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Amide-esters from *Aglaia tenuicaulis* – First representatives of a class of compounds structurally related to bisamides and flavaglines

Harald Greger [a,*], Margit Hofer [a], Klaus Teichmann [a], Johann Schinnerl [a], Caroline M. Pannell [b], Srunya Vajrodaya [c], Otmar Hofer [d,*]

[a] *Comparative and Ecological Phytochemistry, Faculty Center of Botany, University of Vienna, Rennweg 14, A-1030 Wien, Austria*
[b] *Department of Plant Sciences, University of Oxford, South Parks Road, Oxford OX1 3RA, UK*
[c] *Department of Botany, Faculty of Science, Kasetsart University, Bangkok 10900, Thailand*
[d] *Institute of Organic Chemistry, University of Vienna, Währingerstrasse 38, A-1090 Wien, Austria*

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Abstract

Six amide-esters and two sulphur-containing bisamides were isolated from the leaves, stem and root bark of *Aglaia tenuicaulis* together with two bisamides from the leaves of *A. spectabilis*. Their structures were elucidated by spectroscopic methods. The co-occurrence of amide-esters and bisamides suggests close biosynthetic connections replacing only one nitrogen atom of putrescine with oxygen. Putrescine appears to be the common building block linked to various acids from which the cinnamoyl moiety represents the prerequisite for an incorporation of bisamides into flavaglines. Corresponding amide-esters are apparently not incorporated, but closely related amide-alcohol derivatives were found as part of benzopyran and benzofuran flavaglines. The structure of a amide-alcohol is described, representing an artifact due to hydrolysis of an amide-ester during TLC purification. A hypothetical amide-amine building block is suggested to form the characteristic pyrimidinone structures only found in benzofuran flavaglines. Structural and biosynthetic connections between amide-esters, bisamides and flavaglines are discussed and the chemotaxonomic significance of accumulating specific derivatives within the genus *Aglaia* is highlighted.

Keywords: *Aglaia tenuicaulis*; *A. spectabilis*; Meliaceae; Amide-esters; Bisamides; Flavaglines; Putrescine derivatives; Aminopyrrolidines; Chemotaxonomy

1. Introduction

The genus *Aglaia* of the family Meliaceae comprises nearly 120 species mainly distributed in the tropical rain forests of southeast Asia (Pannell, 1992). A number of species have attracted considerable attention due to their accumulation of highly bioactive flavaglines (=rocaglamides), exhibiting insecticidal (e.g. Schneider et al., 2000; Greger et al., 2001), antifungal (Engelmeier et al., 2000), and antiproliferative activity against cancer cell lines (e.g. Wang et al., 2001; Kim et al., 2006a,b). As a consequence, flavagline profiles of many *Aglaia* species have already been investigated leading to isolation and identification of around 110 different derivatives (Proksch et al., 2001; Brem, 2002; Kim et al., 2006b). The occurrence of flavaglines was shown to be closely correlated with the formation of putrescine-derived bisamides, also representing a characteristic chemical feature of *Aglaia* mostly accumulated in the leaves. Structurally, bisamides were found to occur either in an open-chained form or as cyclic 2-aminopyrrolidine derivatives. Based on the literature, the latter have a more restricted distribution and were reported so far only from the genus *Aglaia*. Both forms of bisamides are also known as important building blocks in a number of flavaglines, particularly incorporated into benzopyran and

* Corresponding authors. Tel.: +43 1 4277 54070; fax: +43 1 4277 9541 (H. Greger), tel.: +43 1 4277 52107; fax: +43 1 4277 9521 (O. Hofer).
E-mail addresses: harald.greger@univie.ac.at (H. Greger), otmar.hofer@univie.ac.at (O. Hofer).

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benzoxepine derivatives (e.g. Dumontet et al., 1996; Bacher et al., 1999; Puripattanavong et al., 2000; Xu et al., 2000; Chaidir et al., 2001; Kim et al., 2006b).

The majority of bisamides is characterised by two different acid moieties mostly consisting of cinnamic acid and derivatives of 2-methylbutanoic acid. In addition, isobutanoic, phenylacetic, benzoic, isovaleric, and senecioic acid have been described as acyl parts. As an exception acetic acid was found together with cinnamic and dihydrocinnamic acid in a threefold acylated putrescine, named edulimide (Brader et al., 1998). Of special interest, however, was the formation of sulphur-containing bisamides with methylthiopropenoic acid moieties in *A. edulis* A. Gray (Saifah et al., 1999) and *A. leucophylla* King, published as *A. leptantha* Miq. (Greger et al., 2000). Inada et al. (2000) regarded the whole benzopyran flavagline as acyl part of the putrescine bisamide grandiamide A. However, for the sake of clarity the flavagline nucleus should be seen as a separate biogenetic entity, probably generated by a flavonol linked with a cinnamoyl moiety (Dumontet et al., 1996; Nugroho et al., 1999; Bacher et al., 1999). Interest in bisamides has increased since cytotoxic (Hayashi et al., 1982; Duh et al., 1993; Inada et al., 2001) and antiviral activity (Joshi et al., 1987) was reported for the aminopyrrolidine bisamides odorine (**15**), dehydroodorine (**16**), and odorinol (**17**), respectively.

With respect to the frequent co-occurrence of flavaglines and bisamides, the exclusive accumulation of the latter in *A. edulis* (Saifah et al., 1999) and *A. leucophylla* (Greger et al., 2000) deserves special chemotaxonomic attention. Even more, as in this case new sulphur-containing derivatives were isolated as major constituents not only from the leaves, but also from the stem and root bark. In the course of our current phytochemical comparison within the genus *Aglaia* we have now discovered a series of sulphur-containing amide-esters in *A. tenuicaulis* Hiern, representing a novel class of compounds (**1**–**6**). They also accumulate in the leaves, stem, and rootbark, and their co-occurrence with the two new sulphur-containing bisamides **8** and **9** suggests close structural as well as biosynthetic connections. Moreover, from the leaves of *A. spectabilis* (Miq.) Jain & Bennet two further, new open-chained putrescine bisamides (**10**, **11**) were isolated together with the already known aglairubine (**12**) (Saifah and Suparakchinda, 1998; Detterbeck and Hesse, 2002b; with revised structure Seger et al., 2002).

In the present paper, we report the isolation and structure elucidation of six novel amide-esters (**1**–**6**) together with four new bisamides (**8**–**11**) and discuss their possible structural and biosynthetic connections among each other as well as with flavaglines. In addition, the structure of a new amide-alcohol (**7**), which was created as an artifact during TLC-purification of aglatenin (**4**), is described. The chemotaxonomic significance of accumulating different bisamides and the possibly related amide-esters in the genus *Aglaia* is highlighted with respect to their distribution in various species.

2. Results and discussion

2.1. Structure elucidation of compounds 1–11

Methanolic extracts of dried leaves, stem, and root bark of *A. tenuicaulis*, and of the leaves of *A. spectabilis* were concentrated and partitioned between water and chloroform. The lipophilic fractions were compared with UV-HPLC, and the major compounds were isolated by preparative MPLC and TLC as described previously (Greger et al., 2000, 2001; Seger et al., 2002). The HPLC profiles of three different provenances of *A. tenuicaulis* (HG 869, HG 870, HG 901) collected in south Thailand were nearly identical, and both, the UV-spectra and the retention times of the peaks, resembled those of different collections of *A. leucophylla* (*A. leptantha*) characterised by various suphur-containing bisamides (Greger et al., 2000). Bisamides were also detected in the leaf extract of *A. spectabilis* (HG 864), but its HPLC profile clearly deviated by additional peaks with different UV-spectra. All major compounds of *A. tenuicaulis* could sufficiently be separated by HPLC, either with MeOH–H_2O or acetonitrile–H_2O gradients (see Section 3). Most of the compounds showed similar UV-spectra with dominating maxima at 274–277 nm and a second weak peak at 216–218 nm with a shoulder at 221–222 nm (MeOH/H_2O). Compounds **4** and **7** deviated by very weak, but characteristic second maxima at 224 nm which has already been pointed out, in our earlier report on sulphur-containing bisamides, to indicate the absence of an aromatic acid moiety (Greger et al., 2000). The benzoic acid ester group in compound **6** was indicated by an additional shoulder at 231 nm**.** The IR spectra in CCl_4 were mostly characterized by $\geq$N–H stretching at 3446–3451 cm^{-1}, typical for secondary amides, and by dominating signals at 1670–1680 cm^{-1} for the $\geq$N–C=O stretching region. Compounds **1**–**6** can be clearly distinguished by additional strong signals at 1710–1722 cm^{-1}, indicative for the presence of ester –C=O groups. The IR spectrum of compound **8** with deviating signals at 3259 and 1420 cm^{-1} (CCl_4) showed great similarity with the previously published cyclic 2-aminopyrrolidine bisamide aglepin (Greger et al., 2000).

