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ORGAN-SPECIFIC CHEMICAL DIFFERENCES IN *GLYCOSMIS TRICHANTHERA*

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Key Word Index—*Glycosmis trichanthera*; Rutaceae-Aurantioideae; amides; sulphones; acridones; quinolines; diprenyl indoles; organ-specific differences.

Abstract—The lipophilic leaf, stem and root extracts of *Glycosmis trichanthera* are characterized by distinct chemical profiles, containing sulphur-containing amides in the leaves, prenylated acridone alkaloids in the stem bark, and quinoline alkaloids together with a 3,7-diprenylated indole in the root bark. Two isomeric sulphones derived from methylthio-propenoic acid phenethylamides, named trichanthin-A and -B, and the 3,7-diprenylated indole proved to be new natural products. Structure elucidation of the new compounds is described by spectroscopic evidence. Bioautographic tests with *Cladosporium herbarum* showed only moderate antifungal activity for trichanthin-B and methylgerambullin.

INTRODUCTION

Glycosmis species are characterized by different types of amides mainly accumulated in the leaves. Their acid moieties were shown to be mostly derived from methylthiopropenoic or methylthiocarbonic acid [1, 2], but can also be deduced from anthranilic [3], isovaleric, and senecioic acid [2]. From the root and stem bark, by contrast, different acridone, carbazole and quinoline alkaloids are known which have been isolated so far mainly from three species only, namely from *G. pentaphylla* (Retz.) DC. (= *G. arborea* (Roxb.) DC.), *G. mauritiana* (Lam.) Tanaka, and *G. parviflora* (Sims) Little (= *G. citrifolia* (Willd.) Lindley) [see Ref. 4].

In the course of elaborating the chemical key characters for the genus we have now investigated separately the lipophilic leaf, stem, and root extracts from three individuals of *G. trichanthera* Guillaumin (= *G. calcicola* B. C. Stone) collected in Kho Tarutao (south Thailand). It can easily be distinguished from other species by its emarginate leaflets (terminated with a depressed apex), tetramerous flowers and globose fruits and is found mostly in open and dryer limestone range. From all three individuals each organ was shown to be uniformly characterized by a specific chemical profile from which the leaf and root extract contained three hitherto unknown compounds as major components (Fig. 1). From the leaves we isolated two new isomeric sulphones derived from methylthiopropenoic acid phenethylamides linked with an unusual pentacyclic 4-oxo-2-oxolenyl terpenoid side chain, named trichanthins-A (**1**) and -B (**2**), together with the closely related glyparvin-A [5] and its presumable biogenetic precursor methylgerambullin [1]. The HPLC profile of the stem bark showed a series of already known acridone alkaloids, whereas the root extract afforded large amounts of an as yet undescribed 3,7-diprenyl indole (**3**) along with some known quinoline and acridone alkaloids (Fig. 1). In the present study we have analysed the organ-specific chemical profiles and report on the isolation and structure elucidation of three new compounds.

RESULTS AND DISCUSSION

HPLC analysis of the lipophilic crude extracts of the leaves, root and stem bark of *G. trichanthera* linked with UV diode-array detected show clearly distinguishable chemical profiles (Fig. 1). The leaf extract is characterized by simple UV spectra, suggesting a series of amides. Two compounds were subsequently shown to be identical with the previously published methylgerambulline [1] and glyparvin-A [5]. The UV spectra of the two remaining derivatives (**1**, **2**) look also very much like that of glyparvin-A. With λ_{max} (MeOH) at 224 and 294 nm and a shoulder at 240 nm **1** is especially similar but deviates by its different

