R. *Acta Crystallogr., Sect. C* **1999**, *55*, 1952.

- (348) Jarvis, A. P.; Johnson, S.; Morgan, E. D.; Simmonds, M. S. J.; Blaney, W. M. *J. Chem. Ecol.* **1997**, *23*, 2841.
- (349) Malathi, R.; Rajan, S. S.; Gopalakrishnan, G.; Suresh, G. *Acta Crystallogr., Sect. C* **2002**, *58*, o681.
- (350) Ekong, D. E. U.; Ibiyemi, S. A.; Olagbemi, E. O. *J. Chem. Soc., D* **1971**, *18*, 1117.
- (351) Ekong, D. E. U.; Ibiyemi, S. A. *Phytochemistry* **1985**, *24*, 2259.
- (352) Ekundayo, O. Z. *Pflanzenphysiol.* **1983**, *112*, 139.
- (353) Rani, K.; Akhila, A. *Nat. Prod. Lett.* **1994**, *4*, 179.
- (354) Akhila, A.; Rani, K. *Indian J. Heterocycl. Chem.* **2002**, *11*, 299.
- (355) Anitha, G.; Raj, J. J. L.; Narasimhan, S.; Solomon, K. A.; Rajan, S. S. *J. Agric. Food Chem.* **2006**, *8*, 445.
- (356) Garg, H. S.; Bhakuni, D. S. *Phytochemistry* **1984**, *23*, 2383.
- (357) Henderson, R.; McCrindle, R.; Overton, K. H.; Melera, A. *Tetrahedron Lett.* **1964**, *52*, 3969.
- (358) de Silva, L. B.; Stocklin, W.; Geissman, T. A. *Phytochemistry* **1969**, *8*, 1817.
- (359) Yamasaki, R. B.; Ritland, T. G.; Barnby, M. A.; Klocke, J. A. *J. Chromatogr.* **1988**, *447*, 277.
- (360) Nakatani, M.; Huang, R. C.; Okamura, H.; Iwagawa, T.; Tadera, K. *Chem. Lett.* **1995**, *11*, 995.
- (361) Huang, R. C.; Minami, Y.; Yagi, F.; Nakamura, Y.; Nakayama, N.; Tadera, K.; Nakatani, M. *Heterocycles* **1996**, *43*, 1477.
- (362) Rajab, M. S.; Bentley, M. D.; Alford, A. R.; Mendel, M. J. *J. Nat. Prod.* **1988**, *51*, 168.
- (363) Nakatani, M.; Zhou, J. B.; Nakayama, N.; Okamura, H.; Iwagawa, T. *Phytochemistry* **1996**, *41*, 739.
- (364) Ochi, M.; Kotsuki, H.; Kataoka, T.; Tada, T.; Tokoroyama, T. *Chem. Lett.* **1978**, *4*, 331.
- (365) Rajab, M. S.; Bentley, M. D. *Bull. Chem. Soc. Ethiopia* **1992**, *6*, 97.
- (366) Koul, O.; Singh, G.; Singh, R.; Singh, J.; Daniewski, W. M.; Berlozecki, S. *J. Biosci.* **2004**, *29*, 409.
- (367) Rojatar, S. R.; Bhat, V. S.; Kulkarni, M. M.; Joshi, V. S.; Nagasampagi, B. A. *Phytochemistry* **1989**, *28*, 203.
- (368) Garg, H. S.; Bhakuni, D. S. *Phytochemistry* **1985**, *24*, 866.
- (369) Cui, B. L.; Chai, H. B.; Constant, H. L.; Santisuk, T.; Reutrakul, V.; Beecher, C. W. W.; Farnsworth, N. R.; Cordell, G. A.; Pezzuto, J. M.; Kinghorn, A. D. *Phytochemistry* **1998**, *47*, 1283.
- (370) Fukuyama, Y.; Miura, I.; Ochi, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1139.
- (371) Xie, F.; Zhang, C. F.; Zhang, M.; Wang, Z. T.; Yu, B. Y. *Chin. Chem. Lett.* **2008**, *19*, 183.
- (372) Ekong, D. E. U. *Chem. Commun. (London)* **1967**, *16*, 808.
- (373) Kigodi, P. G. K.; Blask, G.; Thebtaranonth, Y.; Pezzuto, J. M.; Cordell, G. A. *J. Nat. Prod.* **1989**, *52*, 1246.
- (374) Nair, M. S.; Gopal, S.; Issac, D. *Phytochemistry* **1997**, *46*, 1177.
- (375) Malathi, R.; Anitha, G.; Solomon, K. A.; Suresh, G.; Rajan, S. S.; Narasimhan, S.; Raj, J. J. L.; Gopalakrishnan, G. *Acta Crystallogr., Sect. C* **2005**, *61*, o70.
- (376) Uwaifo, A. O. *J. Toxicol. Environ. Health* **1984**, *13*, 521.
- (377) Bokel, M.; Cramer, R.; Gutzeit, H.; Reeb, S.; Kraus, W. *Tetrahedron* **1990**, *46*, 775.
- (378) Mulholland, D. A.; Kotsos, M.; Mahomed, H. A.; Taylor, D. A. H. *Phytochemistry* **1998**, *49*, 2457.
- (379) Siddiqui, S.; Siddiqui, B. S.; Faizi, S.; Mahmood, T. *Heterocycles* **1986**, *24*, 3163.
- (380) Siddiqui, S.; Faizi, S.; Mahmood, T.; Siddiqui, B. S. *Tetrahedron* **1986**, *42*, 4849.
- (381) Zhang, Q.; Liang, J. Y.; Li, Q. S.; Min, Z. D. *Chin. Chem. Lett.* **2010**, *21*, 838.
- (382) Kraus, W.; Bokel, M. *Chem. Ber* **1981**, *114*, 267.
- (383) Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *Heterocycles* **1989**, *29*, 729.
- (384) Zeng, L.; Gu, Z. M.; Fanwick, P. E.; Chang, C. J.; Smith, D. L.; McLaughlin, J. L. *Heterocycles* **1995**, *41*, 741.
- (385) Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *J. Nat. Prod.* **1989**, *52*, 1209.
- (386) Adesida, G. A.; Okorie, D. A. *Phytochemistry* **1973**, *12*, 3007.
- (387) Zhou, H. L.; Hamazaki, A.; Fontana, J. D.; Takahashi, H.; Esumi, T.; Wandscheer, C. B.; Tsujimoto, H.; Fukuyama, Y. *J. Nat. Prod.* **2004**, *67*, 1544.
- (388) Nakai, H.; Shiro, M.; Ochi, M. *Acta Crystallogr., Sect. B* **1980**, *36*, 1698.
- (389) Ochi, M.; Kotsuki, H.; Ido, M.; Nakai, H.; Shiro, M.; Tokoroyama, T. *Chem. Lett.* **1979**, *9*, 1137.
- (390) Yang, M. H.; Wang, J. S.; Luo, J. G.; Wang, X. B.; Kong, L. Y. *J. Nat. Prod.* **2009**, *72*, 2014.
- (391) Tane, P.; Akam, M. T.; Tsopmo, A.; Ndi, C. P.; Sterner, O. *Phytochemistry* **2004**, *65*, 3083.
- (392) Mitra, C. J. *Sci. Ind. Res.* **1956**, *15B*, 425.
- (393) Mitra, C. J. *Sci. Ind. Res.* **1957**, *16B*, 477.
- (394) Narasimhan, N. S. *Chem. Ind. (London, U. K.)* **1957**, 661.
- (395) Narasimhan, N. S. *Chem. Ber.* **1959**, *92*, 769.
- (396) Sengupta, P.; Sengupta, S. K.; Khastgir, H. N. *Tetrahedron* **1960**, *11*, 67.
- (397) Narayanan, C. R.; Pradhan, S. K.; Pachapurkar, R. V.; Narasimhan, N. S. *Chem. Ind. (London, U. K.)* **1962**, *14*, 1283.
- (398) Henderson, R.; McCrindle, R.; Overton, K. H.; Harris, M.; Turner, D. W. *Proc. Chem. Soc., London* **1963**, Sept, 269.
- (399) Narayanan, C. R.; Pachapurkar, R. V.; Pradhan, S. K.; Shah, V. R. *Indian J. Chem.* **1964**, *2*, 108.
- (400) Narayanan, C. R.; Pachapurkar, R. V.; Pradhan, S. K.; Shah, V. R.; Narasimhan, N. S. *Chem. Ind. (London, U. K.)* **1964**, *8*, 322.
- (401) Narayanan, C. R.; Pachapurkar, R. V. *Tetrahedron Lett.* **1965**, *48*, 4333.
- (402) Narayanan, C. R.; Pachapurkar, R. V.; Pradhan, S. K.; Shah, V. R.; Narasimhan, N. S. *Chem. Ind. (London, U. K.)* **1964**, *8*, 324.
- (403) Harris, M.; Henderson, R.; McCrindle, R.; Overton, K. H.; Turner, D. W. *Tetrahedron* **1968**, *24*, 1517.
- (404) Ziffer, H.; Weiss, U.; Narayanan, G. R.; Pachapurkar, R. V. *J. Org. Chem.* **1966**, *31*, 2691.
- (405) Siddiqui, S. *Curr. Sci.* **1942**, *11*, 278.
- (406) Mitra, C.; Rao, P. N.; Siddiqui, S. *J. Sci. Ind. Res.* **1953**, *12B*, 152.
- (407) Narayanan, C. R.; Iyer, K. N. *Indian J. Chem.* **1967**, *5*, 460.
- (408) Siddiqui, S.; Mahmood, T.; Siddiqui, B. S.; Faizi, S. *J. Nat. Prod.* **1986**, *49*, 1068.
- (409) Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *Phytochemistry* **1988**, *27*, 1801.
- (410) Devakumar, C.; Mukerjee, S. K. *Indian J. Chem., Sect. B* **1985**, *24*, 1105.
- (411) Githua, M.; Hassanali, A.; Keriko, J.; Murilla, G.; Ndungu, M.; Nyagah, G. *Afr. J. Tradit., Complementary Altern. Med.* **2010**, *7*, 207.
- (412) Mohamad, K.; Hirasawa, Y.; Lim, C. S.; Awang, K.; Hadi, A. H. A.; Takeya, K.; Morita, H. *Tetrahedron Lett.* **2008**, *49*, 4276.
- (413) Cespedes, C. L.; Calderon, J. S.; Lina, L.; Aranda, E. *J. Agric. Food Chem.* **2000**, *48*, 1903.
- (414) Baldwin, M. A.; Loudon, A. G.; Maccoll, A.; Bevan, C. W. L. *J. Chem. Soc., C* **1967**, *11*, 1026.
- (415) Powell, J. W. *J. Chem. Soc. C* **1966**, *20*, 1794.
- (416) Sutherland, S. A.; Sim, G. A.; Robertson, J. M. *Proc. Chem. Soc., London* **1962**, June, 222.
- (417) Toscano, R. A.; Mata, R.; Calderon, J.; Segura, R. *J. Chem. Crystallogr.* **1996**, *26*, 707.
- (418) Akisanya, A.; Bevan, C. W. L.; Halsall, T. G.; Powell, J. W.; Taylor, D. A. H. *J. Chem. Soc.* **1961**, 3705.
- (419) Hofer, M.; Greger, H.; Mereiter, K. *Acta Crystallogr., Sect. E* **2009**, *65*, o1942.
- (420) Cespedes, C. L.; Calderon, J. S.; King-Diaz, B.; Lotina-Hennsen, B. *J. Agric. Food Chem.* **1998**, *46*, 2810.
- (421) Akisanya, A.; Arene, E. O.; Bevan, C. W. L.; Ekong, D. E. U.; Nwaji, M. N.; Okogun, J. I.; Powell, J. W.; Taylor, D. A. H. *J. Chem. Soc., C* **1966**, *5*, 506.
- (422) Zhang, H. P.; VanDerveer, D.; Chen, F.; Wang, X.; Wargovich, M. J. *Acta Crystallogr., Sect. E* **2007**, *63*, No. o4162.

- (423) Akisanya, A.; Bevan, C. W. L.; Hirst, J.; Halsall, T. G.; Taylor, D. A. H. *J. Chem. Soc.* **1960**, 3827.
- (424) Taylor, D. A. H. *J. Chem. Soc.* **1965**, May, 3495.
- (425) Mulholland, D. A.; Schwikkard, S. L.; Sandor, P.; Nuzillard, J. M. *Phytochemistry* **2000**, 53, 465.
- (426) Li, M. Y.; Yang, X. B.; Pan, J. Y.; Feng, G.; Xiao, Q.; Sinkkonen, J.; Satyanandamurthy, T.; Wu, J. *J. Nat. Prod.* **2009**, 72, 2110.
- (427) Lakshmi, V.; Singh, N.; Shrivastva, S.; Mishra, S. K.; Dharmani, P.; Mishra, V.; Palit, G. *Phytomedicine* **2010**, 17, 569.
- (428) Nazma, B. S. V.; Rao, J. M. *Curr. Sci.* **1977**, 46, 714.
- (429) Khalid, S. A.; Duddeck, H.; Gonzalez-Sierra, M. *J. Nat. Prod.* **1989**, 52, 922.