With respect to the ^1H NMR spectra the amide-esters **1**–**6** were characterised by triplets in the region 4.07–4.37 ppm ($J = 6.2$–6.3) typical for the ester methylene 1-H_2 next to a further methylene group 2-H_2. The corresponding amide methylene groups 4-H_2 were found at higher field at 3.26–3.47 ppm, appearing as quartets (actually dt with almost identical coupling constants 4-H_2 to NH and to 3-H_2). The remaining proton resonances of the 4-aminobutanol moiety were rather close and could not be resolved. However, in all cases the chemical shifts were higher for 2-H_2 compared to 3-H_2 (Table 1). All assignments were clearly derived from 2D NMR spectra (HH-COSY, NOESY, HMQC, and HMBC). In the ^{13}C NMR spectra the resonances for carbon atoms 1–4 agreed fully with the O–$(CH_2)_4$–N chain, with O–CH_2 at 63.7–64.1 ppm,

Table 1
^{1}H NMR data of amide-esters 1–**6** and amide-alcohol **7** (in $CDCl_3$)[a]

No.	**1**	**2**[b]	**3**	**4**	**5**	**6**	**7**
1	4.17 *t* (6.2)	4.18 *t* (6.2)	4.07 *t* (6.2)	4.15 *t* (6.3)	4.26 *t* (6.3)	4.37 *t* (6.3)	3.68 *br.td* (6.4, 4.5)
2	1.73 *m*	1.71 *m*	1.54 *m*	1.70 *m*	1.80 *m*	1.85 *m*	1.61 *m*
3	1.67 *m*	1.66 *m*	1.48 *m*	1.63 *m*	1.71 *m*	1.76 *m*	1.63 *m*
4	3.43 *dt* (6.6, 6.6)	3.43 *dt* (6.6, 6.6)	3.26 *dt* (6.6, 6.6)	3.36 *dt* (6.6, 6.6)	3.47 *dt* (6.6, 6.6)	3.48 *dt* (6.7, 6.7)	3.36 *dt* (6.6, 6.6)
Ester moiety	MTPA[a]	MTPA	MTPA	MTPA	CA	Benzoic acid ester	OH[c]
2′	5.65 *d* (14.9)	5.84 *d* (10.1)	5.64 *d* (14.9)	5.65 *d* (14.9)	6.44 *d* (16.1)		
3′	7.75 *d* (14.9)	7.05 *d* (10.1)	7.73 *d* (14.9)	7.74 *d* (14.9)	7.69 *d* (16.1)		
S-CH_3'	2.33 *s*	2.39 *s*	2.34 *s*	2.33 *s*			
Phenyl *ortho*					7.53 *m*	8.05 *dm* (8.0)	
meta					7.38 *m*	7.44 *br.dd* (8.0, 7.6)	
para					7.38 *m*	7.56 *tt* (7.6, 1.3)	
Amide moiety	CA	CA	CA	MTPA	CA	CA	MTPA
2″	6.39 *d* (15.4)	6.39 *d* (15.4)	6.00 *d* (12.5)	5.61 *d* (14.7)	6.38 *d* (15.6)	6.37 *d* (15.7)	5.61 *d* (14.6)
3″	7.62 *d* (15.4)	7.61 *d* (15.4)	6.78 *d* (12.5)	7.61 *d* (14.7)	7.63 *d* (15.6)	7.62 *d* (15.7)	7.61 *d* (14.6)
S-CH_3''				2.32 *s*			2.32 *s*
Phenyl *ortho*	7.48 *m*	7.49 *m*	7.42 *m*		7.50 *m*	7.50 *m*	
meta	7.34 *m*	7.35 *m*	7.33 *m*		7.36 *m*	7.36 *m*	
para	7.34 *m*	7.35 *m*	7.33 *m*		7.36 *m*	7.36 *m*	
NH	5.82 *br.t* (6.6)	5.80 *br.t* (6.6)	5.51 *br.t* (6.6)	5.45 *br.t* (6.6)	5.69 *br.t* (6.6)	5.68 *br.t* (6.7)	

[a] *Abbreviations*: methylthiopropenoic acid (MTPA), cinnamic acid (CA); dashed numbers are used for the ester forming acid, double dashed numbering for the amide part.
[b] From a mixture **2**:**1** = 1:2.
[c] OH: 1.99 *br.t* (4.5 Hz).

N–CH_2 at 39.0–39.3 ppm, and 25.8–26.3 ppm for the resonances of C-2 and C-3 (Table 2).

In the case of the dominating compound **1,** named tenucaulin A, the ester forming acid was (*E*)-3-methylthiopropenoic acid (MTPA), and the amide forming acid (*E*)-cinnamic acid (CA). This followed clearly from NOESY cross peaks NH → 2″-H, 4-H_2, 3-H_2 and also from long range contacts, ester-CO → 2′-H, 3′-H, 1-H_2 and amide-CO → 2″-H, 3″-H, 4-H_2. The olefinic protons of the two acid moieties could be discriminated easily by means of characteristic coupling constants of the doublets. They were 14.6–14.9 Hz for MTPA derivatives and 15.4–16.1 Hz for those of CA. Exceptions were of course the (*Z*)-configurated acids in compound **2**, (*Z*)-3-methylthiopropenoic ester ($J = 10.1$ Hz) and **3**, (*Z*)-cinnamic amide (12.5 Hz). Compared to compound **1** the amide-ester **2,** designated as isotenucaulin A, showed deviating chemical shifts for the (*Z*)-MTPA-ester moiety. The same was the case for the (Z)-CA-amide rest of **3,** named tenucaulin B (Table 1). Compound **4**, named aglatenin, was characterised by two MTPA moieties. The assignment of either ester-MTPA or amide-MTPA followed again from NOESY and HMBC spectra (Tables 1 and 2). Compound **5** was the corresponding amide-ester with two CA moieties, named tenaglin. The assignments in Tables 1 and 2 were based on 2D NMR measurements. In compound **6**, named caulitenin, the ester forming acid was benzoic acid and the amide part was once again CA. Consequently, the ^{1}H NMR data of the CA moiety were virtually identical for compounds **1**, **2**, **5**, and **6** (Table 1), the remaining resonances of compound **6** could easily be assigned to benzoic acid.