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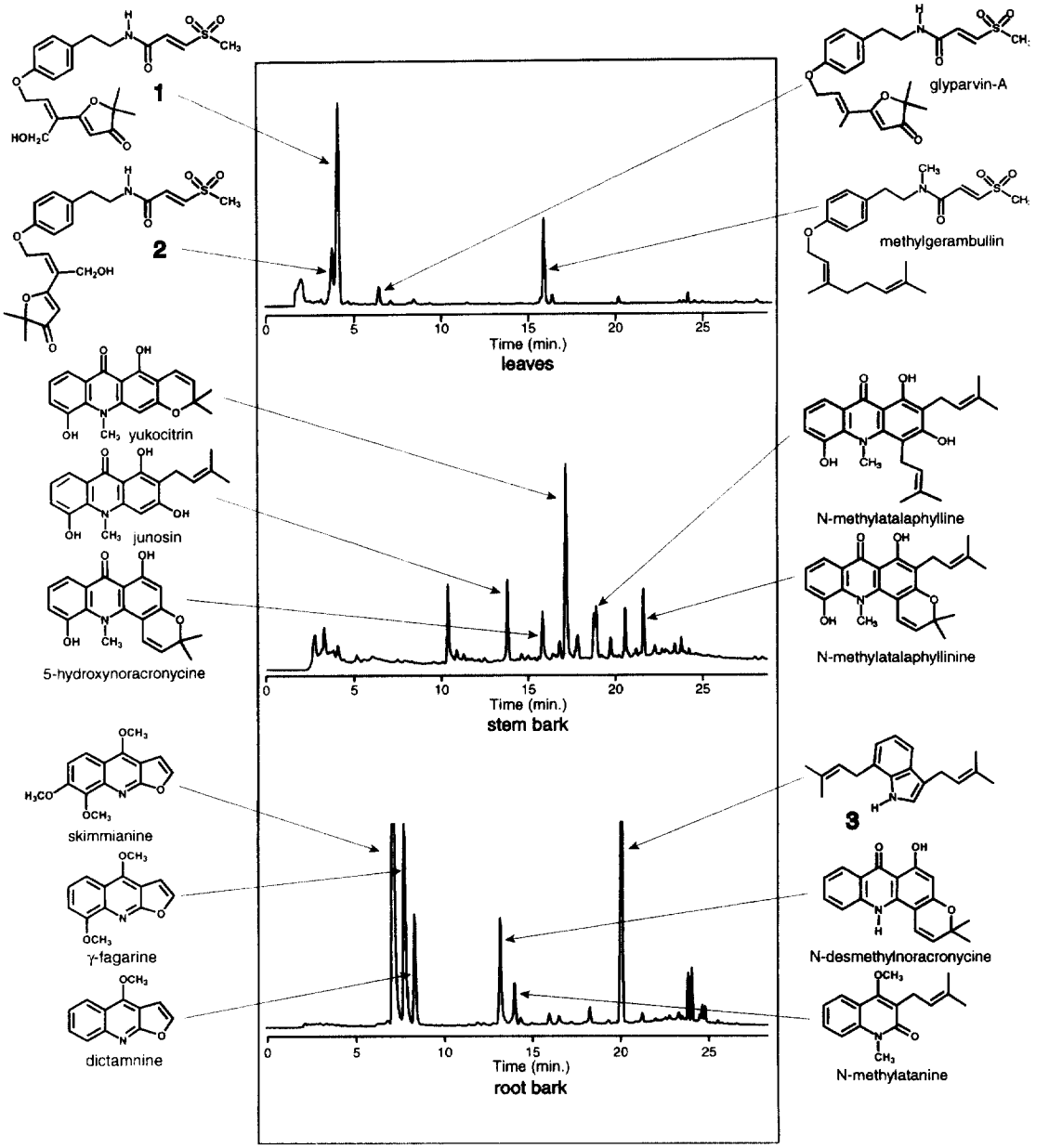
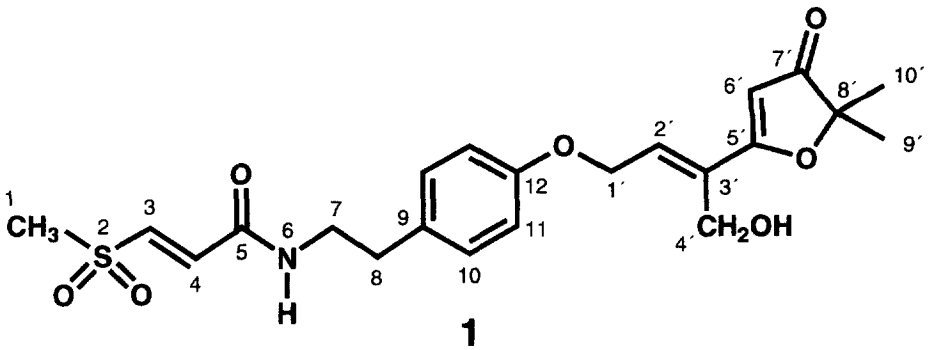


Fig. 1. HPLC profiles of the lipophilic crude extracts from the leaves, stem and root bark of *Glycosmis trichanthera*.