- (430) Madhusudana Rao, M.; Meshulam, H.; Zelnik, R.; Lavie, D. *Phytochemistry* **1975**, 14, 1071.
- (431) Campos, A. M.; Oliveira, F. S.; Machado, M. I. L.; Braz-Filho, R.; Matos, F. J. A. *Phytochemistry* **1991**, 30, 1225.
- (432) MacKinnon, S.; Durst, T.; Arnason, J. T. *J. Nat. Prod.* **1997**, 60, 336.
- (433) Mitsui, K.; Saito, H.; Yamamura, R.; Fukaya, H.; Hitotsuyanagi, Y.; Takeya, K. *J. Nat. Prod.* **2006**, 69, 1310.
- (434) Jimenez, A.; Villarreal, C.; Toscano, R. A.; Cook, M.; Arnason, J. T.; Bye, R.; Mata, R. *Phytochemistry* **1998**, 49, 1981.
- (435) Achnine, L.; Mata, R.; Lotina-Hennsen, B. *Pestic. Biochem. Physiol.* **1999**, 63, 139.
- (436) Bickii, J.; Njifutse, N.; Ayafor Foyere, J.; Basco, L. K.; Ringwald, P. *J. Ethnopharmacol.* **2000**, 69, 27.
- (437) Pereira da Silva, V.; Oliveira, R. R.; Figueiredo, M. R. *Phytochem. Anal.* **2009**, 20, 77.
- (438) Marcelle, G. B.; Mootoo, B. S. *Phytochemistry* **1975**, 14, 2717.
- (439) Fuzzati, N.; Dyatmiko, W.; Rahman, A.; Achmad, F.; Hostettmann, K. *Phytochemistry* **1996**, 42, 1395.
- (440) Connolly, J. D.; McCrindle, R.; Overton, K. H.; Feeney, J. *Tetrahedron* **1966**, 22, 891.
- (441) Saxena, E.; Babu, U. V. *Fitoterapia* **2001**, 72, 186.
- (442) Koul, O.; Multani, J. S.; Singh, G.; Daniewski, W. M.; Berlozecki, S. *J. Agric. Food Chem.* **2003**, 51, 2937.
- (443) Hay, A. E.; Ioset, J. R.; Ahua, K. M.; Diallo, D.; Brun, R.; Hostettmann, K. *J. Nat. Prod.* **2007**, 70, 9.
- (444) Ekong, D. E. U.; Olagbemi, E. O. *Tetrahedron Lett.* **1967**, 8, 3525.
- (445) Mootoo, B. S.; Ali, A.; Motilal, R.; Pingal, R.; Ramlal, A.; Khan, A.; Reynolds, W. F.; McLean, S. *J. Nat. Prod.* **1999**, 62, 1514.
- (446) Adesogan, E. K.; Taylor, D. A. H. *J. Chem. Soc., C* **1970**, 12, 1710.
- (447) Abdelgaleil, S. A.; Hashinaga, F.; Nakatani, M. *Pest Manage. Sci.* **2005**, 61, 186.
- (448) Pudhom, K.; Sommit, D.; Nuclear, P.; Ngamrojanavanich, N.; Petsom, A. *J. Nat. Prod.* **2009**, 72, 2188.
- (449) Ollis, W. D.; Ward, A. D.; Zelnick, R. *Tetrahedron Lett.* **1964**, 37, 2607.
- (450) Ollis, W. D.; Ward, A. D.; de Oliveira, H. M.; Zelnik, R. *Tetrahedron* **1970**, 26, 1637.
- (451) Adesogan, E. K.; Taylor, D. A. H. *J. Chem. Soc., C* **1968**, 16, 1974.
- (452) D'Ambrosio, M.; Guerriero, A. *Phytochemistry* **2002**, 60, 419.
- (453) Tinto, W. F.; Jagessar, P. K.; Ketwaru, P.; Reynolds, W. F.; McLean, S. *J. Nat. Prod.* **1991**, 54, 972.
- (454) Lukacova, V.; Polonsky, J.; Moretti, C.; Pettit, G. R.; Schmidt, J. M. *J. Nat. Prod.* **1982**, 45, 288.
- (455) Waratchareeyakul, W.; Chantrapromma, S.; Fun, H.-K.; Razak, I. A.; Karalai, C.; Ponglimanont, C. *Acta Crystallogr., Sect. E* **2004**, 60, o1964.
- (456) Lin, B. D.; Zhang, C. R.; Yang, S. P.; Zhang, S.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2009**, 72, 1305.
- (457) Abdelgaleil, S. A. M.; Doe, M.; Morimoto, Y.; Nakatani, M. *Phytochemistry* **2006**, 67, 452.
- (458) Lin, B. D.; Yuan, T.; Zhang, C. R.; Dong, L.; Zhang, B.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2009**, 72, 2084.
- (459) Adeoye, S. A.; Bekoe, D. A. *Chem. Commun. (London)* **1965**, 14, 301.
- (460) Saxena, M.; Srivastava, S. K. *Indian J. Chem., Sect. B* **1986**, 25, 1087.
- (461) Burke, B. A.; Chan, W. R.; Magnus, K. E.; Taylor, D. R. *Tetrahedron* **1969**, 25, 5007.
- (462) Cespedes, C. L.; Calderon, J. S.; Salazar, R.; King-Diaz, B.; Lotina-Hennsen, B. *Bol. Soc. Chil. Quim.* **1999**, 44, 173.
- (463) Bevan, C. W. L.; Halsall, T. G.; Nwaji, M. N.; Taylor, D. A. H. *J. Chem. Soc.* **1962**, 768.
- (464) Adesida, G. A.; Adesogan, E. K.; Taylor, D. A. H. *Chem. Commun.* **1967**, 16, 790.
- (465) Adesogan, E. K.; Powell, J. W.; Taylor, D. A. H. *J. Chem. Soc., C* **1967**, 7, 554.
- (466) Tchimine, M. K.; Ngamga, D.; Tane, P.; Sterner, O.; Connolly, J. D. *Bull. Chem. Soc. Ethiopia* **2006**, 20, 69.
- (467) Govindachari, T. R.; Kumari, G. N. K. *Phytochemistry* **1998**, 47, 1423.
- (468) Govindachari, T. R.; Kumari, G. N. K.; Suresh, G. *J. Liq. Chromatogr. Relat. Technol.* **1997**, 20, 3189.
- (469) Taylor, D. A. H. *J. Chem. Soc., C* **1970**, 2, 336.
- (470) Zhang, H. P.; VanDerveer, D.; Chen, F.; Wang, X.; Wargovich, M. J. In *Abstracts of Papers, 236th ACS National Meeting, Philadelphia, PA, United States, August 17–21*; American Chemical Society: Washington, D. C., 2008.
- (471) Zhang, H. P.; VanDerveer, D.; Wang, X.; Chen, F.; Wargovich, M. J. *Acta Crystallogr., Sect. E* **2007**, 63, o4599.
- (472) Abdelgaleil, S. A. M.; Iwagawa, T.; Doe, M.; Nakatani, M. *Fitoterapia* **2004**, 75, 566.
- (473) Zhang, H. P.; Wang, X.; Chen, F.; Androulakis, X. M.; Wargovich, M. J. *Phytother. Res.* **2007**, 21, 731.
- (474) Taylor, D. A. H. *Chem. Commun. (London)* **1968**, 19, 1172.
- (475) Housley, J. R.; King, F. E.; King, T. J.; Taylor, P. R. *J. Chem. Soc.* **1962**, 5095.
- (476) Taylor, D. A. H. *Chem. Commun.* **1967**, 10, 500.
- (477) Connolly, J. D.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 7, 686.
- (478) Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *Fitoterapia* **1992**, 63, 118.
- (479) Siddiqui, S.; Faizi, S.; Siddiqui, B. S. *Heterocycles* **1984**, 22, 295.
- (480) Sabri, N. N.; Abou-Donia, A. H.; Ghazy, N. A. *Alexandria J. Pharm. Sci.* **1987**, 1, 28.
- (481) Gullo, V. P.; Miura, I.; Nakanishi, K.; Cameron, A. F.; Connolly, J. D.; Duncanson, F. D.; Harding, A. E.; McCrindle, R.; Taylor, D. A. H. *J. Chem. Soc., Chem. Commun.* **1975**, 9, 345.
- (482) Cameron, A. F.; Duncanson, F. D. *Acta Crystallogr., Sect. B* **1976**, 32, 1841.
- (483) Luo, X. D.; Wu, S. H.; Yang, X. S.; Teng, R. W.; Ma, Y. B.; Wu, D. G.; Hao, X. J.; Lu, Y.; Liu, X. Y.; Zheng, Q. T. *Heterocycles* **2000**, 53, 2225.
- (484) Brown, D. A.; Taylor, D. A. H. *Phytochemistry* **1978**, 17, 1995.
- (485) Zhang, H. P.; Chen, F.; Wang, X.; Wu, D. G.; Chen, Q. *Magn. Reson. Chem.* **2007**, 45, 189.
- (486) King, T. J.; Taylor, D. A. H. *Phytochemistry* **1983**, 22, 307.
- (487) Connolly, J. D.; Okorie, D. A.; de Wit, L. D.; Taylor, D. A. H. *J. Chem. Soc., Chem. Commun.* **1976**, 22, 909.
- (488) Taylor, D. A. H. *J. Chem. Res., Synop.* **1982**, 2, 55.
- (489) Connolly, J. D.; Labbe, C.; Rycroft, D. S.; Okorie, D. A.; Taylor, D. A. H. *J. Chem. Res., Synop.* **1979**, 8, 256.
- (490) MacLachlan, L. K.; Taylor, D. A. H. *Phytochemistry* **1982**, 21, 2426.
- (491) Daniewski, W. M.; Gumulka, M.; Anczewski, W.; Truszevska, D.; Bloszyk, E.; Drozd, B. *Pol. J. Chem.* **1996**, 70, 1265.
- (492) Rodriguez-Hahn, L.; Cardenas, J.; Arenas, C. *Phytochemistry* **1996**, 43, 457.
- (493) Nakatani, M.; Okamoto, M.; Iwashita, T.; Mizukawa, K.; Naoki, H.; Hase, T. *Heterocycles* **1984**, 22, 2335.
- (494) Koul, O.; Daniewski, W. M.; Multani, J. S.; Gumulka, M.; Singh, G. *J. Agric. Food Chem.* **2003**, 51, 7271.

- (495) Adul, G. O.; Bentley, M. D.; Benson, B. W.; Huang, F. Y.; Gelbaum, L.; Hassanali, A. J. *Nat. Prod.* **1993**, *56*, 1414.
- (496) Garcez, F. R.; Nunez, C. V.; Garcez, W. S.; Almeida, R. M.; Roque, N. F. *Planta Med.* **1998**, *64*, 79.
- (497) Govindachari, T. R.; Suresh, G.; Krishna Kumari, G. N.; Rajamannar, T.; Partho, P. D. *Fitoterapia* **1999**, *70*, 83.
- (498) Sarker, S. D.; Savchenko, T.; Whiting, P.; Sik, V.; Dinan, L. *Arch. Insect Biochem. Physiol.* **1997**, *35*, 211.
- (499) Akinniyi, J. A.; Connolly, J. D.; Rycroft, D. S.; Sondengam, B. L.; Ifeadike, N. P. *Can. J. Chem.* **1980**, *58*, 1865.
- (500) Bray, D. H.; Warhurst, D. C.; Connolly, J. D.; O'Neill, M. J.; Phillipson, J. D. *Phytother. Res.* **1990**, *4*, 29.
- (501) Jolad, S. D.; Hoffmann, J. J.; Schram, K. H.; Cole, J. R.; Tempesta, M. S.; Bates, R. B. *J. Org. Chem.* **1981**, *46*, 641.
- (502) Nagakura, Y.; Yamanaka, R.; Hirasawa, Y.; Hosoya, T.; Rahman, A.; Kusumawati, I.; Zaini, N. C.; Morita, H. *Heterocycles* **2010**, *80*, 1471.
- (503) Mulholland, D. A.; Taylor, D. A. H. *J. Chem. Res., Synop.* **1979**, *9*, 294.
- (504) Musza, L. L.; Killar, L. M.; Speight, P.; McElhiney, S.; Barrow, C. J.; Gillum, A. M.; Copper, R. *Tetrahedron* **1994**, *50*, 11369.
- (505) Kraus, W.; Kypke, K.; Bokel, M.; Grimminger, W.; Sawitzki, G.; Schwinger, G. *Liebigs Ann. Chem.* **1982**, *1*, 87.
- (506) Qi, S. H.; Chen, L.; Wu, D. G.; Ma, Y. B.; Luo, X. D. *Tetrahedron* **2003**, *59*, 4193.
- (507) Luo, X. D.; Wu, S. H.; Wu, D. G.; Ma, Y. B.; Qi, S. H. *Tetrahedron* **2002**, *58*, 7797.
- (508) Zhang, H. P.; Wu, S. H.; Luo, X. D.; Ma, Y. B.; Wu, D. G. *Chin. Chem. Lett.* **2002**, *13*, 341.
- (509) Fraser, L.-A.; Mulholland, D. A.; Taylor, D. A. H. *S. Afr. J. Bot.* **1995**, *61*, 281.
- (510) Kipassa, N. T.; Iwagawa, T.; Okamura, H.; Doe, M.; Morimoto, Y.; Nakatani, M. *Phytochemistry* **2008**, *69*, 1782.