Table 2
^{13}C NMR data of amide-esters **1–5** and amide-alcohol **7** (in $CDCl_3$)[a]

No.	**1**	**2**[b]	**3**	**4**	**5**	**7**
1	63.8 *t*	63.7 *t*	63.7 *t*	63.8 *t*	64.1 *t*	62.4 *t*
2	26.3 *t*	26.3 *t*[c]	26.2 *t*[c]	26.3 *t*	26.3 *t*	29.7 *t*
3	26.3 *t*	26.2 *t*[c]	25.8 *t*[c]	26.3 *t*	26.3 *t*	26.4 *t*
4	39.3 *t*	39.3 *t*	39.0 *t*	39.2 *t*	39.3 *t*	39.3 *t*
Ester moiety	MTPA[a]	MTPA	MTPA	MTPA	CA	
1′	165.3 *s*	166.7 *s*	165.2 *s*	165.3 *s*	167.0 *s*	
2′	112.9 *d*	112.9 *d*	112.9 *d*	112.9 *d*	118.0 *d*	
3′	147.3 *d*	152.1 *d*	147.3 *d*	147.3 *d*	144.9 *d*	
S-CH_3'	14.3 *q*	19.2 *q*	14.3 *q*	14.3 *q*		
Phenyl 4′					134.4 *s*	
ortho					128.9 *d*[c]	
meta					128.1 *d*[c]	
para					130.3 *d*	
Amide moiety	CA	CA	CA	MTPA	CA	MTPA
1″	165.9 *s*	165.9 *s*	167.1 *s*	164.5 *s*	165.9 *s*	164.7 *s*
2″	120.6 *d*	120.7 *d*	125.2 *d*	115.7 *d*	120.6 *d*	115.8 *d*
3″	141.0 *d*	140.9 *d*	136.1 *d*	142.9 *d*	141.1 *d*	142.9 *d*
S-CH_3''				14.6 *q*		14.6 *q*
Phenyl 4″	134.8 *s*	134.9 *s*	135.1 *s*		134.8 *s*	
ortho	127.8 *d*	127.8 *d*	128.6 *d*[c]		127.8 *d*	
meta	128.8 *d*	128.8 *d*	128.8 *d*[c]		128.8 *d*	
para	129.6 *d*	129.6 *d*	128.6 *d*		129.7 *d*	

[a] *Abbreviations*: methylthiopropenoic acid (MTPA), cinnamic acid (CA); dashed numbers are used for the ester forming acid, double dashed numbering for the amide moiety.
[b] From a mixture **2:1** = 1:2.
[c] Interchangeable within the row.

Compound **7** was an amide-alcohol with (*E*)-MTPA forming the amide, which was also the case for compound **4**. Therefore, the ^{13}C resonances of the amide part of **1** and **4** were practical identical (Table 2). In the ^{1}H NMR of **7**

the resonances of 1-CH_2 and 1-OH were rather broad due to coupling between OH and the methyl group 1-H_2. The chemical shifts, the coupling patterns, and all 2D NMR data agreed with the structure of **7,** named aglatenol.

Compounds **8–11** represented either cyclic (**8**) or open-chained bisamides (**9–11**) with identical (*E*)-CA amide moieties but varying second acid components. Compound **8,** named pyrrolotenin**,** showed the ^1H and ^{13}C resonances typical for cyclic bisamides of the aminopyrrolidine type. The acid components were (*E*)-CA and (*E*)-MTPA. These acids could be identified in the NMR and also in the EIMS spectra showing strong peaks for the cinnamoyl and methylthiopropenoyl moiety (see below and in Section 3). It is interesting to note that in $CDCl_3$ two very close but distinct ^1H and ^{13}C NMR data sets were obtained. This was already observed for several other bisamides of the aminopyrrolidine type (Purushothaman et al., 1979; Brader et al., 1998) and was usually explained by epimeric mixtures due to epimerisation at C-4 with its acetal-like N–C–N arrangement. However, in MeOH-d_4 only one set of resonances was obtained. The data of both solvents were listed in Table 3. A possible explanation may be that MeOH as a polar, protic solvent increased the epimerisation rate and only averaged signals could be detected on the NMR time scale. Measurement in MeOH-d_4 allowed the comparison with aglamide A, an already known isomer of pyrrolotenin (**8**) with exchanged acid moieties recently isolated from *A. edulis*. In this case, the cinnamoyl moiety was attached to the ring-nitrogen and the methylthiopropenoyl moiety to the amino group (Kim et al., 2006a). The ^1H and ^{13}C NMR resonances of the pyrrolidine ring were nearly identical, e.g. ^{13}C 63.5, 34.8, 22.0, 46.5 ppm compared to 64.3, 35.1, 22.6, 46.5 for pyrrolotenin (**8**) (Table 3). The acid rests, however, showed small but significant deviations, e.g. the olefinic ^{13}C resonances for MTPA attached to the amino group were 116.0 and 144.1 compared to 114.3 and 146.5 for **8**. These values were consistent with the data of the cyclic bisamide leptanthin also characterised by two MTPA moieties with values 116.0 and 145.2 ppm for MTPA at the amino function, and 114.3, 146.4 for MTPA attached directly to the ring (Greger et al., 2000). Consequently, the MTPA unit of pyrrolotenin (**8**) with resonances at 114.3 and 146.5 was clearly linked to the ring-nitrogen. Compound **9** was an open chain bisamide with CA and MTPA moieties corresponding to the cyclic pyrrolotenin (**8**) after ring opening, and was therefore named secopyrrolotenin (**9**). The structure followed from analysis of the 2D NMR spectra and was supported by EIMS showing peaks for M^+ and the two characteristic acyl fragments (see Table 3 and Section 3).

In compounds **10** and **11**, isolated from *A. spectabilis*, one of the acids was again cinnamic acid, however, the second acids were aliphatic with additional alcohol functions. Cyclic aminopyrrolidine derivatives with similar hydroxylated aliphatic acid components are well known. In odorinol (Hayashi et al., 1982) and piriferinol (Brader et al., 1998) the alcohol functions were tertiary ones (OH at positions 2). The corresponding seco derivatives secoodorinol and secopiriferinol were also isolated from *A. gracilis* (Gre-

Table 3
^1H NMR data of bisamides **8–11** and ^{13}C NMR of bisamides **8–10** (in $CDCl_3$, **8** also in CD_3OD)

No.	^1H NMR					^{13}C NMR			
	8 (CD_3OD)	**8** (60/40%)[a]	**9**[b]	**10**[b]	**11**[b]	**8** (CD_3OD)	**8** (60/40%)[a]	**9**	**10**
1	6.11 *br.d* (5.8)	6.13/6.13 *br.d*	3.38 *q* (6.1)	3.68 *m*	3.72 *m*	64.3 *d*	62.94/62.88 *d*	39.1 *t*	39.0 *t*
2	a: 2.26 *m* b: 1.92 *m*	a: 2.19/2.19 *m* b: 1.98/1.98 *m*	1.63 *m*	1.60 *m*	1.61 *m*	35.1 *t*	34.41/34.35 *t*	27.0 *t*[c]	26.9 *t*[c]
3	1.98 *m*	1.90/1.90 *m*	1.63 *m*	1.60 *m*	1.61 *m*	22.6 *t*	21.67/21.60 *t*	26.8 *t*[c]	26.5 *t*[c]
4	a: 3.67 *ddd* (11.2, 8.4, 3.1) b: 3.43 *ddd* (11.2, 9.3, 7.2)	a: 3.54/3.48 *m* b: 3.38/3.38 *m*	3.43 *q* (6.1)	3.40 *m*	3.42 *m*	47.0 *t*	45.89/45.89 *t*	39.3 *t*	39.4 *t*
1′						166.3 *s*	164.52/164.57 *s*	164.3 *s*	177.1 *s*
2′	6.20 *d* (14.4)	6.14/6.12 *d*	5.66 *d* (14.6)	2.53 *m*	2.48 *m*	114.3 *d*	112.99/ 112.94 *d*	115.8 *d*	38.3 *d*
3′	7.69 *d* (14.4)	7.77/7.81 *d*	7.63 *d* (14.6)	a: 1.83 *m* b: 1.73 *m*	a: 3.41 *m* b: 3.33 *m*	146.5 *d*	145.45/145.49 *d*	142.9 *d*	36.7 *t*
4′	2.33 *s* (SMe)	2.31/2.32 s (SMe)	2.32 *s* (SMe)	a: 3.40 *m* b: 3.24 *m*	1.18 *d* (7.3)	14.5 *q* (SMe)	14.49/14.49 *q* (SMe)	14.6 *q* (SMe)	60.3 *t*
5′				1.19 *d* (7.1)					17.9 *q*
1″						167.1 *s*	164.78/164.83 *s*	166.2 *s*	166.5 *s*
2″	6.58 *d* (15.7)	6.58/6.64 *d*	6.42 *d* (15.6)	6.42 *d* (15.7)	6.40 *d* (15.7)	121.2 *d*	120.26/120.37 *d*	120.7 *d*	120.6 *d*
3″	7.60 *d* (15.7)	7.68/7.70 *d*	7.62 *d* (15.6)	7.62 *d* (15.7)	7.62 *d* (15.7)	143.0 *d*	141.75/141.62 *d*	140.9 *d*	141.2 *d*
4″						136.1 *s*	134.74/134.67 *s*	134.9 *s*	134.8 *s*
5″/9″	7.55 *m*	7.53/7.53 *m*	7.51 *m*	7.50 *m*	7.51 *m*	128.9 *d*	127.90/127.90 *d*	127.8 *d*	127.8 *d*
6″/8″	7.38 *m*	7.36/7.36 *m*	7.36 *m*	7.36 *m*	7.36 *m*	130.0 *d*	128.85/128.85 *d*	128.8 *d*	128.8 *d*
10″	7.38 *m*	7.36/7.36 *m*	7.36 *m*	7.36 *m*	7.36 *m*	131.1 *d*	129.89/129.84 *d*	129.6 *d*	129.7 *d*