retention time (Fig. 1). A close structural relationship between **1** and glyparvin-A can also be deduced from the very similar IR spectra. Besides the typical >N-H stretching band at 3294 cm^{-1} (KBr) and the strong carbonyl band at 1678 cm^{-1} for the furanone ring, **1** shows an additional signal at 3682 cm^{-1} ($CHCl_3$) indicative for an OH group. The ^1H and the ^{13}C NMR spectra of **1** and **2** are also very similar to the data recently published for glyparvin-A [5]. The chemical shifts for protons 1-H–11-H are almost identical; however, the terpenoid side chain shows some significant changes with a lack of CH_3 group at position 4′ as the main difference. That is obviously replaced by a CH_2OH group in **1** and **2**. In the case of **1**, the resonance for 4′-H_2 appears as a *d* (J = 5.9 Hz) at δ 4.48 and the corresponding 4′-OH as a *t* at δ 1.96 (J = 5.9 Hz). The hydroxyl proton (4′-OH) is D_2O exchangeable, changing thereby the *d* at 4.48 to a somewhat broadened *s*. In concentrated or less pure samples the 4′-OH signal is found as a very broad *s* and the 4′-H_2 resonance as a fairly sharp *s*. The 4′-CH_2 resonance for **2** appears as a clear *dd* at δ 4.37 with coupling constants of J = 5.8 and 1.2 Hz, and the 4′-OH resonance at δ 1.88 (J = 5.8 Hz). The long range coupling of 1.2 Hz has its counterpart in the coupling pattern of the 2′-H resonance (a *tt* with J = 5.3 and 1.2 Hz for **2**, compared to a *t* with J = 5.9 Hz for **1**). The ^{13}C NMR spectra of **1** and **2** also



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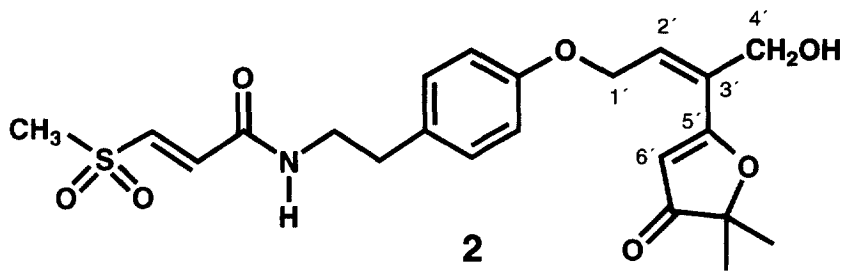

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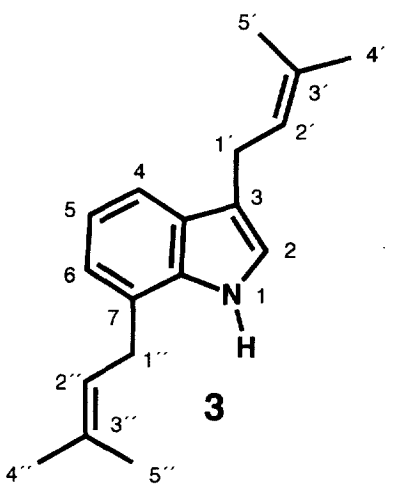

3

support the relationship to glyparvin-A, namely the oxidation of the 4′-methyl to a hydroxymethyl group which is found as a *t* in the typical region of ca 60 ppm (see Experimental). Compounds **1** and **2** are obviously the two possible stereo-isomers characterized by either an (*E*) or (*Z*) configuration at the C-2′=C-3′ double bond. One of the isomers represents the 4′-hydroxylated glyparvin-A (*E*-isomer), the other one the 4′-hydroxylation product of the not yet described glyparvin-B (*Z*-isomer). The molecular formula of $C_{22}H_{27}NO_7S$ for both isomers is in agreement with the MS data with the molecular ion at *m/z* 449 and the characteristic fragments at *m/z* 431 $[M-H_2O]^+$, 268 $[C_{12}H_{14}NO_4S$, $M-$geranyl$]^+$, and 181 $[C_{10}H_{13}O_3$, geranyl moiety$]^+$. The measurement of differential NOEs allows a clear decision which one of the two compounds is (*E*) or (*Z*) configurated. Especially the strong effects 4′ → 1′ and 6′ → 2′ for **1** and the effects 4′ → 2′ and 6′ → 1′ for **2** are only compatible with an (*E*) configuration for **1**, named trichanthin-A, and a (*Z*) configuration for **2**, named trichanthin-B. In the ^{13}C NMR spectra some of the chemical shift differences between **1** and **2** may be interpreted in terms of different steric compressions causing characteristic upfield shifts. The largest upfield shift is observed for the C-4′ resonance, which is found at δ 58.1 for the (*E*) isomer trichanthin-A (**1**), but at δ 65.8 for 63.6 for the (*Z*) isomer trichanthin-B (**2**) (see Experimental). This agrees with the proposed stereochemical assignments, because in the (*E*)-isomer, C-4′ is in close neigh-