- (511) Mitsui, K.; Maejima, M.; Fukaya, H.; Hitotsuyanagi, Y.; Takeya, K. *Phytochemistry* **2004**, *65*, 3075.
- (512) Garcez, F. R.; Garcez, W. S.; Roque, N. F.; Castellano, E. E.; Zukerman-Schpector, J. *Phytochemistry* **2000**, *55*, 733.
- (513) Ahmed, F. R.; Ng, A. S.; Fallis, A. G. *Can. J. Chem.* **1978**, *56*, 1020.
- (514) Ng, A. S.; Fallis, A. G. *Can. J. Chem.* **1979**, *57*, 3088.
- (515) Adesida, G. A.; Taylor, D. A. H. *Phytochemistry* **1972**, *11*, 2641.
- (516) Mulholland, D. A.; Monkhe, T. V.; Pegel, K. H.; Taylor, D. A. H. *Biochem. Syst. Ecol.* **1999**, *27*, 313.
- (517) Jogia, M. K.; Andersen, R. J. *Can. J. Chem.* **1989**, *67*, 257.
- (518) Mulholland, D. A.; Nair, J. J.; Taylor, D. A. H. *Phytochemistry* **1996**, *42*, 1667.
- (519) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G. *Fitoterapia* **2000**, *71*, 492.
- (520) Garcez, F. R.; Garcez, W. S.; Tsutsumi, M. T.; Roque, N. F. *Phytochemistry* **1997**, *45*, 141.
- (521) Marcelle, G. B.; Mootoo, B. S. *Tetrahedron Lett.* **1981**, *22*, 505.
- (522) Jogia, M. K.; Andersen, R. J. *Phytochemistry* **1987**, *26*, 3309.
- (523) Ekong, D. E. U.; Olagbemi, E. O. *J. Chem. Soc. C* **1966**, *10*, 944.
- (524) Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H.; Halsall, T. G.; Toft, P.; Welford, M. J. *Chem. Soc. C* **1967**, *2*, 163.
- (525) Chan, W. R.; Magnus, K. E.; Mootoo, B. S. *J. Chem. Soc. C* **1967**, *2*, 171.
- (526) Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H.; Toft, P.; Welford, M.; Chan, W. R.; Mootoo, B. S.; Halsall, T. G. *Chem. Ind. (London, U. K.)* **1964**, *42*, 1751.
- (527) Sanni, S. B.; Behm, H.; Beurskens, P. T. *Acta Crystallogr., Sect. C* **1987**, *43*, 1398.
- (528) Connolly, J. D.; Thornton, I. M. S.; Taylor, D. A. H. *J. Chem. Soc., D* **1970**, *18*, 1205.
- (529) Connolly, J. D.; Thornton, I. M. S.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, *20*, 2407.
- (530) Adesida, G. A.; Taylor, D. A. H. *Phytochemistry* **1967**, *6*, 1429.
- (531) Connolly, J. D.; Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1972**, *9–10*, 1145.
- (532) Powell, R. G.; Mikolajczak, K. L.; Zilkowski, B. W.; Mantus, E. K.; Cherry, D.; Clardy, J. *J. Nat. Prod.* **1991**, *54*, 241.
- (533) Okorie, D. A.; Taylor, D. A. H. *Phytochemistry* **1968**, *7*, 1683.
- (534) Agnihotri, V. K.; Srivastava, S. D.; Srivastava, S. *Planta Med.* **1987**, *53*, 298.
- (535) Agnihotri, V. K.; Srivastava, S. D.; Srivastava, S. K. *Curr. Sci.* **1987**, *56*, 770.
- (536) Srivastava, S. K.; Srivastava, S. D.; Srivastava, S. *Indian J. Chem., Sect. B* **2003**, *42*, 3155.
- (537) Purushothaman, K. K.; Chandrasekharan, S. *Indian J. Chem.* **1974**, *12*, 207.
- (538) Purushothaman, K. K.; Chandrasekharan, S.; Connolly, J. D.; Rycroft, D. S. *J. Chem. Soc., Perkin Trans. 1* **1977**, *16*, 1873.
- (539) Agarwal, S. K.; Verma, S.; Singh, S. S.; Kumar, S. *Indian J. Chem., Sect. B* **2001**, *40*, 536.
- (540) Chandrasekharan, S.; Kundu, A. B.; Chakraborty, T. *Sci. Cult.* **1968**, *34*, 362.
- (541) Chakraborty, T.; Chandrasekharan, S.; Kundu, A. B. *Indian J. Med. Res.* **1969**, *4*, 121.
- (542) Chatterjee, A.; Kundu, A. B.; Chakraborty, T.; Chandrasekharan, S. *Tetrahedron* **1970**, *26*, 1859.
- (543) Mulholland, D. A.; Nair, J. J.; Taylor, D. A. H. *Phytochemistry* **1996**, *42*, 1239.
- (544) Fang, X.; Zhang, Q.; Tan, C. J.; Mu, S. Z.; Lu, Y.; Lu, Y. B.; Zheng, Q. T.; Di, Y. T.; Hao, X. J. *Tetrahedron* **2009**, *65*, 7408.
- (545) Kipassa, N. T.; Okamura, H.; Doe, M.; Morimoto, Y.; Iwagawa, T.; Nakatani, M. *Heterocycles* **2008**, *75*, 157.
- (546) Ambaye, R. Y.; Indap, M. A.; Panse, T. B. *Curr. Sci.* **1971**, *40*, 158.
- (547) Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Doe, M.; Nakatani, M. *Heterocycles* **2000**, *53*, 2233.
- (548) Nakatani, M.; Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Sato, A.; Doe, M. *Tetrahedron Lett.* **2000**, *41*, 6473.
- (549) Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Sato, A.; Miyahara, I.; Doe, M.; Nakatani, M. *Tetrahedron* **2001**, *57*, 119.
- (550) Abdelgaleil, S. A. M.; Nakatani, M. *J. Appl. Entomology* **2003**, *127*, 236.
- (551) Nakatani, M.; Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Doe, M. *Chem. Lett.* **2000**, *8*, 876.
- (552) Tchimine, M. K.; Tane, P.; Ngamga, D.; Connolly, J. D.; Farrugia, L. J. *Phytochemistry* **2005**, *66*, 1088.
- (553) Tchuendem, M.-H. K.; Foyere Ayafor, J.; Connolly, J. D.; Sterner, O. *Tetrahedron Lett.* **1998**, *39*, 719.
- (554) Zhang, B.; Yang, S. P.; Yin, S.; Zhang, C. R.; Wu, Y.; Yue, J. M. *Phytochemistry* **2009**, *70*, 1305.
- (555) Taylor, D. A. H. *Chem. Commun. (London)* **1969**, *2*, 58.
- (556) Mootoo, B. S.; Ramsewak, R.; Khan, A.; Tinto, W. F.; Reynolds, W. F.; McLean, S.; Yu, M. J. *Nat. Prod.* **1996**, *59*, 544.
- (557) Naidoo, D.; Mulholland, D. A.; Randrianarivelojosia, M.; Coombes, P. H. *Biochem. Syst. Ecol.* **2003**, *31*, 1047.
- (558) Zhang, J.; Yang, S. X.; Yang, X. B.; Li, M. Y.; Feng, G.; Pan, J. Y.; Satyanandamurthy, T.; Wu, J. *Chem. Pharm. Bull.* **2010**, *58*, 552.
- (559) Abdelgaleil, S. A. M.; Saad, M. M. G.; Nakatani, M. *Alex. J. Pharm. Sci.* **2005**, *19*, 141.
- (560) Connolly, J. D.; McCrindle, R.; Overton, K. H.; Warnock, W. D. C. *Tetrahedron* **1967**, *23*, 4035.
- (561) Agbedahunsi, J. M.; Elujoba, A. A. *Niger. J. Nat. Prod. Med.* **1998**, *2*, 34.
- (562) Pancharoen, O.; Haboonmee, P.; Taylor, W. C. *Acta Hort.* **2005**, *677*, 51.
- (563) Fang, X.; Di, Y. T.; Li, C. S.; Geng, Z. L.; Zhang, Z.; Zhang, Y.; Lu, Y.; Zheng, Q. T.; Yang, S. Y.; Hao, X. J. *J. Nat. Prod.* **2009**, *72*, 714.
- (564) Zhang, Z. G.; Yao, K.; Hu, G. L.; Zhang, J. *Helv. Chim. Acta* **2010**, *93*, 698.
- (565) Kehrli, A. R. H.; Taylor, D. A. H.; Niven, M. *Phytochemistry* **1990**, *29*, 153.
- (566) Taylor, A. R. H.; Taylor, D. A. H. *Phytochemistry* **1984**, *23*, 2676.

- (567) Taylor, D. A. H. *Phytochemistry* **1981**, *20*, 2263.
- (568) Wu, J.; Yang, S. X.; Li, M. Y.; Feng, G.; Pan, J. Y.; Xiao, Q.; Sinkkonen, J.; Satyanandamurthy, T. J. *Nat. Prod.* **2010**, *73*, 644.
- (569) Pancharoen, O.; Pipatanapatikarn, A.; Taylor, W. C.; Bansiddhi, J. *Nat. Prod. Res., Part A* **2009**, *23*, 10.
- (570) Segura, R.; Calderon, J.; Toscano, R.; Gutierrez, A.; Mata, R. *Tetrahedron Lett.* **1994**, *35*, 3437.
- (571) Cespedes, C. L.; Calderon, J. S.; Salazar, J. R.; Lotina-Hennsen, B.; Segura, R. *J. Chem. Ecol.* **2001**, *27*, 137.
- (572) Chen, Y. Y.; Wang, X. N.; Fan, C. Q.; Yin, S.; Yue, J. M. *Tetrahedron Lett.* **2007**, *48*, 7480.
- (573) Wang, X. N.; Fan, C. Q.; Yin, S.; Gan, L. S.; Yue, J. M. *Phytochemistry* **2008**, *69*, 1319.
- (574) Nakatani, M.; Abdelgaleil, S. A. M.; Kassem, S. M. I.; Takezaki, K.; Okamura, H.; Iwagawa, T.; Doe, M. *J. Nat. Prod.* **2002**, *65*, 1219.
- (575) Nakatani, M.; Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Doe, M.; Hirotsu, K. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **2000**, *42*, 37.
- (576) Adesogan, E. K.; Taylor, D. A. H. *J. Chem. Soc., D* **1969**, *15*, 889.
- (577) Nishizawa, M.; Nademoto, Y.; Sastrapradja, S.; Shiro, M.; Hayashi, Y. *J. Org. Chem.* **1985**, *50*, 5487.
- (578) Nishizawa, M.; Nademoto, Y.; Sastrapradja, S.; Shiro, M.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1985**, *7*, 395.
- (579) Ndung'u, M.; Hassanali, A.; Hooper, A. M.; Chhabra, S.; Miller, T. A.; Paul, R. L.; Torto, B. *Phytochemistry* **2003**, *64*, 817.
- (580) Cameron, A. F.; Connolly, J. D.; Maltz, A.; Taylor, D. A. H. *Tetrahedron Lett.* **1979**, *11*, 967.
- (581) Kimbu, S. F.; Ayafor, J. F.; Sondengam, B. L.; Connolly, J. D.; Rycroft, D. S. *Tetrahedron Lett.* **1984**, *25*, 1613.
- (582) Kimbu, S. F.; Ayafor, J. F.; Sondengam, B. L.; Tsamo, E.; Connolly, J. D.; Rycroft, D. S. *Tetrahedron Lett.* **1984**, *25*, 1617.
- (583) Nishizawa, M.; Nademoto, Y.; Sastrapradja, S.; Shiro, M.; Hayashi, Y. *Phytochemistry* **1988**, *27*, 237.
- (584) Fun, H. K.; Chantapromma, S.; Boonnak, N.; Chaiyadej, K.; Chantapromma, K.; Yu, X. L. *Acta Crystallogr., Sect. E* **2006**, *62*, o3725.
- (585) Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H. *Chem. Commun. (London)* **1965**, *13*, 281.
- (586) Connolly, J. D.; McCrindle, R.; Overton, K. H. *Tetrahedron* **1968**, *24*, 1497.
- (587) Connolly, J. D.; McCrindle, R.; Overton, K. H. *Chem. Commun. (London)* **1965**, *8*, 162.
- (588) Connolly, J. D.; McCrindle, R.; Overton, K. H. *Tetrahedron* **1968**, *24*, 1489.
- (589) Sanni, S. B.; Behm, H.; Beurskens, P. T. *Acta Crystallogr., Sect. C* **1987**, *43*, 1400.
- (590) Sondengam, B. L.; Kamga, C. S.; Connolly, J. D. *Phytochemistry* **1980**, *19*, 2488.
- (591) Gan, L. S.; Wang, X. N.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 1344.
- (592) Connolly, J. D.; McCrindle, R.; Overton, K. H.; Warnock, W. D. C. *Tetrahedron Lett.* **1965**, *6*, 2937.
- (593) Chakraborty, T.; Connolly, J. D.; McCrindle, R.; Overton, K. H.; Schwarz, J. C. P. *Tetrahedron* **1968**, *24*, 1503.