[a] **8** in $CDCl_3$ as a mixture of epimers in the ratio 60:40%.

[b] NH and OH resonances. **9**: 6.15 (*br. t*, cinnamic amide), 5.79 (*br. t*, methylthiopropenoic amide); **10**: 6.29 and 6.21 (2 × *br. t*, 2 × NH), 3.03 *br. s* (OH); **11**: 6.23 and 5.87 (2 × *br. t*, 2 × NH), 2.95 *br. s* (OH).

[c] Exchangeable within the row.

ger et al., 2001). The present seco compounds **10** and **11** were isomers with OH positioned at the end of the short chains at positions 3′ and 4′, resulting in primary alcohol functions. The aliphatic acid component of compound **10,** named secoisoodorinol, was shown to be 4-hydroxy-2-methylbutanoic acid, whereas that of compound **11**, named secoisopiriferinol, was the closely related 3-hydroxy-2-methylpropanoic acid. Comparison of chemical shifts and additional 2D NMR measurements proved unambiguously the proposed structures.

Structures **1**–**11** were also confirmed by EIMS. The expected molecular masses M^+ appeared as peaks of 8–21% relative intensity and the HR-EIMS agreed in all cases with the molecular formulae of the compounds. The 100% peaks were represented by the acyl ions, either the cinnamoyl rest Ph–CH=CH–CO^+, $m/z = 131$ (**1–3**, **5**, **6**, **9–11**) or the methylthiopropenoyl moiety CH_3S–CH=CH–CO^+, $m/z = 101$ (**4**, **7**, and **8**). For compounds with both acyl rests both peaks were observed. Further prominent fragments included Ph–CH=CH^+, $m/z = 103$ and CH_3S–CH=CH^+, $m/z = 73$ as a consequence of loss of CO of the acyl ions (see Section 3).

2.2. Distribution and structural correlations of amide-esters, bisamides, and flavaglines

Based on extensive UV-HPLC analyses and TLC comparisons sprayed with anisaldehyde–sulphuric acid various chemical capacities of different *Aglaia* species were analysed and compared in our laboratory. Apart from a number of triterpenoids (Brader et al., 1998; Joycharat et al., 2007), especially flavaglines (Bacher et al., 1999; Greger et al., 2001; Brem, 2002; Hofer, 2002), bisamides, and lignans (Greger et al., 2000; Teichmann, 2002) were shown to constitute the typical chemical make-up of the genus. Due to the small amount of plant material used for most comparative studies only accumulated constituents could be detected and were taken into consideration. In contrast to many other *Aglaia* species, the HPLC profile of *A. tenuicaulis* was characterised by rather uniform UV-spectra usually indicative for bisamides. However, they turned out to belong mainly to amide-esters with tenucaulin A (**1**) and aglatenin (**4**) as major constituents in the leaf extract. The isomers isotenucaulin A (**2**) and tenucaulin B (**3**) were isolated as minor constituents only. The composition of the stem and root bark differed by the formation of tenaglin (**5**) and caulitenin (**6**), whereas aglatenin (**4**) was only detected in trace amounts. Tenucaulin A (**1**) was shown to be the dominating derivative in all three plant parts accompanied by big amounts of the cyclic bisamide pyrrolotenin (**8**).

As shown in Fig. 1, the newly described amide-esters **1–6** were mostly characterized by two different acid moieties, mainly consisting of cinnamic and methylthiopropenoic acid. Both of which were shown to form either the amide or the ester group. Only caulitenin (**6**) deviated by a combination of cinnamic and benzoic acid. By contrast, two identical acyl moieties were found in aglatenin (**4**) and tenaglin (**5**), where either two methylthiopropenoyl moieties in the former or two cinnamoyl moieties in the latter were symmetrically linked to an aminoalcohol. The corresponding putrescine-bisamide aglaidithioduline with two methylthiopropenoyl moieties was already isolated from *A. edulis* (Saifah et al., 1999) and *A. leucophylla* (*A. leptantha*) (Greger et al., 2000). However, in the latter species aglaidithioduline was erroneously interpreted as the amide-amine hemileptaglin due to contaminated basic material. This error has been corrected by Detterbeck and Hesse (2002a). In addition, leptanthin, the corresponding cyclic aminopyrrolidine derivative of aglaidithioduline was also isolated from *A. leucophylla* (Greger et al., 2000). Comparing the open-chained structures of tenucaulin A (**1**) and secopyrrolotenin (**9**), close structural connections between amide-esters and bisamides became evident. Moreover, secopyrrolotenin (**9**) could be directly deduced from pyrrolotenin (**8**) by opening the pyrrolidine ring (Fig. 1). Hence, putrescine appeared to be the central building block for all structures mentioned above. However, in the case of the amide-esters **1**–**6** and the amide-alcohol **7** one nitrogen atom was obviously replaced with oxygen. The latter compound **7** was shown to be a product of hydrolysis created by TLC purification of aglatenin (**4**) and could not be detected in the HPLC profile of the original crude extract.