bourhood to 1′ and 6′ (or to the ring oxygen, depending on the conformation about the 3′,5′-single bond). In the (*Z*)-isomer only 6′ (or the ring oxygen) is that close. In the case of glyparvin-A, the *s*-(*z*) conformation about the C-3′—C-5′ single bond is favoured [5], for **1** and **2** both conformations *s*-(*z*) and *s*-(*e*) are substantially populated. This can be concluded from the NOEs which are equally strong for 6′ → 2′ and 6′ → 4′ in **1** and for 6′ → 1′ and 6′ → 4′ in **2** [in the formula scheme only the 3′,5′-*s*-(*z*) conformers are shown].

The lipophilic crude extract of the stem bark is mainly characterized by different acridone alkaloids whose structures have already been described previously (Fig. 1). The main component, yukocitrin [6], was isolated and its structure confirmed by spectroscopic methods. All the other derivatives were identified by HPLC-UV comparison with authentic samples.

The chemical pattern of the root bark clearly deviates by the accumulation of the furoquinolines skimmianine, γ-fagarine and dictamnine [see Ref. 4] together with the unknown compound **3** accompanied by the acridone *N*-desmethylnoracronycine and the quinoline *N*-methylatanine as minor components (Fig. 1). Whereas the two latter compounds were identified by HPLC-UV comparison only, all major components were isolated and their structures elucidated or confirmed by spectroscopic evidence, respectively. The UV-spectrum of the unknown **3** is characterized by the typical indole chromophore with λ_{max} (MeOH) at 292 sh, 282, 275 sh, and 225 nm [7], recently also determined for tryptamine derived amides from *Clausena indica* (Dalz.) Oliver (Rutaceae) [8]. The indole structure was further supported by a strong IR absorption at 3486 cm^{-1}, indicating the N–H vibration. The ^1H NMR spectrum also supports the postulated indole skeleton showing the typical broad indole N–H resonance in the region of δ ca 8 ppm. From the other four aromatic indole protons, three are positioned on the benzene ring at directly linked carbon atoms (two *d* at δ 7.46 and 6.99 and one *dd* at 7.05; see Experimental). The fourth one is a *br s* at δ 6.94, belonging to the pyrrole ring. The characteristic resonances for two prenyl groups (2 × —CH_2—CH= and 4 methyl groups) complete the ^1H NMR spectrum. The molecular formula of $C_{18}H_{23}N$ for a diprenylindole is confirmed by HR-MS (see Experimental). The resonance pattern would allow either positions 4 or 7 at the benzene ring for one of the prenyl groups, and positions 2 or 3 at the pyrrole ring for the other one. The chemical shift values or the coupling constants do not allow to discriminate the possible structures (the chemical shifts for 4-H and 7-H are comparable and the coupling constants $J(1,3)$ and $J(1,2)$ are both in the range of 2–2.5 Hz). Measurement of differential NOEs allowed a clear decision. Irradiation at N1-H (δ 7.89) gave strong effects for one —CH_2—CH= group (1″-H_2 at 3.55 and 2″-H at 5.41) and the broad *s* at the pyrrole ring (2-H at 6.94). This is only compatible with a prenyl group at position C-7. Irradiation at the other prenyl CH_2 group (1′-H_2 at δ 3.45) showed strong effects for 4-H (7.46) and 2-H (6.94), indicating position 3 for that prenyl rest. Additional NOEs from 1′ to 2′ and 5′ helped to assign the remaining prenyl resonances. Reverse C,H-COSY shift correlation allowed the unambiguous assignment of all 6 CH doublets as well as the two CH_2 triplets and the four CH_3 quartets of the ^{13}C NMR spectrum. The assignment of the quaternary carbon atoms followed the literature data for C-3 and C-7 prenyl substituted indoles [9–11].

Apart from a previously described monosubstituted 7-prenyl indole [15] and a series of prenylated bisindoles, the annonidines [10], most of the other already known derivatives belong to a group of 3,5- and 3,6-diprenylated indoles, the hexalobines, isolated from the African Annonaceae genera *Uvaria* [11], *Hexalobus* [9, 13], and *Isolona* [14]. Interestingly, a 3,7-diprenylated indole has so far been reported only for the Brazilian Rutaceae *Esenbeckia leiocarpa*, named leiocarpadiol [16]. However, in this case the nature of the two prenyl groups clearly deviates from those of the new indole derivative **3**.