- (594) Connolly, J. D.; McCrindle, R.; Overton, K. H.; Warnock, W. D. C. *Tetrahedron* **1968**, *24*, 1507.
- (595) Goh, B. H.; Abdul Kadir, H.; Abdul Malek, S. N.; Ng, S. W. *Acta Crystallogr., Sect. E* **2010**, *66*, o1396.
- (596) Zelnik, R.; Rosito, C. M. *Tetrahedron Lett.* **1966**, *52*, 6441.
- (597) Lavie, D.; Levy, E. C.; Rosito, C.; Zelnik, R. *Tetrahedron* **1970**, *26*, 219.
- (598) Zelnik, R.; Rosito, C. *Phytochemistry* **1971**, *10*, 1166.
- (599) Taylor, D. A. H. *Tetrahedron Lett.* **1970**, *32*, 2797.
- (600) Taylor, D. A. H.; Wehrli, F. W. J. *Chem. Soc., Perkin Trans. 1* **1973**, *15*, 1599.
- (601) Khalid, S. A.; Friedrichsen, G. M.; Kharazmi, A.; Theander, T. G.; Olsen, C. E.; Christensen, S. B. *Phytochemistry* **1998**, *49*, 1769.
- (602) Adesogan, E. K.; Taylor, D. A. H. *Chem. Commun.* **1967**, *S*, 225.
- (603) Govindachari, T. R.; Suresh, G.; Banumathy, B.; Masilamani, S.; Gopalakrishnan, G.; Kumari, G. N. K. *J. Chem. Ecol.* **1999**, *25*, 923.
- (604) Wu, J.; Zhang, S.; Xiao, Q.; Li, Q. X.; Huang, J. S.; Xiao, Z. H.; Long, L. J. *Z. Naturforsch., B* **2003**, *58*, 1216.
- (605) Wu, J.; Zhang, S.; Song, Y.; Xiao, Z. H.; Xiao, Q.; Li, Q. X. *Z. Naturforsch., B* **2005**, *60*, 1291.
- (606) Chakraborty, T.; Chatterjee, A. J. *Indian Chem. Soc.* **1957**, *34*, 117.
- (607) Connolly, J. D.; Henderson, R.; McCrindle, R.; Overton, K. H.; Bhacca, N. S. *Tetrahedron Lett.* **1964**, *5*, 2593.
- (608) Chakravarty, T.; Chatterjee, A. J. *Indian Chem. Soc.* **1955**, *32*, 179.
- (609) Connolly, J. D.; Henderson, R.; McCrindle, R.; Overton, K. H.; Bhacca, N. S. *J. Chem. Soc.* **1965**, *Dec*, 6935.
- (610) McPhail, A. T.; Sim, G. A. *Tetrahedron Lett.* **1964**, *37–38*, 2599.
- (611) McPhail, A. T.; Sim, G. A. *J. Chem. Soc., B* **1966**, *4*, 318.
- (612) Solomon, K. A.; Malathi, R.; Rajan, S. S.; Narasimhan, S.; Nethaji, M. *Acta Crystallogr., Sect. E* **2003**, *S9*, o1519.
- (613) Mulholland, D. A.; Taylor, D. A. H. *Phytochemistry* **1988**, *27*, 1741.
- (614) Kojima, K.; Isaka, K.; Ogihara, Y. *Chem. Pharm. Bull.* **1998**, *46*, 523.
- (615) Rao, M. M.; Krishna, E. M.; Gupta, P. S.; Singh, P. P. *Indian J. Chem., Sect. B* **1978**, *16*, 823.
- (616) Govindachari, T. R.; Banumathy, B.; Gopalakrishnan, G.; Suresh, G. *Fitoterapia* **1999**, *70*, 106.
- (617) Leite, A. C.; Fernandes, J. B.; da Silva, M. F. das G. F.; Vieira, P. C. Z. *Naturforsch., B* **2005**, *60*, 351.
- (618) Marpaung, L.; Nakamura, N.; Kaduda, H.; Hattori, M. *Nat. Med. (Tokyo, Jpn.)* **2001**, *55*, 220.
- (619) Okorie, D. A.; Taylor, D. A. H. *Phytochemistry* **1971**, *10*, 469.
- (620) Daniewski, W. M.; Gumulka, M.; Danikiewicz, W.; Gluzinski, P.; Krajewski, J.; Pankowska, E.; Bloszyk, E.; Jacobsson, U.; Norin, T.; Szafrański, F. *Phytochemistry* **1993**, *33*, 1534.
- (621) Daniewski, W. M.; Gumulka, M.; Danikiewicz, W.; Gluzinski, P.; Krajewski, J.; Sitkowski, J.; Bloszyk, E.; Drozd, B.; Jacobsson, U.; Szafrański, F. *Phytochemistry* **1994**, *36*, 1001.
- (622) Yuan, T.; Yang, S. P.; Zhang, C. R.; Zhang, S.; Yue, J. M. *Org. Lett.* **2009**, *11*, 617.
- (623) Yuan, T.; Zhang, C. R.; Yang, S. P.; Yue, J. M. *J. Nat. Prod.* **2010**, *73*, 669.
- (624) Roy, A. D.; Kumar, R.; Gupta, P.; Khaliq, T.; Narender, T.; Aggarwal, V.; Roy, R. *Magn. Reson. Chem.* **2006**, *44*, 1054.
- (625) Connolly, J. D.; MacLellan, M.; Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, *19*, 1993.
- (626) Alvi, K. A.; Crews, P.; Aalbersberg, B.; Prasad, R. *Tetrahedron* **1991**, *47*, 8943.
- (627) Xiao, Z. H.; Wu, J.; Zhang, S.; Li, Q. X. *Chin. J. Magn. Reson.* **2005**, *22*, 315.
- (628) Wu, J.; Xiao, Z. H.; Song, Y.; Zhang, S.; Xiao, Q.; Ma, C.; Ding, H. X.; Li, Q. X. *Magn. Reson. Chem.* **2006**, *44*, 87.
- (629) Segura-Correa, R.; Mata, R.; Anaya, A. L.; Hernandez-Bautista, B.; Villena, R.; Soriano-Garcia, M.; Bye, R.; Linares, E. *J. Nat. Prod.* **1993**, *56*, 1567.
- (630) Saad, M. M. G.; Iwagawa, T.; Okamura, H.; Doe, M.; Nakatani, M. *Heterocycles* **2004**, *63*, 389.
- (631) Yuan, X. H.; Li, B. G.; Zhou, M.; Qi, H. Y.; Zhang, G. L. *Org. Lett.* **2005**, *7*, 5051.
- (632) Yin, S.; Wang, X. N.; Fan, C. Q.; Lin, L. P.; Ding, J.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 682.
- (633) Cui, J. X.; Wu, J.; Deng, Z. W.; Proksch, P.; Lin, W. H. *J. Nat. Prod.* **2007**, *70*, 772.
- (634) Huo, C. H.; Guo, D.; Shen, L. R.; Yin, B. W.; Sauriol, F.; Li, L. G.; Zhang, M. L.; Shi, Q. W.; Kiyota, H. *Tetrahedron Lett.* **2010**, *51*, 754.
- (635) Wu, J.; Zhang, S.; Long, L. J. CN Patent 1513853, 2004; *Chem. Abstr.* **2005**, *143*, 363956.
- (636) Wu, J.; Zhang, S.; Xiao, Q.; Li, Q. X.; Huang, J. S.; Long, L. J.; Huang, L. M. *Tetrahedron Lett.* **2004**, *45*, 591.

- (637) Yin, S.; Fan, C. Q.; Wang, X. N.; Lin, L. P.; Ding, J.; Yue, J. M. *Org. Lett.* **2006**, *8*, 4935.
- (638) Wu, J.; Zhang, S.; Bruhn, T.; Xiao, Q.; Ding, H.; Bringmann, G. *Chem.—Eur. J.* **2008**, *14*, 1129.
- (639) Wu, J.; Zhang, S.; Zhou, Y.; Xiao, Q. *Chem. Pharm. Bull.* **2006**, *54*, 1582.
- (640) Yuan, T.; Zhu, R. X.; Zhang, H.; Odeku, O. A.; Yang, S. P.; Liao, S. G.; Yue, J. M. *Org. Lett.* **2010**, *12*, 252.
- (641) Adesogan, E. K.; Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H. *J. Chem. Soc. C* **1966**, *23*, 2127.
- (642) Zelnik, R.; Rosito, C. *Phytochemistry* **1971**, *10*, 1955.
- (643) Leite, A. C.; Neto, A. P.; Ambrozini, A. R. P.; Fernandes, J. B.; Vieira, P. C.; da Silva, M. F. das G. F.; de Albuquerque, S. *Rev. Bras. Farmacogn.* **2010**, *20*, 1.
- (644) Zelnik, R. *Phytochemistry* **1972**, *11*, 1866.
- (645) Chantrapromma, K.; Saewan, N.; Fun, H.-K.; Chantrapromma, S.; Rahman, A. A. *Acta Crystallogr., Sect. E* **2004**, *60*, o312.
- (646) Coombes, P. H.; Mulholland, D. A.; Randrianarivelojosia, M. *Phytochemistry* **2005**, *66*, 1100.
- (647) Fang, X.; Di, Y. T.; Hu, G. W.; Li, S. L.; Hao, X. J. *Biochem. Syst. Ecol.* **2009**, *37*, 528.
- (648) Vanucci, C.; Lange, C.; Lhomme, G.; Dupont, B.; Davoust, D.; Vauchot, B.; Clement, J. L.; Brunck, F. *Phytochemistry* **1992**, *31*, 3003.
- (649) Rahman, A. K. M. S.; Chowdhury, A. K. A.; Ali, H.-A.; Raihan, S. Z.; Ali, M. S.; Nahar, L.; Sarker, S. D. *J. Nat. Med.* **2009**, *63*, 41.
- (650) Inada, A.; Konishi, M.; Murata, H.; Nakanishi, T. *J. Nat. Prod.* **1994**, *57*, 1446.
- (651) Fang, X.; Di, Y. T.; Geng, Z. L.; Tan, C. J.; Guo, J.; Ning, J.; Hao, X. J. *Eur. J. Org. Chem.* **2010**, *2010*, 1381.
- (652) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Tetrahedron Lett.* **1989**, *30*, 1111.
- (653) Chen, J. J.; Huang, S. S.; Liao, C. H.; Wei, D. C.; Sung, P. J.; Wang, T. C.; Cheng, M. J. *Food Chem.* **2010**, *120*, 379.
- (654) Chan, K. C.; Tang, T. S.; Toh, H. T. *Phytochemistry* **1976**, *15*, 429.
- (655) Adesogan, E. K.; Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H. *Chem. Commun. (London)* **1966**, *1*, 27.
- (656) Matos Andreia, P.; Leite Ana, C.; Batista-Pereira Luciane, G.; Vieira Paulo, C.; Fernandes Josao, B.; da Silva, M. F. das G. F. *Z. Naturforsch., C* **2009**, *64*, 441.
- (657) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G. *Phytochemistry* **2000**, *55*, 867.
- (658) Nakatani, M.; Abdelgaleil, S. A. M.; Kurawaki, J.; Okamura, H.; Iwagawa, T.; Doe, M. *J. Nat. Prod.* **2001**, *64*, 1261.
- (659) Wu, J.; Xiao, Q.; Li, Q. X. *Biochem. Syst. Ecol.* **2006**, *34*, 838.
- (660) Li, M. Y.; Wu, J.; Zhang, S.; Xiao, Q.; Li, Q. X. *Magn. Reson. Chem.* **2007**, *45*, 705.
- (661) Guha-Sircar, S. S.; Chakravarty, T. *J. Indian Chem. Soc.* **1951**, *28*, 207.
- (662) Dewanjee, S.; Maiti, A.; Das, A. K.; Mandal, S. C.; Dey, S. P. *Fitoterapia* **2009**, *80*, 249.
- (663) Daily, A.; Seligmann, O.; Lotter, H.; Wagner, H. *Z. Naturforsch., C* **1985**, *40*, 519.
- (664) Saad, M. M. G.; Iwagawa, T.; Doe, M.; Nakatani, M. *Tetrahedron* **2003**, *59*, 8027.
- (665) Jimenez, A.; Mata, R.; Pereda-Miranda, R.; Calderon, J.; Isman, M. B.; Nicol, R.; Arnason, J. T. *J. Chem. Ecol.* **1997**, *23*, 1225.
- (666) Mikolajczak, K. L.; Weisleder, D.; Parkanyi, L.; Clardy, J. *J. Nat. Prod.* **1988**, *51*, 606.
- (667) Awang, K.; Lim, C. S.; Mohamad, K.; Morita, H.; Hirasawa, Y.; Takeya, K.; Thoisson, O.; Hadi, A. H. A. *Bioorg. Med. Chem.* **2007**, *15*, S997.
- (668) Kadota, S.; Yanagawa, K.; Kikuchi, T.; Tanaka, K. *Tetrahedron Lett.* **1990**, *31*, S943.
- (669) Wu, J.; Li, M.; Zhang, S.; Xiao, Q.; Li, Q. *Z. Naturforsch., B* **2007**, *62*, 859.
- (670) Arene, E. O.; Bevan, C. W. L.; Powell, J. W.; Taylor, D. A. H. *Chem. Commun. (London)* **1965**, *14*, 302.