The two new open-chained bisamides secoisoodorinol (**10**) and secoisopiriferinol (**11**) were isolated from the leaf extract of *A. spectabilis* together with the closely related aglairubin (**12**) (Teichmann, 2002). Aglairubine (**12**) was originally described for *A. rubiginosa* (Hiern) C.M. Pannell (Saifah and Suparakchinda, 1998) and later with a revised structure for the two Australian species *A. australiensis* C.M. Pannell and *A. meridionalis* C.M. Pannell (Seger et al., 2002; Teichmann, 2002). Since all four species were grouped together in the section Amoora the accumulation of **10** and/or **12** may be regarded as an important chemical marker for an infrageneric classification of *Aglaia* (Muellner et al., 2005). The structure of aglairubine (**12**) was also published as dasyclamide isolated from the leaves of a plant identified as *A. dasyclada* Miq. (Chaidir et al., 2001). This name has not yet been typified (Pannell, 1992). Chromatographic comparison of leaf extracts of different geographical provenances of *A. spectabilis* showed pronounced variation in the accumulation of bisamides. Based on more detailed investigations within single individuals the highest amount of bisamides was always found in the youngest terminal leaves. This could impressively be demonstrated in the unifoliolate leaves of a seedling of *A. spectabilis* (HG 809), where the terminal leaf accumulated large amounts of secoisoodorinol (**10**), whereas in the basal leaf no bisamides could be detected at all (Teichmann, 2002). Structurally, secoisoodorinol (**10**) is also directly related with the well-known cyclic bisamides odorine (**15**), dehydroodorine (**16**), and odorinol (**17**) (Shiengthong et al., 1979; Duh et al., 1993). Similarily, secoisopiriferinol

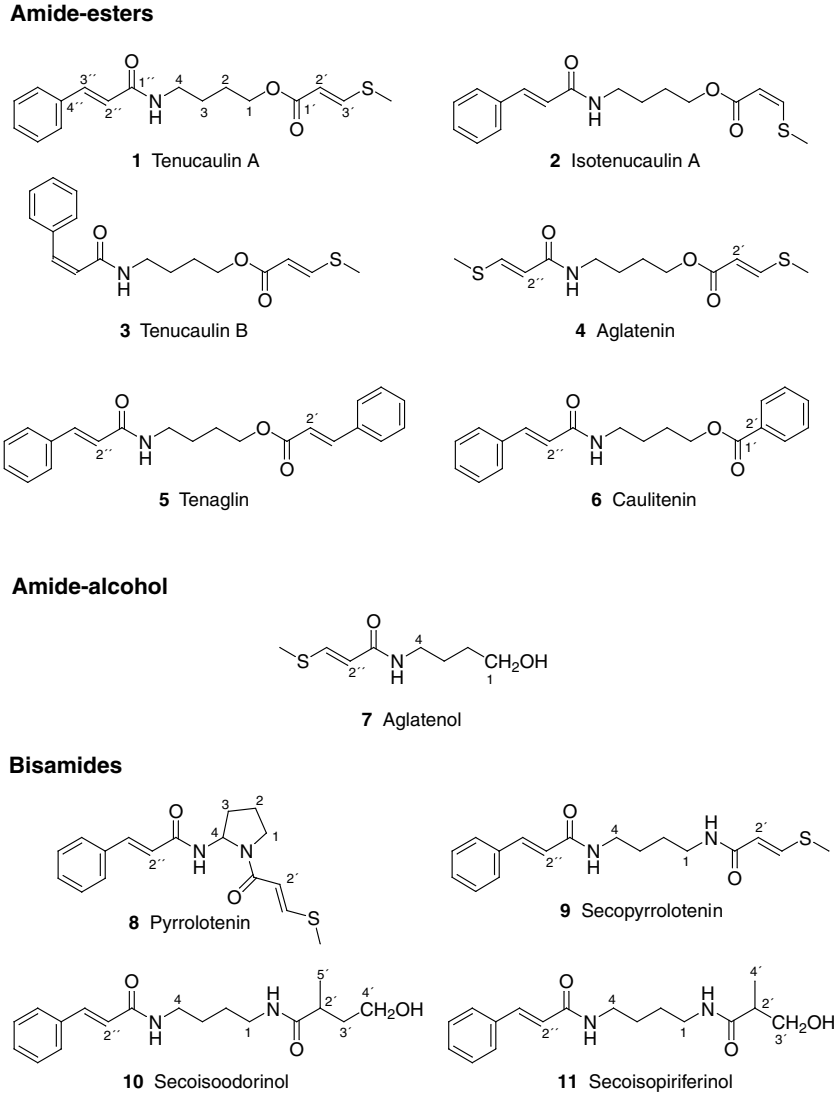

Fig. 1. Amide-esters and structurally related bisamides.

(**11**) is related to piriferine (**14**) (Saifah et al., 1988) and piriferinol (Brader et al., 1998). Common to all bisamides mentioned above is a cinnamoyl moiety combined with different derivatives of methylbutanoic or isobutanoic acid.

Bisamides also represent important building blocks of flavaglines, especially incorporated into benzopyran and benzoxepin derivatives (Fig. 2). A prerequisite for such an insertion appears to be the presence of a cinnamoyl moiety most likely leading to a cycloaddition reaction with a flavonol (Bacher et al., 1999; Xu et al., 2000). In this case both the open-chained (**12**, **13**) and the cyclic bisamides (**14**–**18**) are inserted as a whole maintaining their overall structure and substitution pattern. This became especially clear with the formation of aglain A and aglaforbesin A, where odorine (**15**) is incorporated in two different positions (Dumontet et al., 1996). Apart from the essential cinnamoyl moiety most bisamides are also characterised by derivatives of methylbutanoic acid as second acyl moiety (**12**, **15**–**17**). As shown in Fig. 2, benzoic (**13**), isobutanoic (**14**), and isovaleric acid (**18**) were also identified to be part of bisamides incorporated into benzopyran flavaglines (Puripattanavong et al., 2000; Joycharat et al., 2007; Kim et al., 2006a) (Fig. 2).

Although no amide-esters have so far been found as building blocks of flavaglines, closely related derivatives have been reported, in which amide-alcohol derived moieties are incorporated into benzopyrans and benzofurans (Nugroho et al., 1997; Salim et al., 2007). In this case one of the nitrogen atoms of putrescine has obviously also been replaced with oxygen (Fig. 3). Further transformation then probably led to a methoxylated pyrrolidin ring in the recently published ponapensin isolated from *A. mariannensis* Merr. (syn = *A. ponapensis* Kaneh.). Ponapensin was shown to be a benzopyran flavagline with potent NF-κB inhibitory activity (Salim et al., 2007). The corresponding building block aglamide D (**19**) has already been isolated from *A. edulis* (Roxb.) Wall. (Kim et al., 2006a). From