Of particular phytochemical interest is the formation of the unusual terminal 4-oxo-2-oxolene five-membered ring in the sulphur-containing amides trichanthin-A (**1**) and -B (**2**). The same non lactonic dihydrofuranone moiety has recently also been reported for four other amides isolated from *Glycosmis parva* Craib. named glyparvin-A, dihydroglyparvin, khaochamide, and puhinamide [5]. Apart from that, this rare terpenoid moiety was only known so far as a substituent from a coumarin, geiparvarin, isolated from *Geijera parviflora* [17, 18], again a member of the Rutaceae.

Since antifungal activities have been reported not only for some sulphur-containing amides [2], but also for prenylated indoles [12, 13], the fungitoxic properties of the leaf and root extract as well as of the isolated pure compounds have also been tested by bioautography with our test fungus *Cladosporium herbarum* (Pers.: Fr.) Link. [2]. However, only trichanthin-B (**2**) and methylgerambullin showed a moderate antifungal activity. In the case of the 3,7-diprenylated indole (**3**), its inactivity is in agreement with the results of Achenbach *et al.*, where only indole derivatives with oxidated prenyl groups are active against the fungi *Saprolegnia asterophora* [12] and *Rhizoctonia solani* [13].

EXPERIMENTAL

General

NMR: Bruker AM 400 WB, 400 MHz, $CDCl_3$; MS: Finnigan MAT 900 S; IR: Perkin-Elmer 16 PC FT-IR; HPLC: Hewlett–Packard HP 1090 II, UV diode array detection at 230 nm, column 290 × 4 mm (Spherisob ODS, 5 μm), mobile phase MeOH (gradi-

ent 60–100%) in aq. buffer (0.015 M phosphoric acid, 0.0015 M tetrabutylammoniumhydroxide, pH 3), flow rate 1 ml min^{-1}.

Plant material

G. trichanthera was collected from Pha Toh Bu, Tarutao National Park, Satun Province (south Thailand), 12 February 1996. Voucher specimens are deposited at the Herbarium of the Dept. of Botany, Faculty of Science, Kasetsart University, Bangkok and the Herbarium of the Institute of Botany, University of Vienna (WU).

Extraction and isolation

Dried leaves, stem and root bark from three individuals were ground and extracted separately with MeOH at room temp. for 7 days, filtered and concd. The aq. residue was extracted with $CHCl_3$. The $CHCl_3$ fractions were evapd to dryness and roughly sepd by column chromatography (Merck silica gel 60, 35–70 mesh) and further by prep. MPLC (400 × 40 mm column, Merck Lichroprep silica gel 60, 25–40 micrometre, UV detection, 254 nm).

Leaf extract

476 mg of lipophilic crude extract from 148 g dried leaves was roughly sepd by column chromatography (silica gel). The fractions eluted with 75%, 50% Et_2O in MeOH and 100% MeOH, containing the amides, were combined, concd (283 mg) and further sepd by MPLC with 70% EtOAc in hexane to afford 84 mg trichanthin-A (**1**) and 24 mg trichanthin-B (**2**). The fractions eluted with 100% Et_2O and 75% Et_2O in MeOH, were combined and the precipitation (91 mg) was sepd by MPLC with 70% EtOAc in hexane to afford 6 mg glyparvin-A, 43 mg trichanthin-A (**1**), and 33 mg trichanthin-B (**2**). The residue after precipitation was concd (415 mg) and further sepd by MPLC with 50% EtOAc in hexane to afford 88 mg methylgerambullin, sepd with 70% EtOAc in hexane affording 100 mg trichanthin-A (**1**) and 33 mg trichanthin-B (**2**).

Stem bark extract

375 mg lipophilic crude extract from 113 g dried stem bark was roughly sepd by column chromatography (silica gel). The fractions were eluted with 75% and 50% Et_2O in MeOH. The acridone-containing fractions were combined, concd (94 mg) and further sepd by MPLC with 10% EtOAc in hexane to afford 14 mg yukocitrin.

Root extract

660 mg lipophilic crude extract from 39 g dried root bark was roughly sepd by column chromatography (silica gel). The combined fractions (175 mg) were eluted with 90% and 75% hexane in Et_2O was sepd by MPLC with 5% EtOAc in hexane to give the alkaloid containing fraction (119 mg). This fraction was further sepd by MPLC with 5% EtOAc in hexane to give 76 mg residue and further purified by cyclic MPLC (11 cycles) with 5% EtOAc in hexane to afford 33 mg 3,7-diprenylindole (**3**). The fractions eluted by 90%, 75%, 50% Et_2O in MeOH and 100% MeOH were combined (288 mg) and sepd by MPLC with 30% EtOAc in hexane to give 20 mg crystals of skimmianine. The concd residue (96 mg) was further sepd by cyclic MPLC (3 cycles) with 50% EtOAc affording 44 mg skimmianine and 28 mg γ-fagarine.