- (671) Leite, A. C.; Bueno, F. C.; Oliveira, C. G.; Fernandes, J. B.; Vieira, P. C.; da Silva, M. F. das G. F.; Bueno, O. C.; Pagnocca, F. C.; Jose, M.; Hebling, A.; Bacci, M., Jr. *J. Braz. Chem. Soc.* **2005**, *16*, 1391.
- (672) Connolly, J. D.; Handa, K. L. *J. Chem. Soc., C* **1969**, *18*, 2435.
- (673) Cheng, F.; Zhou, Y.; Wub, J.; Zoua, K. *Z. Naturforsch., B* **2006**, *61*, 626.
- (674) Krajewski, J. W.; Gluzinski, P.; Daniewski, W. M.; Gumulka, M.; Kemme, A.; Mishnev, A. *Pol. J. Chem.* **1994**, *68*, 2641.
- (675) Shen, L. R.; Dong, M.; Guo, D.; Yin, B. W.; Zhang, M. L.; Shi, Q. W.; Huo, C. H.; Kiyota, H.; Suzuki, N.; Cong, B. *Z. Naturforsch., C* **2009**, *64*, 37.
- (676) Huo, C.; Guo, D.; Shen, L.; Wang, W.; Zhang, Q.; Zhang, M.; Shi, Q. *Zhongcaoyao* **2010**, *41*, 176.
- (677) Cui, J. X.; Deng, Z. W.; Xu, M. J.; Proksch, P.; Li, Q. S.; Lin, W. H. *Helv. Chim. Acta* **2009**, *92*, 139.
- (678) El-Aswad Ahmed, F.; Abdelgaleil Samir, A. M.; Nakatani, M. *Pest Manage. Sci.* **2004**, *60*, 199.
- (679) Zhang, H.; Odeku Oluwatoyin, A.; Wang, X. N.; Yue, J. M. *Phytochemistry* **2008**, *69*, 271.
- (680) Ferreira, I. C. P.; Cortez, D. A. G.; da Silva, M. F. das G. F.; Fo, E. R.; Vieira, P. C.; Fernandes, J. B. *J. Nat. Prod.* **2005**, *68*, 413.
- (681) Veitch, N. C.; Wright, G. A.; Stevenson, P. C. *J. Nat. Prod.* **1999**, *62*, 1260.
- (682) Kokpol, U.; Chavasiri, W.; Tip-Pyang, S.; Veerachato, G.; Zhao, F. L.; Simpson, J.; Weavers, R. T. *Phytochemistry* **1996**, *41*, 903.
- (683) Taylor, D. A. H. *Phytochemistry* **1983**, *22*, 1297.
- (684) Perusquia, M.; Hernandez, R.; Jimenez, M. A.; Pereda-Miranda, R.; Mata, R. *Phytother. Res.* **1997**, *11*, 354.
- (685) Okorie, D. A.; Taylor, D. A. H. *J. Chem. Soc., C* **1970**, *2*, 211.
- (686) Mootoo, B. S.; Jatava, C.; Tinto, W. F.; Reynolds, W. F.; McLean, S. *Can. J. Chem.* **1992**, *70*, 1260.
- (687) Wu, J.; Ding, H.; Li, M.; Zhang, S. *Z. Naturforsch., B* **2007**, *62*, 569.
- (688) Taylor, D. A. H. *Phytochemistry* **1977**, *16*, 1847.
- (689) Arndt, R. R.; Baarschers, W. H. *Tetrahedron* **1972**, *28*, 2333.
- (690) Coetzer, J.; Baxter, W. J.; Gafner, G. *Acta Crystallogr., Sect. B* **1971**, *27*, 1434.
- (691) Haenni, R.; Tamm, C. *J. Chem. Soc., Chem. Commun.* **1972**, *22*, 1253.
- (692) Haenni, R.; Tamm, C.; Gullo, V.; Nakanishi, K. *J. Chem. Soc., Chem. Commun.* **1975**, *14*, 563.
- (693) Guex, M.; Tamm, C. *Helv. Chim. Acta* **1984**, *67*, 885.
- (694) Taylor, D. A. H. *Phytochemistry* **1979**, *18*, 1574.
- (695) Niven, M. L.; Taylor, D. A. H. *Phytochemistry* **1988**, *27*, 1542.
- (696) Luo, J.; Wang, J. S.; Wang, X. B.; Huang, X. F.; Luo, J. G.; Kong, L. Y. *Tetrahedron* **2009**, *65*, 3425.
- (697) Zhang, C. R.; Fan, C. Q.; Zhang, L.; Yang, S. P.; Wu, Y.; Lu, Y.; Yue, J. M. *Org. Lett.* **2008**, *10*, 3183.
- (698) Harrison, H. R.; Hodder, O. J. R.; Bevan, C. W. L.; Taylor, D. A. H.; Halsall, T. G. *J. Chem. Soc. D* **1970**, *21*, 1388.
- (699) Wu, J.; Xiao, Q.; Huang, J. S.; Xiao, Z. H.; Qi, S. H.; Li, Q. X.; Zhang, S. *Org. Lett.* **2004**, *6*, 1841.
- (700) Wu, J.; Xiao, Q.; Zhang, S.; Li, X.; Xiao, Z. H.; Ding, H. X.; Li, Q. X. *Tetrahedron* **2005**, *61*, 8382.
- (701) Cui, J. X.; Deng, Z. W.; Li, J.; Fu, H. Z.; Proksch, P.; Lin, W. H. *Phytochemistry* **2005**, *66*, 2334.
- (702) Connolly, J. D.; Labbe, C.; Rycroft, D. S. *J. Chem. Soc., Perkin Trans. 1* **1978**, *3*, 285.
- (703) Ansell, S. M.; Taylor, D. A. H. *Phytochemistry* **1988**, *27*, 1218.
- (704) Coombes, P. H.; Mulholland, D. A.; Randrianarivelojosia, M. *J. Nat. Prod.* **2003**, *66*, 735.
- (705) Mallavarapu, G. R.; Muralikrishna, E.; Connolly, J. D. *Phytochemistry* **1985**, *24*, 305.
- (706) Nakatani, M.; Abdelgaleil, S. A. M.; Saad, M. M. G.; Huang, R. C.; Doe, M.; Iwagawa, T. *Phytochemistry* **2004**, *65*, 2833.
- (707) Zhang, C. R.; Yang, S. P.; Chen, X. Q.; Wu, Y.; Zhen, X. C.; Yue, J. M. *Helv. Chim. Acta* **2008**, *91*, 2338.

- (708) Rao, M. M.; Gupta, P. S.; Singh, P. P.; Krishna, E. M. *Indian J. Chem., Sect. B* **1979**, *17*, 158.
- (709) Randrianarivelojosia, M.; Kotsos, M. P.; Mulholland, D. A. *Phytochemistry* **1999**, *52*, 1141.
- (710) Connolly, J. D.; Phillips, W. R.; Mulholland, D. A.; Taylor, D. A. H. *Phytochemistry* **1981**, *20*, 2596.
- (711) Ragettli, T.; Tamm, C. *Helv. Chim. Acta* **1978**, *61*, 1814.
- (712) Zhang, C. R.; Yang, S. P.; Zhu, Q.; Liao, S. G.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 1616.
- (713) Fan, C. Q.; Wang, X. N.; Yin, S.; Zhang, C. R.; Wang, F. D.; Yue, J. M. *Tetrahedron* **2007**, *63*, 6741.
- (714) Halsall, T. G.; Wragg, K.; Connolly, J. D.; McLellan, M. A.; Bredell, L. D.; Taylor, D. A. H. *J. Chem. Res., Synop.* **1977**, *6*, 154.
- (715) Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1974**, *4*, 437.
- (716) Nascimento da Silva, M.; Arruda, M. S. P.; Castro, K. C. F.; da Silva, M. F. das G. F.; Fernandes, J. B.; Vieira, P. C. *J. Nat. Prod.* **2008**, *71*, 1983.
- (717) Tan, S.-K.; Osman, H.; Wong, K.-C.; Boey, P.-L. *Food Chem.* **2009**, *115*, 1279.
- (718) Wangenstein, H.; Duong, G. M.; Alamgir, M.; Sarder, M.; Samuelsen, A. B.; Malterud, K. E. *Nat. Prod. Commun.* **2006**, *1*, 985.
- (719) Tchouankeu, J. C.; Tsamo, E.; Sondengam, B. L.; Connolly, J. D. *Phytochemistry* **1989**, *28*, 2855.
- (720) Olmo, L. R. V.; da Silva, M. F. das G. F.; Rodrigues, F. O.; Vieira, P. C.; Fernandes, J. B.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1997**, *44*, 1157.
- (721) Olmo, L. R. V.; da Silva, M. F. das G. F.; Rodrigues, F. O.; Vieira, P. C.; Fernandes, J. B.; Marsaioli, A. J.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1996**, *42*, 831.
- (722) Zhang, H. P.; Tan, J. J.; VanDerveer, D.; Wang, X.; Wargovich, M. J.; Chen, F. *Phytochemistry* **2009**, *70*, 294.
- (723) Pudhom, K.; Sommit, D.; Nuclear, P.; Ngamrojanavanich, N.; Petsom, A. *J. Nat. Prod.* **2010**, *73*, 263.
- (724) Brown, D. A.; Taylor, D. A. H. *J. Chem. Res., Synop.* **1978**, *1*, 20.
- (725) Tchouankeu, J. C.; Tsamo, E.; Sondengam, B. L.; Connolly, J. D. *Phytochemistry* **1990**, *29*, 3999.
- (726) Cui, J. X.; Ou, Y. J.; Deng, Z. W.; Lin, W. H. *Magn. Reson. Chem.* **2008**, *46*, 894.
- (727) Zhou, Y.; Cheng, F.; Wu, J.; Zou, K. *J. Nat. Prod.* **2006**, *69*, 1083.
- (728) Fall, A. B.; Vanhaelen-Fastre, R.; Vanhaelen, M.; Lo, I.; Toppet, M.; Ferster, A.; Fondou, P. *Planta Med.* **1999**, *65*, 209.
- (729) Purushothaman, K. K.; Venkatanarasimham, M.; Sarada, A.; Connolly, J. D.; Rycroft, D. S. *Can. J. Chem.* **1987**, *65*, 35.
- (730) Mulholland, D. A.; Iourine, S. E. *Phytochemistry* **1998**, *47*, 1357.
- (731) Geng, Z. L.; Fang, X.; Di, Y. T.; Zhang, Q.; Zeng, Y.; Shen, Y. M.; Hao, X. J. *Tetrahedron Lett.* **2009**, *50*, 2132.
- (732) Hill, R. A.; Sutherland, A. *Nat. Prod. Rep.* **2009**, *26*, 725.
- (733) Mulholland, D. A.; Schwikkard, S. L.; Randrianarivelojosia, M. *Phytochemistry* **1999**, *52*, 705.
- (734) Venkatanarasimhan, M.; Kundu, A. B. *Indian J. Chem., Sect. B* **1990**, *29*, 970.
- (735) Di, Y. T.; He, H. P.; Liu, H. Y.; Yi, P.; Zhang, Z.; Ren, Y. L.; Wang, J. S.; Sun, Q. Y.; Yang, F. M.; Fang, X.; Li, S. L.; Zhu, H. J.; Hao, X. J. *J. Nat. Prod.* **2007**, *70*, 1352.
- (736) Ismail, I. S.; Ito, H.; Hatano, T.; Taniguchi, S.; Yoshida, T. *Phytochemistry* **2003**, *64*, 1345.
- (737) Yoshida, T.; Ismail, I. S.; Ito, H. In *Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22–26, 2004*; American Chemical Society: Washington, D. C., 2004.
- (738) Ismail, I. S.; Ito, H.; Hatano, T.; Taniguchi, S.; Yoshida, T. *Chem. Pharm. Bull.* **2004**, *52*, 1145.
- (739) Yin, S.; Wang, X. N.; Fan, C. Q.; Liao, S. G.; Yue, J. M. *Org. Lett.* **2007**, *9*, 2353.
- (740) Fang, X.; Di, Y. T.; He, H. P.; Liu, H. Y.; Zhang, Z.; Ren, Y. L.; Gao, Z. L.; Gao, S.; Hao, X. J. *Org. Lett.* **2008**, *10*, 1905.
- (741) Fang, X.; Di, Y. T.; He, H. P.; Liu, H. Y.; Zhang, Z.; Ren, Y. L.; Gao, Z. L.; Gao, S.; Hao, X. J. *Org. Lett.* **2008**, *10*, 3169.
- (742) Bruhn, A.; Bokel, M.; Kraus, W. *Tetrahedron Lett.* **1984**, *25*, 3691.
- (743) Nakatani, M.; Zhou, J. B.; Tadera, K.; Naoki, H. *Chem. Lett.* **1998**, *12*, 1279.
- (744) Rogers, L. L.; Zeng, L.; McLaughlin, J. L. *Tetrahedron Lett.* **1998**, *39*, 4623.
- (745) Kashiwada, Y.; Fujioka, T.; Chang, J. J.; Chen, I. S.; Mihashi, K.; Lee, K. H. *J. Org. Chem.* **1992**, *57*, 6946.