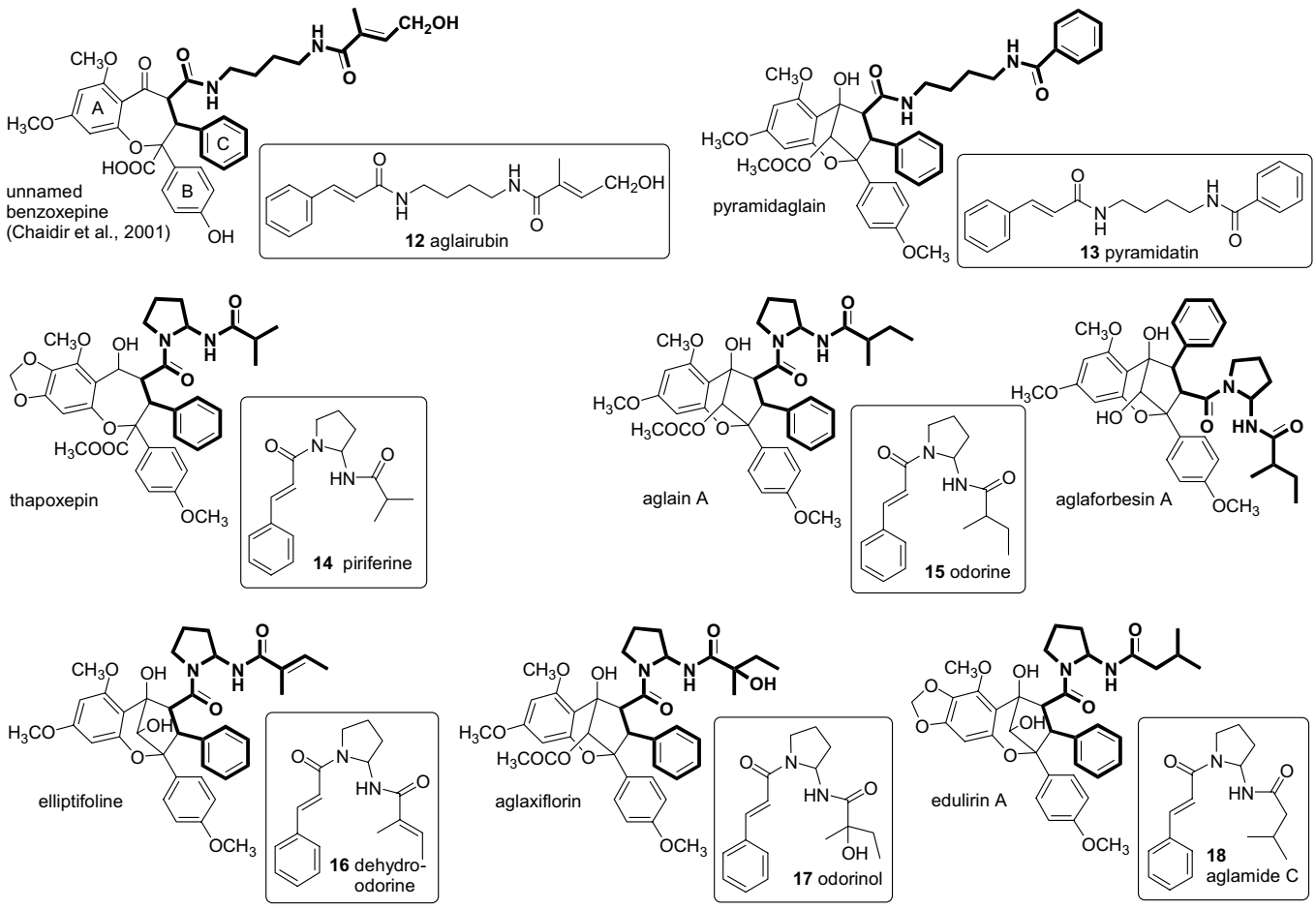

Fig. 2. Various bisamides as building blocks of benzopyran and benzoxepine flavaglines.

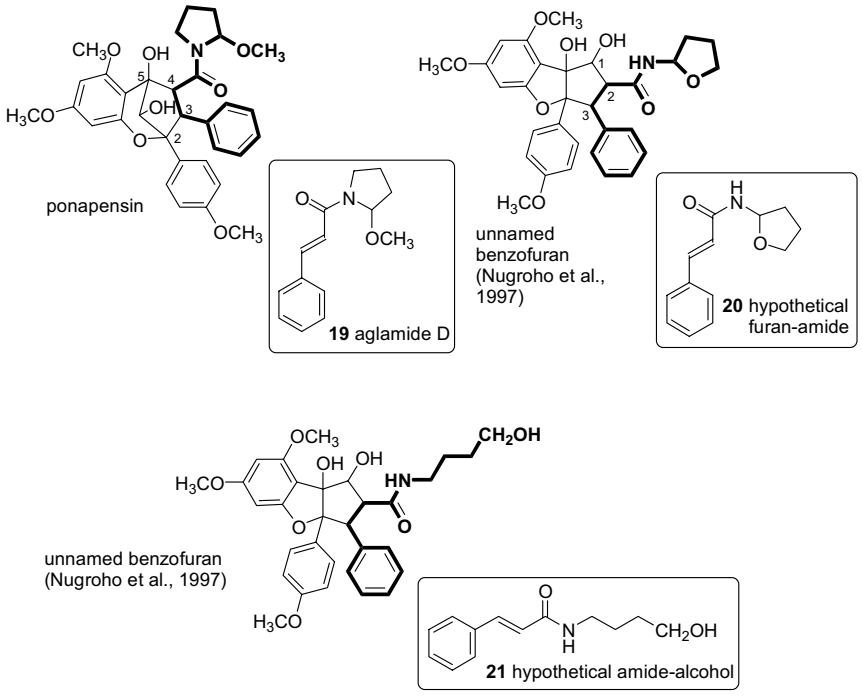

Fig. 3. Benzopyran and benzofuran flavaglines with amide-alcohol derived moieties.

the fruits of *A. elliptica* Bl. two benzofurans have been described (Nugroho et al., 1997), from which **20** and **21** can be assumed as hypothetical building blocks so far unknown as discrete natural products. The open-chained amide-alcohol **21** may be regarded as precursor of the furan-amide **20**, and both appear to be derived from a putrescine amide (Fig. 3).

For sake of completeness it should be pointed out that putrescine-derived amides were also found in flavaglines attached in another way, forming a pyrimidinone structure, e.g. in aglaiastatin (Ohse et al., 1996) and marikarin (Greger et al., 2001) (Fig. 4). These structures are most likely derived from a flavonol linked with a putrescine-derived cyclic amide-amine moiety. However, the corresponding hypothetical building block **22** has not yet been isolated. Aglaiastatin was shown to block cell cycle progression in the mitotic prophase and induce apoptosis in colorectal cancer cells (Hausott et al., 2004). Together with the related dehydroaglaiastatin and marikarin it was isolated from *A. gracilis* A.C. Smith and also exhibited pronounced insecticidal activity (Greger et al., 2001). The typical pyrimidinone structure of this type of flavaglines can be explained by a condensation reaction between the free amino group of the hypothetical putrescine amide **22** and the OH group at position C-1 of the cyclopentane ring of the benzofuran skeleton (Fig. 4).

2.3. Concluding remarks

Based on the flavagline structures known so far it became evident that the putrescine-derived bisamides are essential building blocks incorporated in benzopyran and benzoxepine flavaglines (Fig. 2), but were only rarely found in benzofuran derivatives. On the other hand, pyrimidinone structures appeared to be exclusively formed in the latter (Fig. 4). Although the newly described amide-esters (**1**–**6**) showed obvious structural similarities with putrescine-derived bisamides, only closely related amide-alcohol derivatives could be detected so far in benzopyran and benzofuran flavaglines. However, taking into account the rapid hydrolysis of the amide-ester aglatenin (**4**) into the amide-alcohol aglatenol (**7**) during TLC separation, similar reactions cannot be excluded for the formation of the flavaglines shown in Fig. 3.

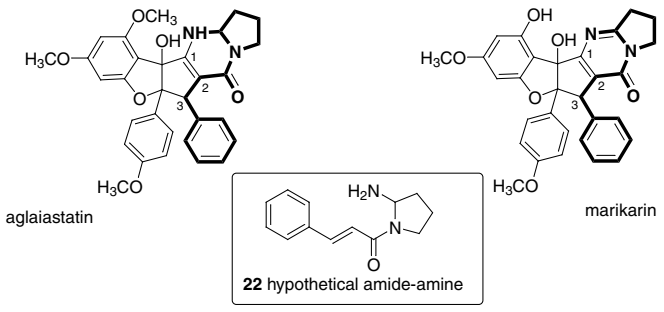

Fig. 4. Benzofuran flavaglines with amide-amine moieties.