Trichanthin-A [*(E)-3-(methylsulfonyl)-propenoic acid (E)-4-[4-hydroxy-3-(4-oxo-2-oxolen-2-yl)-2-butenyloxy]-phenethylamide*] (**1**). Crystals (Et_2O), mp 154–156°. UV λ^{MeOH} nm: 296, 240 (sh), 224; IR ν^{KBr} cm^{-1}: 3294 *m*, 3068 *w*, 2978 *w*, 2928 *w*, 1678 *s*, 1558 *s*, 1512 *s*, 1456 *w*, 1380 *m*, 1364 *w*, 1304 *s*, 1242 *s*, 1176 *s*, 1130 *s*, 1018 *m*, 972 *m*, 910 *w*, 856 *w*, 824 *w*, 810 *w*, 774 *w*, 620 *w*, 570 *w*, 514 *m*; ν^{CHCl_3}: 3682 *w*, 3421 *w*, 2928 *w*, 1686 *s*, 1647 *w*, 1560 *m*, 1512 *s*, 1318 *s*, 1178 *m*, 1140 *m*, 970 *w*, 961 *w*, 516 *m*; ^{1}H NMR ($CDCl_3$, TMS): δ 7.36 (*d*, 1H, *J* = 14.7 Hz, 3-H), 7.13 (*d*, 2H, *J* = 8.6 Hz, 10-H and 14-H), 6.92 (*t*, 1H, *J* = 5.9 Hz, 2′-H), 6.90 (*d*, 2H, *J* = 8.6 Hz, 11-H and 13-H), 6.80 (*d*, 1H, *J* = 14.7 Hz, 4-H), 5.96 (*br t*, 1H, *J* = 6.0, 6-H), 5.73 (*s*, 1H, 6′-H), 4.89 (*d*, 2H, *J* = 5.9 Hz, 1′-H), 4.48 (*d*, 2H, *J* = 5.9 Hz, 4′-H), 3.62 (*dt*, 2H, *J* = 6.0 and 6.8 Hz, 7-H), 3.00 (*s*, 3H, 1-H), 2.83 (*t*, 2H, *J* = 6.8 Hz, 8-H), 1.96 (*t*, 1H, *J* = 5.9 Hz, 4′-OH), 1.42 (*s*, 6H, 9′-H and 10′-H), differential NOEs 1′ ↔ 4′, 1′ → 11, 4′ ↔ 6′, 6′ → 2′; ^{13}C NMR ($CDCl_3$, TMS): δ 161.5 (*s*, C-5), 157.0 (*s*, C-12), 139.1 (*d*, C-3), 135.3 (*d*, C-2′), 135.3 (*d*, C-4), 132.0 and 131.1 (2 × *s*, C-9 and C-3′), 129.9 (*d*, C-10 and C-14), 115.1 (*d*, C-11 and C-13), 100.5 (*d*, C-6′), 88.5 (*s*, C-8′), 64.6 (*t*, C-1′), 58.1 (*t*, C-4′), 42.5 (*q*, C-1), 41.3 (*t*, C-7), 34.3 (*t*, C-8), 23.1 (*q*, C-9′ and C-10′), the quaternary carbon atom resonances for C-5′ and C-7′ were too weak for detection, assignments based on Ref. [5]; MS (70 eV, 130°) *m/z*: 449 (3) $[M]^+$, 431 (8) $[M-H_2O]^+$, 419 (7), 340 (7), 281 (8), 270 (25), 268 (12) [M − geranyl]$^+$, 181 (25) [geranyl moiety, $C_{10}H_{13}O_3]^+$, 165 (11), 151 (10), 135 (11), 133 (12), 123 (14), 121 (20), 120 (100), 111 (18), 109 (18), 107 (66), 97 (29), 91 (20), 85 (29), 83 (34), 71 (44), 69 (58), 65 (32), 57 (76), 44 (81).