- (746) Kalinowski, H.-O.; Ermel, K.; Schmutterer, H. *Liebigs Ann. Chem.* **1993**, *31*, 1033.
- (747) Rojatk, S. R.; Nagasampagi, B. A. *Nat. Prod. Lett.* **1994**, *5*, 69.
- (748) Ramji, N.; Venkatakrishnan, K.; Madyastha, K. M. *Phytochemistry* **1996**, *42*, 561.
- (749) Malathi, R.; Kabaleeswaran, V.; Rajan, S. S.; Gopalakrishnan, G.; Govindachari, T. R. *J. Chem. Crystallogr.* **2003**, *33*, 229.
- (750) Zhang, C. R.; Yang, S. P.; Liao, S. G.; Fan, C. Q.; Wu, Y.; Yue, J. M. *Org. Lett.* **2007**, *9*, 3383.
- (751) Luo, J.; Wang, J. S.; Luo, J. G.; Wang, X. B.; Kong, L. Y. *Org. Lett.* **2009**, *11*, 2281.
- (752) Luo, J.; Wang, J. S.; Wang, X. B.; Luo, J. G.; Kong, L. Y. *J. Nat. Prod.* **2010**, *73*, 835.
- (753) Siddiqui, B. S.; Ghiasuddin, Faizi, S.; Siddiqui, S. *Phytochemistry* **1992**, *31*, 4275.
- (754) Mulholland, D. A.; Randrianarivelojosia, M.; Lavaud, C.; Nuzillard, J.-M.; Schwikkard, S. L. *Phytochemistry* **2000**, *53*, 115.
- (755) Govindachari, T. R.; Geetha, G.; Rajan, S. S.; Kabaleeswaran, V.; Lessinger, L. *Acta Crystallogr., Sect. B* **1996**, *52*, 145.
- (756) Govindachari, T. R.; Gopalakrishnan, G.; Malathi, R.; Singh, N. D. *P. Nat. Prod. Lett.* **1999**, *13*, 157.
- (757) Cortez, D. A. G.; Fernandes, J. B.; Vieira, P. C.; da Silva, M. F. das G. F.; Ferreira, A. G. *Phytochemistry* **2000**, *55*, 711.
- (758) Kraus, W.; Cramer, R. *Chem. Ber.* **1981**, *114*, 2375.
- (759) Zhang, H. P.; Wu, S. H.; Shen, Y. M.; Ma, Y. B.; Wu, D. G.; Qi, S. H.; Luo, X. D. *Can. J. Chem.* **2003**, *81*, 253.
- (760) Tchouankeu, J. C.; Tsamo, E.; Sondengam, B. L.; Connolly, J. D.; Rycroft, D. S. *Tetrahedron Lett.* **1990**, *31*, 4505.
- (761) Daniewski, W. M.; Gumulka, M.; Pankowska, E.; Bloszyk, E.; Szafranski, F.; Jacobsson, U.; Norin, T. *Pol. J. Chem.* **1994**, *68*, 499.
- (762) Daniewski, W. M.; Gumulka, M.; Danikiewicz, W.; Sitkowski, J.; Jacobsson, U.; Norin, T. *Phytochemistry* **1995**, *40*, 903.
- (763) Coggon, P.; McPhail, A. T. *J. Chem. Soc. B* **1970**, *8*, 1521.
- (764) Xie, B. J.; Yang, S. P.; Yue, J. M. *Phytochemistry* **2008**, *69*, 2993.
- (765) Qi, S. H.; Wu, D. G.; Chen, L.; Ma, Y. B.; Luo, X. D. *J. Agric. Food Chem.* **2003**, *51*, 6949.
- (766) Kraus, W.; Klenk, A.; Bokel, M.; Vogler, B. *Liebigs Ann. Chem.* **1987**, *4*, 337.
- (767) Adesida, G. A.; Taylor, D. A. H. *Phytochemistry* **1972**, *11*, 1520.
- (768) da Silva, M. F. das G. F.; Agostinho, S. M. M.; de Paula, J. R.; Oiano Neto, J.; Castro-Gamboa, L.; Rodrigues Filho, E.; Fernandes, J. B.; Vieira, P. C. *Pure Appl. Chem.* **1999**, *71*, 1083.
- (769) Pennington, T. D.; Styles, B. T. *Blumea* **1975**, *22*, 419.
- (770) Veitch, G. E.; Beckmann, E.; Burke, B. J.; Boyer, A.; Maslen, S. L.; Ley, S. V. *Angew. Chem., Int. Ed.* **2007**, *46*, 7629.
- (771) Denholm, A. A.; Jennens, L.; Ley, S. V.; Wood, A. *Tetrahedron* **1995**, *51*, 6591.
- (772) Kolb, H. C.; Ley, S. V. *Tetrahedron Lett.* **1991**, *32*, 6187.
- (773) Kolb, H. C.; Ley, S. V.; Slawin, A. M. Z.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, *21*, 2735.
- (774) Ley, S. V. *Pure Appl. Chem.* **1994**, *66*, 2099.
- (775) Ley, S. V.; Lovell, P. J.; Smith, S. C.; Wood, A. *Tetrahedron Lett.* **1991**, *32*, 6183.
- (776) Ley, S. V.; Lovell, P. J.; Slawin, A. M. Z.; Smith, S. C.; Williams, D. J.; Wood, A. *Tetrahedron* **1993**, *49*, 1675.
- (777) Koot, W. J.; Ley, S. V. *Tetrahedron* **1995**, *51*, 2077.
- (778) Kanoh, N.; Ishihara, J.; Murai, A. *Synlett* **1995**, *9*, 895.
- (779) Haag, D.; Chen, X.-T.; Fraser-Reid, B. *Chem. Commun. (Cambridge)* **1998**, *23*, 2577.

- (780) Goldenstein, K.; Nerenz, F.; Winterfeldt, E. *Pol. J. Chem.* **1999**, 73, 3.
- (781) Ishihara, J.; Yamamoto, Y.; Kanoh, N.; Murai, A. *Tetrahedron Lett.* **1999**, 40, 4387.
- (782) Yamamoto, Y.; Ishihara, J.; Kanoh, N.; Murai, A. *Synthesis* **2000**, 13, 1894.
- (783) Ley, S. V.; Abad Somovilla, A.; Broughton, H. B.; Craig, D.; Slawin, A. M. Z.; Toogood, P. L.; Williams, D. J. *Tetrahedron* **1989**, 45, 2143.
- (784) Brasca, M. G.; Broughton, H. B.; Craig, D.; Ley, S. V.; Somovilla, A. A.; Toogood, P. L. *Tetrahedron Lett.* **1988**, 29, 1853.
- (785) Kanoh, N.; Ishihara, J.; Yamamoto, Y.; Murai, A. *Synthesis* **2000**, 13, 1878.
- (786) Kanoh, N.; Ishihara, J.; Murai, A. *Synlett* **1997**, 6, 737.
- (787) Ley, S. V.; Gutteridge, C. E.; Pape, A. R.; Spilling, C. D.; Zumburn, C. *Synlett* **1999**, 8, 1295.
- (788) Nicolaou, K. C.; Sasmal, P. K.; Koftis, T. V.; Converso, A.; Loizidou, E.; Kaiser, F.; Roecker, A. J.; Dellios, C. C.; Sun, X. W.; Petrovic, G. *Angew. Chem., Int. Ed.* **2005**, 44, 3447.
- (789) Nicolaou, K. C.; Sasmal, P. K.; Roecker, A. J.; Sun, X. W.; Mandal, S.; Converso, A. *Angew. Chem., Int. Ed.* **2005**, 44, 3443.
- (790) Watanabe, H.; Mori, N.; Itoh, D.; Kitahara, T.; Mori, K. *Angew. Chem., Int. Ed.* **2007**, 46, 1512.
- (791) Watanabe, H.; Watanabe, T.; Mori, K.; Kitahara, T. *Tetrahedron Lett.* **1997**, 38, 4429.
- (792) Ley, S. V.; Santafianos, D.; Blaney, W. M.; Simmonds, M. S. J. *Tetrahedron Lett.* **1987**, 28, 221.
- (793) Anderson, J. C.; Ley, S. V. *Tetrahedron Lett.* **1990**, 31, 3437.
- (794) Anderson, J. C.; Ley, S. V.; Santafianos, D.; Sheppard, R. N. *Tetrahedron* **1991**, 47, 6813.
- (795) Grossman, R. B.; Ley, S. V. *Tetrahedron* **1994**, 50, 11553.
- (796) Nishikimi, Y.; Iimori, T.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, 54, 3354.
- (797) Schlesiger, H.; Winterfeldt, E. *Chirality* **1997**, 9, 454.
- (798) Schlesiger, H.; Winterfeldt, E. *Chirality* **1998**, 10, 190.
- (799) de la Puente, M. L.; Ley, S. V.; Simmonds, M. S.; Blaney, W. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 13, 1523.
- (800) Pflieger, D.; Muckensturm, B.; Robert, P. C.; Simonis, M. T.; Kienlen, J. C. *Tetrahedron Lett.* **1987**, 28, 1519.
- (801) Henry, K. J., Jr.; Fraser-Reid, B. *J. Org. Chem.* **1994**, 59, 5128.
- (802) Ishihara, J.; Fukuzaki, T.; Murai, A. *Tetrahedron Lett.* **1999**, 40, 1907.
- (803) de la Puente, M. L.; Grossman, R. B.; Ley, S. V.; Simmonds, M. S. J.; Blaney, W. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 13, 1517.
- (804) Watanabe, H.; Watanabe, T.; Mon, K. *Tetrahedron* **1996**, 52, 13939.
- (805) Anderson, J. C.; Ley, S. V. *Tetrahedron Lett.* **1990**, 31, 431.
- (806) Ley, S. V.; Durand-Reville, T.; Gobbi, L. In *Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26–30*; American Chemical Society: Washington, D.C., 2001.
- (807) Durand-Reville, T.; Gobbi, L. B.; Gray, B. L.; Ley, S. V.; Scott, J. S. *Org. Lett.* **2002**, 4, 3847.
- (808) Fukuzaki, T.; Kobayashi, S.; Hibi, T.; Ikuma, Y.; Ishihara, J.; Kanoh, N.; Murai, A. *Org. Lett.* **2002**, 4, 2877.
- (809) Murai, A. *Toxin Rev.* **2003**, 22, 617.
- (810) Nicolaou, K. C.; Roecker, A. J.; Follmann, M.; Baati, R. *Angew. Chem., Int. Ed.* **2002**, 41, 2107.
- (811) Nicolaou, K. C.; Roecker, A. J.; Monenschein, H.; Guntupalli, P.; Follmann, M. *Angew. Chem., Int. Ed.* **2003**, 42, 3637.
- (812) Nicolaou, K. C.; Follmann, M.; Roecker, A. J.; Hunt, K. W. *Angew. Chem., Int. Ed.* **2002**, 41, 2103.
- (813) Veitch, G. E.; Beckmann, E.; Burke, B. J.; Boyer, A.; Ayats, C.; Ley, S. V. *Angew. Chem., Int. Ed.* **2007**, 46, 7633.
- (814) Jauch, J. *Angew. Chem., Int. Ed.* **2008**, 47, 34.
- (815) Veitch, G. E.; Pinto, A.; Boyer, A.; Beckmann, E.; Anderson, J. C.; Ley, S. V. *Org. Lett.* **2008**, 10, 569.
- (816) Bilton, J. N.; Jones, P. S.; Ley, S. V.; Robinson, N. G.; Sheppard, R. N. *Tetrahedron Lett.* **1988**, 29, 1849.
- (817) Grossman, R. B.; Ley, S. V. *Tetrahedron* **1994**, 50, 8871.
- (818) Fernandez Mateos, A.; Lopez Barba, A. M. *J. Org. Chem.* **1995**, 60, 3580.
- (819) Corey, E. J.; Hahl, R. W. *Tetrahedron Lett.* **1989**, 30, 3023.
- (820) Sastry, B. S.; Babu, K. S.; Babu, T. H.; Chandrasekhar, S.; Srinivas, P. V.; Saxena, A. K.; Rao, J. M. *Bioorg. Med. Chem. Lett.* **2006**, 16, 4391.
- (821) Fernández-Mateos, A.; Ramos Silvo, A. I.; Rubio González, R.; Simmonds, M. S. J. *Tetrahedron* **2006**, 62, 7809.
- (822) Buchanan, J. G. S. C.; Halsall, T. G. *Chem. Commun.* **1969**, 5, 242.
- (823) Buchanan, J. G. S. C.; Halsall, T. G. *J. Chem. Soc. D* **1969**, 2, 48.
- (824) Fukuyama, Y.; Tokoroyama, T.; Kubota, T. *Tetrahedron Lett.* **1972**, 33, 3401.
- (825) Tokoroyama, T.; Fukuyama, Y.; Kubota, T.; Yokotani, K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 5, 1557.
- (826) Okamura, H.; Yamauchi, K.; Miyawaki, K.; Iwagawa, T.; Nakatani, M. *Tetrahedron Lett.* **1997**, 38, 263.
- (827) Trudeau, S.; Morken, J. P. *Org. Lett.* **2005**, 7, 5465.
- (828) Corey, E. J.; Reid, J. G.; Myers, A. G.; Hahl, R. W. *J. Am. Chem. Soc.* **1987**, 109, 918.