The predominant accumulation of specific bisamides, both in free form and/or as building block of flavaglines, may serve as important chemical marker in the genus *Aglaia*. For instance, the restricted distribution of the open-chained aglairubin (**12**) and secoisoodorinol (**10**) characterised the species of the section Amoora (Muellner et al., 2005). Hence, an affiliation of '*A. dasyclada*' from China to this group should be reconsidered with respect to the dominating aglairubin (**12**) and corresponding benzopyran and benzoxepine flavaglines found in that species (Chaidir et al., 2001). Specific bisamide patterns may also help to clarify taxonomic delimitations of complex species like *A. edulis*. As already pointed out in our previous paper (Bacher et al., 1999), the sole accumulation of the threefold acylated putrescine edulimide in *A. edulis* of southeast Thailand (HG 12) (Brader et al., 1998) clearly deviated from another collection of southwest Thailand (HG 515) (Bacher et al., 1999), characterised by a number of benzopyran and benzoxepine flavaglines, mainly containing pirriferine (**14**) as bisamide moiety. Moreover, in *A. edulis* from Kaeng Krachan National Park in west Thailand only bisamides were shown to be accumulated containing methylthiopropenoic and phenylacetic acid moieties (Saifah et al., 1999). Surprisingly, this rare chemical pattern was also found in a parallel investigation of *A. leptantha* collected in southeast Thailand (Greger et al., 2000). However, more detailed morphological studies carried out by one of us (C.M.P) led to a re-identification of the voucher specimen of the latter as *A. leucophylla*. After comparing the voucher specimens of *A. edulis* from Kaeng Krachan with those of *A. leucophylla* morphological similarities became evident suggesting an amalgamation of both collections into *A. leucophylla*. In a more recent investigation of *A. edulis* from Indonesia various flavaglines were isolated together with bisamides characterised by cinnamic and methylthiopropenoic acid moieties (Kim et al., 2006a). In this case, the substitution pattern of aromatic ring A of the flavaglines was shown to be the same as already previously reported for a collection from southwest Thailand (Bacher et al., 1999) containing a methylenedioxy and methoxy group (e.g. in thapoxepine and edulirin A, Fig. 2). However, the incorporated bisamides differed, showing methylthiopropenoic and isovaleric acid moieties in the Indonesian, and isobutanoic and methylbutanoic acid moieties in the Thai collection. On the other hand, a nearly identical chemical profile of the latter (Bacher et al., 1999) was also reported for a collection from Vietnam, which, however, was identified as *A. oligophylla* Miq. (Dreyer et al., 2001). A critical re-investigation of corresponding voucher specimens would help to clarify the taxonomic position of these collections. The examples presented should demonstrate, that to date any chemotaxonomic conclusion in the genus *Aglaia* is premature, since many species investigated so far have not been accurately identified and documented. At the same time, it should be pointed out that attempts to recover valuable bioactive compounds from some species fail if the name cited for the

plant material from which they were extracted is incorrect or if there is no voucher specimen with a unique identifier cited in the published report of the new compound.

3. Experimental

3.1. General

NMR: Bruker, DRX 400 WB ($CDCl_3$, ^1H δ 7.26, ^{13}C δ 77.0; CD_3OD, ^1H δ 3.31, ^{13}C δ 49.0). MS: Finnigan MAT 900 S. IR: Perkin-Elmer 16PC FT-IR. Optical rotation: Perkin-Elmer Polarimeter 241. HPLC: Agilent 1100, UV diode array detection at 230 nm, column Hypersil BDS-C18 250 × 4.6 mm, 5 μm, mobile gradient either MeOH 20–100% or acetonitrile 20–60% in aqueous buffer (0.015 M H_3PO_4, 0.0015 M tetrabutylammoniumhydroxide), flow rate 1 ml/min.

3.2. Plant material

Leaves, stem, and root bark of three different provenances of *A. tenuicaulis* were collected separately in evergreen forests: (a) from Ton Tae waterfall, near Trang, S-Thailand (HG 869, HG 870) and (b) from Ban Tung Sung community forest, 50 km NW of Krabi, S-Thailand (HG 901). Leaves of *A. spectabilis* were collected in the evergreen forest of Adang Island, Satun, S-Thailand (HG 864). Voucher specimens are deposited at the Herbarium of the Faculty Center of Botany, University of Vienna, Austria, WU.

3.3. Extraction and isolation

Dried leaves, stem and root bark of three collections of *A. tenuicaulis*, and leaves of *A. spectabilis* were ground separately and extracted twice with MeOH at room temperature for 5 days, filtered, and concentrated. The aqueous residues were extracted with $CHCl_3$ and the concentrated $CHCl_3$ fractions dissolved in MeOH were used for comparative UV-HPLC and TLC, respectively. For preparative isolation, lipophilic crude extracts were roughly separated by column chromatography (Merck Silica gel 60, 0.2–0.5) with solvent mixtures of hexane, EtOAc, and MeOH. Further separation was achieved by MPLC (400 × 40 mm column, Merck LiChroprep silica 60, 25–40 μm) with mixtures of MeOH in EtOAc as mobile phase and prep TLC.

From 120 g leaves of *A. tenuicaulis* (HG 901) a portion (2000 mg) of the $CHCl_3$ fraction (3486 mg) was roughly separated by CC. The combined amide containing fractions (500 mg), monitored by HPLC and TLC, were eluted with 100% EtOAc and further separated by prep MPLC with 30% EtOAc in hexane to afford 50 mg tenucaulin A (**1**), 40 mg of a mixture of **2** and **3,** and 25 mg of aglatenin (**4**). The mixture containing **2** and **3** was further separated by prep TLC (CH_2Cl_2:EtOAc = 40:60) to afford 8 mg pure tenucaulin B (**3**) and 4 mg pure isotenucaulin A **(2)**. A more polar CC fraction (15% MeOH in EtOAc) afforded an additional amide-fraction separated by prep MPLC with 30% EtOAc leading to three different fractions containing impure **4**, **8**, and **9,** from which one fraction afforded 28 mg pure pyrrolotenin (**8**) by prep TLC (CH_2Cl_2:EtOAc = 50:50). The two other MPLC fractions containing 10 mg impure **4** and 10 mg impure **9** were further separated by prep TLC (CH_2Cl_2:EtOAc = 50:50) to afford 4 mg secopyrrolotenin (**9**) and 4 mg aglatenol (**7**). The latter obviously represented a hydrolysation product of aglatenin (**4**) created by TLC purification.

From 47 g stem bark of *A. tenuicaulis* (HG 869) 610 mg of the $CHCl_3$ fraction were separated in the same way as described above. The amide-containing CC fractions eluted with 15% MeOH in EtOAc were further separated by prep MPLC using 30% EtOAc in hexane to afford 9 mg tenaglin (**5**) and 5 mg caulitenin (**6**).

From 48 g leaves of *A. spectabilis* (HG 864) a portion (900 mg) of the $CHCl_3$ fraction (1800 mg) was roughly separated by CC and the amide-containing fractions were eluted with 15% and 30% MeOH in EtOAc. Prep MPLC with 5% MeOH in EtOAc and prep TLC (CH_2Cl_2:EtOAc:MeOH = 65:23:12) yielded 3 mg secoisopiriferinol (**11**), 14 mg secoisoodorinol (**10**) and 3 mg aglairubin (**12**).

3.4. Tenucaulin A (*1*)

Colourless crystals, m.p.: 75–77 °C; UV λ_{MeOH/H_2O} 216 (4.18), 221 sh (4.12), 276 (4.52) nm (log ε). IR ν_{CCl_4} cm^{-1} 3450 w, 3337 w, 3029 w, 2925 m, 2858 w, 1711 s, 1679 s, 1632 m, 1582 s, 1507 m, 1449 w, 1322 w, 1296 m, 1252 s, 1211 w, 1161 s, 975 w, 944 w. EIMS (70 eV, 140 °C): $m/z = 319$ (11%, M^+), 220 (14), 131 (100, $PhCH{=}CHCO^+$), 103 (30, 131–CO), 101 (25, $SCH_3CH{=}CHCO^+$); HREIMS: $m/z = 319.1253$ (calcd. 319.1242 for $C_{17}H_{21}NO_3S$).

3.5. Isotenucaulin A (*2*)

UV λ_{MeOH/H_2O} 216 (4.17), 221sh (4.12), 282 (4.48) nm (log ε). IR ν_{CCl_4} cm^{-1} 3449 w, 3349 w, 3029 w, 2925 m, 2856 w, 1710 s, 1679 s, 1633 m, 1582 s, 1506 m, 1449 w, 1322 w, 1296 m, 1252 s, 1210 m, 1163 s, 975 w, 945 w. EIMS (70 eV, 140 °C): $m/z = 319$ (12%, M^+), 220 (18), 131 (100, $PhCH{=}CHCO^+$), 103 (25, 131–CO), 101 (28, $SCH_3CH{=}CHCO^+$); HREIMS: $m/z = 319.1249$ (calcd. 319.1242 for $C_{17}H_{21}NO_3S$).