Trichanthin-B [*(E)-3-(methylsulfonyl)-propenoic acid (Z)-4-[4-hydroxy-3-(4-oxo-2-oxolen-2-yl)-2-butenyloxy]-phenethylamide*] (**2**). Crystals (Et_2O), mp 112–114°. UV λ^{MeOH} nm: 292, 286 (sh), 240 (sh), 220; IR ν^{KBr} cm^{-1}: 3302 *m*, 3066 *w*, 2978 *w*, 2924 *w*, 1674 *s*, 1658 *s*, 1554 *s*, 1512 *s*, 1458 *w*, 1400 *w*, 1380 *w*, 1364 *w*, 1302 *s*, 1242 *m*, 1176 *m*, 1132 *s*, 1082 *w*, 1050 *w*, 1016 *m*, 972 *m*, 912 *w*, 856 *w*, 822 *m*, 780 *w*, 658 *w*, 620 *w*, 514 *m*. ^{1}H NMR ($CDCl_3$, TMS): δ 7.34 (*d*, 1H, *J* = 14.8 Hz, 3-H), 7.10 (*d*, 2H, *J* = 8.5 Hz, 10-H and 14-H), 6.86 (*d*, 1H, *J* = 14.8 Hz, 4-H), 6.82 (*d*, 2H, *J* = 8.5 Hz, 11-H and 13-H), 6.50 (*br t*, 1H, *J* = 6.0,

6-H), 6.42 (*tt*, 1H, J = 5.3 and 1.2 Hz, 2′-H), 5.61 (*s*, 1H, 6′-H), 4.95 (*d*, 2H, J = 5.3 Hz, 1′-H), 4.37 (*dd*, 2H, J = 5.8 and 1.2 Hz, 4′-H), 3.57 (*dt*, 2H, J = 6.0 and 6.8 Hz, 7-H), 2.98 (*s*, 3H, 1-H), 2.81 (*t*, 2H, J = 6.8 Hz, 8-H), 1.88 (*t*, 1H, J = 5.8 Hz, 4′-OH), 1.44 (*s*, 6H, 9′-H and 10′-H), differential NOEs 1′ ↔ 6′, 1′ → 11, 4′ ↔ 6′, 4′ → 2′; ^{13}C NMR ($CDCl_3$, TMS): δ 207.0 (*s*, C-7′), 181.4 (*s*, C-5′), 161.6 (*s*, C-5), 156.9 (*s*, C-12), 138.8 (*d*, C-3), 137.0 (*d*, C-2′), 135.5 (*d*, C-4), 130.9 and 130.7 (2 × *s*, C-9 and C-3′, exchangeable), 129.8 (*d*, C-10 and C-14), 115.0 (*d*, C-11 and C-13), 102.6 (*d*, C-6′), 88.3 (*s*, C-8′), 65.8 and 63.6 (2 × *t*, C-4′ and C-1′, exchangeable; however, according to the concept of steric compression, the C-1′ resonance should be shifted upfield relative to the value of 64.6 for the (*E*)-isomer **2**; this argument is in favour of the assignment 63.6 for C-1′ and 65.8 for C-4′), 42.5 (*q*, C-1), 41.3 (*t*, C-7), 34.3 (*t*, C-8), 23.2 (*q*, C-9′ and C-10′); MS (70 eV, 130°) *m/z*: 449 (4) $[M]^+$, 431 (5) $[M-H_2O]^+$, 419 (6), 372 (9), 302 (13), 282 (25), 269 (20), 268 (80) [M − geranyl]$^+$, 181 (84) [geranyl moiety, $C_{10}H_{13}O_3]^+$, 176 (13), 165 (45), 153 (34), 152 (31), 151 (21), 149 (30), 135 (66), 133 (36), 123 (16), 121 (80), 120 (100), 111 (22), 109 (52), 107 (94), 97 (23), 95 (51), 91 (50), 83 (42), 81 (64), 77 (49), 71 (70), 69 (98), 65 (75), 55 (74), 44 (68).