- (829) Lavie, D.; Levy, E. C. *Tetrahedron* **1971**, 27, 3941.
- (830) Connolly, J. D.; Labbe, C. J. *Chem. Soc., Perkin Trans. 1* **1980**, 2, 529.
- (831) Buchanan, J. G. S. C.; Halsall, T. G. *J. Chem. Soc., D* **1969**, 24, 1493.
- (832) Obasi, M. E.; Okogun, J. I.; Ekong, D. E. U. *J. Chem. Soc., D* **1971**, 14, 727.
- (833) Obasi, M. E.; Okogun, J. I.; Ekong, D. E. U. *J. Chem. Soc., Perkin Trans. 1* **1972**, 15, 1943.
- (834) Connolly, J. D.; Thornton, I. M. S.; Taylor, D. A. H. *J. Chem. Soc., D* **1971**, 1, 17.
- (835) Kehrli, A. R. H.; Taylor, D. A. H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 7, 2067.
- (836) Ohochuku, N. S.; Taylor, D. A. H. *J. Chem. Soc. C* **1970**, 3, 421.
- (837) Adesogan, E. K.; MacLachlan, L. K.; Taylor, D. A. H. *S. Afr. J. Chem.* **1987**, 40, 25.
- (838) Madyastha, K. M.; Venkatakrishnan, K. *Perkin 1* **2000**, 18, 3055.
- (839) Ley, S. V.; Gray, B. L.; Durand-Reville, T.; Gobbi, L. B. In *Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18–22*; American Chemical Society: Washington, D.C., 2002.
- (840) Rembold, H.; Puhlmann, I. *Recent Adv. Phytochem.* **1993**, 27, 153.
- (841) Kraus, W. *Stud. Org. Chem. (Amsterdam)* **1984**, 17, 331.
- (842) Suresh, G. *Biotechnol. Perspect. Chem. Ecol. Insects* **1996**, 63.
- (843) Kubo, I.; Klocke, J. *ACS Symp. Ser.* **1986**, 296, 206.
- (844) Isman, M. B.; Arnason, J. T.; Towers, G. H. N. *Other Meliaceae Plants Containing Ingredients for Integrated Pest Management and Further Purposes. Chemistry and Biological Activity of Ingredients of Other Species of Meliaceae*; VCH: Weinheim, Germany, 1995; p 652.
- (845) Pettit, G. R.; Barton, D. H. R.; Herald, C. L.; Polonsky, J.; Schmidt, J. M.; Connolly, J. D. *J. Nat. Prod.* **1983**, 46, 379.
- (846) Mulla, M. S.; Su, T. J. *Am. Mosq. Control Assoc.* **1999**, 15, 133.
- (847) Kraus, W. *Biologically Active Ingredients: Azadirachtin and Other Triterpenoids*; VCH: Weinheim, Germany, 1995; p 35.
- (848) Immaraju, J. A. *Pestic. Sci.* **1998**, 54, 285.
- (849) Raizada, R. B.; Srivastava, M. K.; Kaushal, R. A.; Singh, R. P. *Food Chem. Toxicol.* **2001**, 39, 477.
- (850) Glinesukon, T.; Somjaree, R.; Piyachaturawat, P.; Thebtaranonth, Y. *Toxicol. Lett.* **1986**, 30, 159.
- (851) Redfern, R. E.; Warthen, J. D., Jr.; Uebel, E. C.; Mills, G. D., Jr. *The Antifeedant and Growth-Disrupting Effects of Azadirachtin on Spodoptera Frugiperda and Oncopeltus Fasciatus*; Ger. Agency Tech. Coop.: Eschborn, Germany, 1981; p 129.
- (852) Nasiruddin, M.; Mordue, A. J. *Tissue Cell* **1993**, 25, 875.
- (853) Reed, D. K.; Warthen, J. D., Jr.; Uebel, E. C.; Reed, G. L. *J. Econ. Entomol.* **1982**, 75, 1109.

- (854) Stokes, J. B.; Redfern, R. E. *J. Environ. Sci. Health, Part A* **1982**, 17, 57.
- (855) Fagoonee, I. *Effect of Azadirachtin and of a Neem Extract on Food Utilization by Crocidolomia Binotalis*; Deutsche Gesellschaft für Technische Zusammenarbeit: Eschborn, Germany, 1984; p 211.
- (856) West, A. J.; Mordue, A. J. *Entomol. Exp. Appl.* **1992**, 62, 75.
- (857) Meisner, J.; Ascher, K. R. S.; Aly, R.; Warthen, J. D. *Phytoparasitica* **1981**, 9, 27.
- (858) Murugan, K.; Jeyabalan, D.; Kumar, N. S.; Babu, R.; Sivaramakrishnan, S.; Nathan, S. S. *Insect Sci. Appl.* **1998**, 18, 157.
- (859) Senthil Nathan, S.; Kalaivani, K.; Murugan, K. *Acta Trop.* **2005**, 96, 47.
- (860) Nasiruddin, M.; Mordue, A. J. *Entomol. Exp. Appl.* **1994**, 70, 247.
- (861) Senthil Nathan, S.; Kalaivani, K.; Murugan, K.; Chung, P. G. *Pestic. Biochem. Physiol.* **2005**, 81, 113.
- (862) Senthil Nathan, S.; Kalaivani, K.; Murugan, K.; Gene Chung, P. *Crop Prot.* **2005**, 24, 760.
- (863) Jeyabalan, D.; Murugan, K. *Entomol.* **1997**, 22, 15.
- (864) Schoonhoven, L. M.; Luo, L.-E. *J. Comp. Physiol., A* **1994**, 175, 519.
- (865) Koul, O.; Multani, J. S.; Singh, G.; Wahab, S. *Curr. Sci.* **2002**, 83, 1387.
- (866) Lin-Er, L.; Van Loon, J. J. A.; Schoonhoven, L. M. *Physiol. Entomol.* **1995**, 20, 134.
- (867) Ortego, F.; Lopez-Olguin, J.; Ruiz, M.; Castanera, P. *Pestic. Biochem. Physiol.* **1999**, 63, 76.
- (868) Koul, O.; Shankar, J. S.; Kapil, R. S. *Entomol. Exp. Appl.* **1996**, 79, 43.
- (869) Govindachari, T. R.; Narasimhan, N. S.; Suresh, G.; Partho, P. D.; Gopalakrishnan, G.; Krishna Kumari, G. N. *J. Chem. Ecol.* **1995**, 21, 1585.
- (870) Suresh, G.; Gopalakrishnan, G.; Wesley, S. D.; Singh, N. D. P.; Malathi, R.; Rajan, S. S. *J. Agric. Food Chem.* **2002**, 50, 4484.
- (871) Ley, S. V.; Anderson, J. C.; Blaney, W. M.; Morgan, E. D.; Sheppard, R. N.; Simmonds, M. S. J.; Slawin, A. M. Z.; Smith, S. C.; Williams, D. J.; Wood, A. *Tetrahedron* **1991**, 47, 9231.
- (872) Mordue, A. J.; Simmonds, M. S. J.; Ley, S. V.; Blaney, W. M.; Mordue, W.; Nasiruddin, M.; Nisbet, A. J. *Pestic. Sci.* **1998**, 54, 277.
- (873) Ley, S. V.; Anderson, J. C.; Blaney, W. M.; Jones, P. S.; Lidert, Z.; Morgan, E. D.; Robinson, N. G.; Santafianos, D.; Simmonds, M. S. J.; Toogood, P. L. *Tetrahedron* **1989**, 45, 5175.
- (874) Blaney, W. M.; Simmonds, M. S. J.; Ley, S. V.; Anderson, J. C.; Toogood, P. L. *Entomol. Exp. Appl.* **1990**, 55, 149.
- (875) Simmonds, M. S. J.; Blaney, W. M.; Ley, S. V.; Anderson, J. C.; Toogood, P. L. *Entomol. Exp. Appl.* **1990**, 55, 169.
- (876) Yamasaki, R. B.; Klocke, J. A. *J. Agric. Food Chem.* **1987**, 35, 467.
- (877) Simmonds, M. S. J.; Blaney, W. M.; Ley, S. V.; Anderson, J. C.; Banteli, R.; Denholm, A. A.; Green, P. C. W.; Grossman, R. B.; Gutteridge, C.; Jennens, L.; Smith, S. C.; Toogood, P. L.; Wood, A. *Entomol. Exp. Appl.* **1995**, 77, 69.
- (878) MacLeod, J. K.; Moeller, P. D. R.; Molinski, T. F.; Koul, O. *J. Chem. Ecol.* **1990**, 16, 2511.
- (879) Yamasaki, R. B.; Klocke, J. A. *J. Agric. Food Chem.* **1989**, 37, 1118.
- (880) Carpinella, M. C.; Defago, M. T.; Valladares, G.; Palacios, S. M. *J. Agric. Food Chem.* **2003**, 51, 369.
- (881) Mordue, A. J.; Nasiruddin, M. *Ser. Entomol.* **1992**, 49, 176.
- (882) Mordue, A. J.; Nisbet, A. J.; Nasiruddin, M.; Walker, E. *Entomol. Exp. Appl.* **1996**, 80, 69.
- (883) Arnason, J. T.; Philogene, B. J. R.; Donskov, N.; Hudon, M.; McDougall, C.; Fortier, G.; Morand, P.; Gardner, D.; Lambert, J.; Morris, C.; Nozzolillo, C. *Entomol. Exp. Appl.* **1985**, 38, 29.
- (884) Koul, O.; Isman, M. B. *J. Insect Physiol.* **1991**, 37, 591.
- (885) Meisner, J.; Mitchell, B. K. Z. *Pflanzenkr. Pflanzenschutz* **1982**, 89, 463.
- (886) Serit, M.; Ishida, M.; Hagiwara, N.; Kim, M.; Yamamoto, T.; Takahashi, S. *J. Chem. Ecol.* **1992**, 18, 593.
- (887) de Souza Garcia, E.; Rembold, H. *J. Insect Physiol.* **1984**, 30, 939.
- (888) Garcia, E. S.; de Azambuja, P.; Forster, H.; Rembold, H. Z. *Naturforsch., C* **1984**, 39, 1155.
- (889) Ruscoe, C. N. E. *Nat., New Biol.* **1972**, 236, 159.
- (890) Koul, O. *Indian J. Exp. Biol.* **1985**, 23, 160.
- (891) Schlueter, U. *Entomol. Exp. Appl.* **1985**, 39, 191.
- (892) Koul, O. *Entomol. Exp. Appl.* **1984**, 36, 85.
- (893) George, J.; Potter, D. A. *Acta Hort.* **2008**, 783, 499.
- (894) Al-rajhy, D. H.; Alahmed, A. M.; Hussein, H. I.; Kheir, S. M. *Pest Manag. Sci.* **2003**, 59, 1250.
- (895) Gaaboub, I. A.; Hayes, D. K. *Environ. Entomol.* **1984**, 13, 803.
- (896) Garcia, E. S.; Gonzalez, M. S.; Azambuja, P.; Rembold, H. Z. *Naturforsch., C* **1989**, 44, 317.
- (897) Malczewska, M.; Gelman, D. B.; Cymborowski, B. *J. Insect Physiol.* **1988**, 34, 725.
- (898) Sieber, K. P.; Rembold, H. *J. Insect Physiol.* **1983**, 29, 523.
- (899) Koolman, J.; Bidmon, H. J.; Lehmann, M.; Kausser, G. *Pr. Nauk. Inst. Chem. Org. Fiz. Politech. Wroclaw.* **1988**, 33, 55.
- (900) Adel, M. M.; Sehnal, F. *J. Insect Physiol.* **2000**, 46, 267.
- (901) Mordue, A. J.; Evans, K. A.; Charlet, M. *Comp. Biochem. Physiol., C* **1986**, 85, 297.
- (902) Josephraj Kumar, A.; Subrahmanyam, B.; Srinivasan, Eur. *J. Entomol.* **1999**, 96, 347.
- (903) Schlueter, U.; Bidmon, H. J.; Grewe, S. *J. Insect Physiol.* **1985**, 31, 773.
- (904) Dorn, A.; Rademacher, J. M.; Sehn, E. *J. Insect Physiol.* **1986**, 32, 231.
- (905) Barnby, M. A.; Klocke, J. A. *J. Insect Physiol.* **1990**, 36, 125.
- (906) Rembold, H.; Subrahmanyam, B.; Mueller, T. *Experientia* **1989**, 45, 361.
- (907) Rembold, H.; Sharma, G. K.; Czoppelt, C.; Schmutterer, H. Z. *Angew. Entomol.* **1982**, 93, 12.
- (908) Gonzalez, M. S.; Nogueira, N. F. S.; Mello, C. B.; De Souza, W.; Schaub, G. A.; Azambuja, P.; Garcia, E. S. *Exp. Parasitol.* **1999**, 92, 100.
- (909) Rembold, H. *Mem. Inst. Oswaldo Cruz* **1987**, 82, 61.
- (910) Smith, S. L.; Mitchell, M. J. *Biochem. Biophys. Res. Commun.* **1988**, 154, 559.
- (911) Lowery, D. T.; Isman, M. B. *J. Econ. Entomol.* **1996**, 89, 602.
- (912) Dorn, A. *J. Appl. Entomol.* **1986**, 102, 313.