3.6. Tenucaulin B (*3*)

UV λ_{MeOH/H_2O} 274 (4.16) nm (log ε). IR ν_{CCl_4} cm^{-1} 3446 w, 3026 w, 2925 m, 2855 w, 1712 s, 1672 s, 1625 w, 1583 s, 1506 m, 1435 w, 1321 w, 1296 m, 1252 s, 1221 w, 1161 s, 945 w. EIMS (70 eV, 140 °C): $m/z = 319$ (12%, M^+), 220 (13), 131 (100, $PhCH{=}CHCO^+$), 103 (47, 131–CO), 101 (36, $SCH_3CH{=}CHCO^+$); HREIMS: $m/z = 319.1247$ (calcd. 319.1242 for $C_{17}H_{21}NO_3S$).

3.7. Aglatenin (**4**)

Colourless crystals, m.p.: 81–83 °C; UV λ_{MeOH/H_2O} 224 (3.75), 274 (4.49) nm (log ε). IR ν_{CCl_4} cm^{-1} 3451 w, 2924 m, 2856 w, 1711 s, 1672 s, 1583 s, 1504 m, 1436 w, 1321 w, 1296 m, 1251 s, 1161 s, 943 m. EIMS (70 eV, 150 °C): $m/z = 289$ (13%, M^+), 101 (100, $SCH_3CH{=}CHCO^+$), 73 (17, 101–CO); HREIMS: $m/z = 289.0800$ (calcd. 289.0806 for $C_{12}H_{19}NO_3S_2$).

3.8. Tenaglin (**5**)

UV λ_{MeOH/H_2O} 216 (4.40), 221sh (4.35), 274 (4.54) nm (log ε). IR ν_{CCl_4} cm^{-1} 3449 w, 3029 w, 2927 m, 2855 w, 1716 s, 1679 s, 1635 s, 1506 m, 1449 w, 1327 w, 1309 w, 1268 w, 1202 m, 1167 s, 986 w, 976 w, 863 w. EIMS (70 eV, 160 °C): $m/z = 349$ (18%, M^+), 218 (12), 148 (17), 131 (100, $PhCH{=}CHCO^+$), 103 (26, 131–CO); HREIMS: $m/z = 349.1670$ (calcd. 349.1678 for $C_{22}H_{23}NO_3$).

3.9. Caulitenin (**6**)

UV λ_{MeOH/H_2O} 218sh (4.32), 222 (4.32), 231sh (4.18), 274 (4.35) nm (log ε). IR ν_{CCl_4} cm^{-1} 3450 w, 2927 m, 2855 w, 1722 s, 1680 s, 1634 m, 1506 m, 1450 w, 1381 w, 1271 s, 1118 s, 1070 w, 1026 w, 975 w. EIMS (70 eV, 180 °C): $m/z = 323$ (8%, M^+), 301 (10), 131 (100, $PhCH{=}CHCO^+$), 119 (35), 105 (32, $PhCO^+$), 103 (35, 131–CO), 84 (37), 77 (40, Ph^+); HREIMS: $m/z = 323.1513$ (calcd. 323.1521 for $C_{20}H_{21}NO_3$).

3.10. Aglatenol (**7**)

UV λ_{MeOH/H_2O} 224 (3.78), 274 (4.32) nm (log ε). IR ν_{CCl_4} cm^{-1} 3638 w, 3451 w, 2926 m, 2855 w, 1670 s, 1583 s, 1505 m, 1437 w, 1323 w, 1248 w, 1178 w, 1163 w, 1023 w, 942 m. EIMS (70 eV, 90 °C): $m/z = 189$ (12%, M^+), 174 (16), 128 (17), 101 (100, $SCH_3CH{=}CHCO^+$), 73 (25, 101–CO); HREIMS: $m/z = 189.0832$ (calcd. 189.0824 for $C_8H_{15}NO_2S$).

3.11. Pyrrolotenin (**8**)

Colourless crystals, m.p.: 167–170 °C. $[\alpha]_D^{20} = -24°$ ($c = 0.5$, MeOH). UV λ_{MeOH/H_2O} 217 (4.20), 223sh (4.16), 277 (4.48) nm (log ε). IR ν_{CCl_4} cm^{-1} 3259 m, 3029 w, 2925 m, 2879 w, 1673 s, 1622 s, 1557 m, 1535 s, 1420 s, 1356 m, 1329 w, 1298 w, 1212 m, 1194 m, 1172 w, 1156 w, 1121 w, 987 w, 978 w, 944 w, 887 w, 868 w. EIMS (70 eV, 170 °C): $m/z = 316$ (20%, M^+), 215 (28, $M^+ - SCH_3CH{=}CHCO$), 185 (20, $M^+ - PhCH{=}CHCO$), 131 (70, $PhCH{=}CHCO^+$), 103 (38, 131–CO), 101 (100, $SCH_3CH{=}CHCO^+$), 85 (63), 73 (16, 101–CO), 70 (23); HREIMS: $m/z = 316.1254$ (calcd. 316.1246 for $C_{17}H_{20}N_2O_2S$).

3.12. Secopyrrolotenin (**9**)

UV λ_{MeOH/H_2O} 217 (4.20), 221sh (4.17), 274 (4.53) nm (log ε). IR ν_{CCl_4} cm^{-1} 3450 w, 3290 w, 2926 m, 2854 w, 1664 m, 1628 s, 1582 m, 1476 m, 1382 m, 1215 m, 1102 w, 1088 w, 942 w. EIMS (70 eV, 180 °C): $m/z = 318$ (8%, M^+), 201 (18), 162 (14), 131 (100, $PhCH{=}CHCO^+$), 103 (70, 131–CO), 101 (66, $SCH_3CH{=}CHCO^+$), 77 (51), 73 (20, 101–CO); HREIMS: $m/z = 318.1415$ (calcd. 318.1402 for $C_{17}H_{22}N_2O_2S$).

3.13. Secoisoodorinol (**10**)

Colourless needles, m.p.: 131–132 °C. $[\alpha]_D^{20} = +12°$ ($c = 0.4$, MeOH). UV λ_{MeOH/H_2O} 216 (4.12), 222sh (4.04), 274 (4.25) nm (log ε). IR ν CHCl3 cm^{-1} 3670 w, 3442 m, 3324 m, 2934 m, 2876 w, 1662 s, 1624 s, 1522 s, 1450 m, 1374 w, 1336 m, 1074 m, 1050 w, 988 w, 976 m, 856 w. EIMS (70 eV, 180 °C): $m/z = 318$ (11%, M^+), 300 (14), 201 (35), 131 (100, $PhCH{=}CHCO^+$), 126 (45), 103 (38, 131–CO), 70 (72); HREIMS: $m/z = 318.1938$ (calcd. 318.1943 for $C_{18}H_{26}N_2O_3$).

3.14. Secoisopiriferinol (**11**)

$[\alpha]_D^{20} = +21°$ ($c = 0.2$, MeOH). UV λ_{MeOH/H_2O} 216 (4.31), 222sh (4.19), 276 (4.24) nm (logε). IR ν CHCl3 cm^{-1} 3686 w, 3442 m, 2930 m, 2856 w, 1662 s, 1626 s, 1518 s, 1450 m, 1382 w, 1334 w, 1110 m, 1016 w, 976 w, 856 w. EIMS (70 eV, 180 °C): $m/z = 304$ (21%, M^+), 201 (37), 156 (22), 131 (100, $PhCH{=}CHCO^+$), 103 (34, 131 – CO), 70 (77); HREIMS: $m/z = 304.1781$ (calcd. 304.1787 for $C_{17}H_{24}N_2O_3$).

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