3,7-*Diprenylindole* [3,7-*bis*(3-*methyl*-2-*butenyl*)-1H-*indole*] (**3**). Oil. UV λ^{MeOH} nm: 292 (sh), 282, 275 (sh), 225; IR ν^{CCl4} cm^{-1}: 3486 *m*, 3053 *w*, 2970 *m*, 2914 *s*, 2856 *m*, 1450 *m*, 1434, *s*, 1406 *w*, 1376 *m*, 1344 *w*, 1282 *w*, 1218 *w*, 1168 *w*, 1118 *w*, 1100 *w*, 1074 *w*, 1056 *w*, 984 *w*, 922 *w*, 844 *w*. ^{1}H NMR ($CDCl_3$, TMS): δ 7.89 (*br s*, 1H, $w_{1/2}$ = 12 Hz, 1-H), 7.46 (*d*, 1H, J = 7.9 Hz, 4-H), 7.05 (*dd*, 1H, J = 7.9 and 7.1 Hz, 5-H), 6.99 (*d*, 1H, J = 7.1 Hz, 6-H), 6.94 (*br s*, $w_{1/2}$ = 5 Hz, 1H, 2-H), 5.43 (*tm*, 1H, J = 7.0 Hz, 2′-H), 5.41 (*tm*, 1H, J = 7.0 Hz, 2″-H), 3.55 (*d*, 2H, J = 7.0 Hz, 1″-H), 3.45 (*d*, 2H, J = 7.0 Hz, 1′-H), 1.81 (*s*, 3H, 5″-H), 1.77 (*s*, 3H, 4″-H), 1.77 (*s*, 3H, 5′-H), 1.75 (*s*, 3H, 4′-H), assignments based on NOE difference measurements: 1 → 2, 1 → 1″, 1 → 2″, 4 → 5, 4 → 1′, 4 → 2′, 1′ → 2, 1′ → 4, 1′ → 2′, 1′ → 5′; ^{13}C NMR ($CDCl_3$, TMS): δ 135.8 (*s*, C-7a), 133.1 (*s*, C-3″), 131.8 (*s*, C-3′), 127.5 (*s*, C-3a), 123.9 (*s*, C-7), 123.2 (*d*, C-2′), 122.4 (*d*, C-2″), 121.5 (*d*, C-6), 120.9 (*d*, C-2), 119.4 (*d*, C-5), 117.0 (*d*, C-4), 116.5 (*s*, C-3), 30.1 (*t*, C-1″), 25.7 (*q*, C-4′), 25.7 (*q*, C-4″), 24.2 (*t*, C-1′), 17.9 (*q*, C-5′), 17.9 (*q*, C-5″), assignments based on Refs. [9, 10] and reverse C,H-shift correlation (reverse C,H-COSY with BIRD sequence); MS (70 eV, 90°C) *m/z*: 253 (100) $[M]^+$, 238 (75), 198 (38), 196 (25), 185 (27), 184 (29), 182 (65), 170 (50), 154 (24), 142 (35), 130 (25), 115 (15), 69 (52), 41 (56); HR-MS: $C_{18}H_{23}N$, M_{calc} = 253.1830, M_{exp} = 253.1835.

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REFERENCES

1. Greger, H., Hofer, O., Zechner, G., Hadacek, F. and Wurz, G., *Phytochemistry*, 1994, **37**, 1305.
2. Greger, H., Zechner, G., Hofer, O. and Vajrodaya, S., *Journal of Natural Products*, 1996, **59**, 1163.
3. Hofer, O., Zechner, G., Vajrodaya, S., Lutz, G. and Greger, H., *Liebigs Annalen*, 1995, 1789.
4. Waterman, P. G. and Grundon, M. F. ed., *Chemistry and Chemical Taxonomy of the Rutales*. Academic Press, London, 1983.
5. Hofer, O., Vajrodaya, S. and Greger, H., *Monatshefte fu[fadi]r Chemie*, 1998, **129**, 213.
6. Takemura, Y., Uchida, H., Ju-Ichi, M., Omura, M., Ito, C., Nakagawa, K., Ono, T. and Furukawa, H., *Heterocycles*, 1992, **34**, 2123.
7. Shoji, N., Umeyama, A., Iuchi, A., Saito, N., Takemoto, T., Nomoto, K. and Ohizumi, Y., *Journal of Natural Products*, 1988, **51**, 161.
8. Riemer, B., Hofer, O. and Greger, H., *Phytochemistry*, 1997, **45**, 337.
9. Achenbach, H., Renner, C. and Addae-Mensah, I., *Heterocycles*, 1984, **22**, 2501.
10. Achenbach, H. and Renner, C., *Heterocycles*, 1985, **23**, 2075.
11. Achenbach, H. and Raffelsberger, B., *Tetrahedron Letters*, 1979, 2571.
12. Achenbach, H., *Pure and Applied Chemistry*, 1986, **58**, 653.
13. Achenbach, H., Renner, C. and Waibel, R., *Liebigs Annalen*, 1995, 1327.
14. Achenbach, H. and Löwel, M., *Phytochemistry*, 1995, **40**, 967.
15. Benesova, V., Samek, Z., Herout, V. and Sorm, F., *Collection of Czechoslovak Chemical Communications*, 1969, **34**, 1807.
16. Delle Monache, F., Delle Monache, G., De Moraes e Souza, M. A., Da Salete Cavalcanti, M. and Chiapetta, A., *Gazzetta Chimica Italiana*, 1989, **119**, 435.
17. Lahey, F. N. and MacLeod, J. K., *Australian Journal of Chemistry*, 1967, **20**, 1943.
18. Dreyer, D. L. and Lee, A., *Phytochemistry*, 1972, **11**, 763.