- (913) Rembold, H.; Sieber, K. P. Z. *Naturforsch., C* **1981**, 36, 466.
- (914) Steets, R.; Schmutterer, H. Z. *Pflanzenkr. Pflanzenschutz* **1975**, 82, 176.
- (915) Ludlum, C. T.; Sieber, K. P. *Physiol. Entomol.* **1988**, 13, 177.
- (916) Sayah, F.; Fayet, C.; Idaomar, M.; Karlinsky, A. *Tissue Cell* **1996**, 28, 741.
- (917) Sayah, F. *Tissue Cell* **2002**, 34, 53.
- (918) Sayah, F.; Idaomar, M.; Soranzo, L.; Karlinsky, A. *Tissue Cell* **1998**, 30, 86.
- (919) Shimizu, T. *Entomol. Exp. Appl.* **1988**, 46, 197.
- (920) Nisbet, A. J.; Mordue, A. J.; Williams, L. M.; Hannah, L.; Jennens, L.; Ley, S. V.; Mordue, W. *Tissue Cell* **1996**, 28, 725.
- (921) Subrahmanyam, B.; Rao, P. J. *Curr. Sci.* **1986**, 55, 534.
- (922) Subrahmanyam, B.; Mueller, T.; Rembold, H. *J. Insect Physiol.* **1989**, 35, 493.
- (923) Subrahmanyam, B.; Rembold, H. *Cell Tissue Res.* **1989**, 256, 513.
- (924) Rembold, H.; Forster, H.; Czoppelt, C.; Rao, P. J.; Sieber, K. P. *Schriften. GTZ* **1984**, 161, 153.
- (925) Simmonds, M. S. J.; Blaney, W. M. *Some Neurophysiological Effects of Azadirachtin on Lepidopterous Larvae and Their Feeding Response*; Deutsche Gesellschaft für Technische Zusammenarbeit: Eschborn, Germany, 1984; p 163.
- (926) Mordue, A. J.; Cottee, P. K.; Evans, K. A. *Physiol. Entomol.* **1985**, 10, 431.
- (927) Timmins, W. A.; Reynolds, S. E. *Entomol. Exp. Appl.* **1992**, 63, 47.

- (928) Senthil Nathan, S.; Kalaivani, K.; Chung, P. G. *Pestic. Biochem. Physiol.* **2005**, *83*, 46.
- (929) Anuradha, A.; Annadurai, R. S.; Shashidhara, L. S. *Insect Biochem. Mol. Biol.* **2007**, *37*, 627.
- (930) Pravin Kumar, R.; Manoj, M. N.; Kush, A.; Annadurai, R. S. *Insect Biochem. Mol. Biol.* **2007**, *37*, 635.
- (931) Mitchell, M. J.; Smith, S. L.; Johnson, S.; Morgan, E. D. *Arch. Insect Biochem. Physiol.* **1997**, *35*, 199.
- (932) Senthil Nathan, S.; Kalaivani, K.; Chung, P. G.; Murugan, K. *Chemosphere* **2006**, *62*, 1388.
- (933) Senthil Nathan, S.; Kalaivani, K.; Sehoon, K.; Murugan, K. *Chemosphere* **2006**, *62*, 1381.
- (934) Govindachari, T. R.; Narashimhan, N. S.; Suresh, G.; Partho, P. D.; Gopalakrishnan, G. *J. Chem. Ecol.* **1996**, *22*, 1453.
- (935) Koul, O.; Isman, M. B. *Entomol. Exp. Appl.* **1992**, *64*, 281.
- (936) Kubo, I.; Klocke, J. A. *Agric. Biol. Chem.* **1982**, *46*, 1951.
- (937) Govindachari, T. R.; Gopalakrishnan, G. *J. Indian Chem. Soc.* **1998**, *75*, 655.
- (938) Lowery, D. T.; Isman, M. B. *Entomol. Exp. Appl.* **1994**, *72*, 77.
- (939) Miller, J. A.; Chamberlain, W. F. *J. Econ. Entomol.* **1989**, *82*, 1375.
- (940) Rembold, H.; Annadurai, R. S. *Z. Naturforsch., C* **1993**, *48*, 495.
- (941) Cohen, E.; Quistad, G. B.; Casida, J. E. *Life Sci.* **1996**, *58*, 1075.
- (942) Salehzadeh, A.; Akhkh, A.; Cushley, W.; Adams, R. L. P.; Kusel, J. R.; Strang, R. H. C. *Insect Biochem. Mol. Biol.* **2003**, *33*, 681.
- (943) Rembold, H.; Puhlmann, I. In *Neem Tree, Azadirachta Indica A. Juss. Other Meliaceae Plants*; Schmutterer, H., Ed.; VCH: Weinheim, Germany, 1995.
- (944) Gurulingappa, H.; Tare, V.; Pawar, P.; Tungikar, V.; Jorapur Yogesh, R.; Madhavi, S.; Bhat Sujata, V. *Chem. Biodiversity* **2009**, *6*, 897.
- (945) Govindachari, T. R.; Suresh, G.; Gopalakrishnan, G.; Masilamani, S.; Banumathi, B. *Fitoterapia* **2000**, *71*, 317.
- (946) Verma, V. S. *Acta Microbiol. Pol., Ser. B* **1974**, *6*, 9.
- (947) Chiruvella, K. K.; Mohammed, A.; Dampuri, G.; Ghanta, R. G.; Raghavan, S. C. *Int. J. Biomed. Sci.* **2007**, *3*, 269.
- (948) Cherry, R.; Nuessly, G. *Fla. Entomol.* **2010**, *93*, 52.
- (949) Cespedes, C. L.; Calderon, J. S.; Gomez-Garibay, F.; Segura, R.; King-Diaz, B.; Lotina-Hennsen, B. *J. Chem. Ecol.* **1999**, *25*, 2665.
- (950) Akudugu, J.; Gade, G.; Bohm, L. *Life Sci.* **2001**, *68*, 1153.
- (951) Harish Kumar, G.; Vidya Priyadarsini, R.; Vinothini, G.; Vidjaya Letchoumy, P.; Nagini, S. *Invest. New Drugs* **2010**, *28*, 392.
- (952) Priyadarsini, R. V.; Manikandan, P.; Harish Kumar, G.; Nagini, S. *Free Radical Res.* **2009**, *43*, 492.
- (953) Priyadarsini, R. V.; Murugan, R. S.; Sripriya, P.; Karunakaran, D.; Nagini, S. *Free Radical Res.* **2010**, *44*, 624.
- (954) Harish Kumar, G.; Chandra Mohan, K. V. P.; Jagannadha Rao, A.; Nagini, S. *Invest. New Drugs* **2009**, *27*, 246.
- (955) Kumar, G. H.; Mohan, K. V. P. C.; Rao, A. J.; Nagini, S. *Invest. New Drugs* **2009**, *27*, 236.
- (956) Roy, M. K.; Kobori, M.; Takenaka, M.; Nakahara, K.; Shinmoto, H.; Isobe, S.; Tsushida, T. *Phytother. Res.* **2007**, *21*, 245.
- (957) Roy, M. K.; Kobori, M.; Takenaka, M.; Nakahara, K.; Shinmoto, H.; Tsushida, T. *Planta Med.* **2006**, *72*, 917.
- (958) Chiruvella, K. K.; Kari, V.; Choudhary, B.; Nambiar, M.; Ghanta, R. G.; Raghavan, S. C. *FEBS Lett.* **2008**, *582*, 4066.
- (959) Brandt, G. E. L.; Schmidt, M. D.; Prinszano, T. E.; Blagg, B. S. J. *J. Med. Chem.* **2008**, *51*, 6495.
- (960) Zhang, B.; Wang, Z. F.; Tang, M. Z.; Shi, Y. L. *Invest. New Drugs* **2005**, *23*, 547.
- (961) Cohen, E.; Quistad, G. B.; Jefferies, P. R.; Casida, J. E. *Pestic. Sci.* **1996**, *48*, 135.
- (962) Rojanapo, W.; Suwanano, S.; Somjaree, R.; Glinsukon, T.; Thebtaranont, Y. *J. Sci. Soc. Thailand* **1985**, *11*, 177.
- (963) Kim, M.; Kim, S. K.; Park, B. N.; Lee, K. H.; Min, G. H.; Seoh, J. Y.; Park, C. G.; Hwang, E. S.; Cha, C. Y.; Kook, Y. H. *Antiviral Res.* **1999**, *43*, 103.
- (964) Barquero, A. A.; Alche, L. E.; Coto, C. E. *J. Gen. Virol.* **2004**, *85*, 483.
- (965) Bueno, C. A.; Barquero, A. A.; Di Consoli, H.; Maier, M. S.; Alche, L. E. *Virus Res.* **2009**, *141*, 47.
- (966) Bueno, C. A.; Alche, L. E.; Barquero, A. A. *Biochem. Biophys. Res. Commun.* **2010**, *393*, 32.
- (967) Omar, S.; Zhang, J.; MacKinnon, S.; Leaman, D.; Durst, T.; Philogene, B. J. R.; Arnason, J. T.; Sanchez-Vindas, P. E.; Poveda, L.; Tamez, P. A.; Pezzuto, J. M. *Curr. Top. Med. Chem. (Hilversum, Neth.)* **2003**, *3*, 133.
- (968) Lee, S. E.; Kim, M. R.; Kim, J. H.; Takeoka, G. R.; Kim, T. W.; Park, B. S. *Phytomedicine* **2008**, *15*, 533.
- (969) Omar, S.; Godard, K.; Ingham, A.; Hussain, H.; Wongpanich, V.; Pezzuto, J.; Durst, T.; Ekl, C.; Gbeassor, M.; Sanchez-Vindas, P.; Poveda, L.; Philogene, B. J. R.; Arnason, J. T. *Ann. Appl. Biol.* **2003**, *143*, 135.
- (970) Garcia, E. S.; Gonzales, M. S.; Azambuja, P. *Mem. Inst. Oswaldo Cruz* **1991**, *86* (Suppl 2), 107.
- (971) Gonzalez, M. S.; Garcia, E. S. *J. Invertebr. Pathol.* **1992**, *60*, 201.
- (972) Jones, I. W.; Denholm, A. A.; Ley, S. V.; Lovell, H.; Wood, A.; Sinden, R. E. *FEMS Microbiol. Lett.* **1994**, *120*, 267.
- (973) Billker, O.; Shaw, M. K.; Jones, I. W.; Ley, S. V.; Mordue, A. J.; Sinden, R. E. *J. Eukaryotic Microbiol.* **2002**, *49*, 489.
- (974) Rochanakij, S.; Thebtaranonth, Y.; Yenjai, C.; Yuthavong, Y. *Southeast Asian J. Trop. Med. Public Health* **1985**, *16*, 66.
- (975) Penido, C.; Costa, K. A.; Pennaforte, R. J.; Costa, M. F. S.; Pereira, J. F. G.; Siani, A. C.; Henriques, M. G. M. O. *Inflammation Res.* **2005**, *54*, 295.
- (976) Penido, C.; Conte, F. P.; Chagas, M. S. S.; Rodrigues, C. A. B.; Pereira, J. F. G.; Henriques, M. G. M. O. *Inflammation Res.* **2006**, *55*, 457.
- (977) Thoh, M.; Kumar, P.; Nagarajaram, H. A.; Manna, S. K. *J. Biol. Chem.* **2010**, *285*, 5888.
- (978) Shi, Y. L.; Kishio, F.; Wang, W. P.; Susumu, T.; Xu, K.; Shunichi, Y. *Chin. Sci. Bull.* **1993**, *38*, 1489.
- (979) Ding, J.; Xu, T. H.; Shi, Y. L. *Neurosci. Res.* **2001**, *41*, 243.
- (980) Wang, Z. F.; Shi, Y. L. *Neurosci. Res.* **2001**, *40*, 211.
- (981) Wang, Z. F.; Shi, Y. L. *Neurosci. Lett.* **2001**, *303*, 13.
- (982) Chen, W. Y.; Yin, P. B.; Ye, W. L.; Shi, Y. L. *Chin. Sci. Bull.* **1999**, *44*, 1106.
- (983) Madhu, D. C.; Nair, G. R. N. *Indian Drugs* **2001**, *38*, 629.
- (984) Njar, V. C.; Adesanwo, J. K.; Raji, Y. *Planta Med.* **1995**, *61*, 91.
- (985) Orisadipe, A.; Amos, S.; Adesomoju, A.; Binda, L.; Emeje, M.; Okogun, J.; Wambebe, C.; Gamaniel, K. *Biol. Pharm. Bull.* **2001**, *24*, 364.
- (986) Amos, S.; Orisadipe, A.; Binda, L.; Emeje, M.; Adesomoju, A.; Okogun, J.; Akah, P.; Wambebe, C.; Gamaniel, K. *Pharmacol. Toxicol.* **2002**, *91*, 71.
- (987) Ekimoto, H.; Irie, Y.; Araki, Y.; Han, G.; Kadota, S.; Kikuchi, T. *Planta Med.* **1991**, *57*, 56.
- (988) Penido, C.; Costa, K. A.; Costa, M. F. de S.; Pereira, J. de F. G.; Siani, A. C.; Henriques, M. das G. M. de O. *Int. Immunopharmacol.* **2006**, *6*, 109.