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# Axially Chiral Dimeric Naphthalene and Naphthoquinone Metabolites, from Root Cultures of the West African Liana *Triphyophyllum peltatum*

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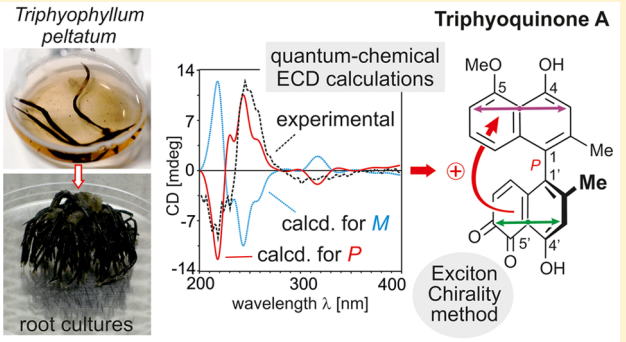
Supporting Information

**ABSTRACT:** Root cultures of the West African liana *Triphyophyllum peltatum* were initiated from stem explants of in vitro cultivated shoots. From these organ cultures, three new binaphthalenes, one binaphthoquinone, and two (bi)-naphthalene glucosides were isolated, with substitution patterns related to those of the naphthylisoquinoline alkaloids, which are the "normal" main metabolites of *T. peltatum*. The structures of the diglucoside dioncoquinoside A (**1**) and of the axially chiral biaryls triphyoquinols $A_1$ (**3**), $A_2$ (**4**), and B (**5**), triphyoquinoside A (**6**), and triphyoquinone A (**7**) were elucidated by spectroscopic analysis (HRESIMS, 1D and 2D NMR) and by application of electronic circular dichroism (ECD) spectroscopy in combination with the exciton chirality method and quantum-chemical ECD calculations. The root cultures likewise produced the known alkaloids dioncophylline A (**8**), 5′-*O*-demethyldioncophylline A (**9**), dioncopeltine A (**10**), habropetaline A (**11**), and 5′-*O*-methyldioncophylline D (**12a**/**b**), the naphthalene glucoside plumbaside A (**2**), and the naphthoquinones plumbagin (**13**), droserone (**14**), and 8-hydroxydroserone (**15**).




During the past years, axially chiral binaphthalenes have attracted great attention as potent ligands in stereoselective total synthesis (e.g., BINAP, BINOL, or BINAM),[1] in particular for transition-metal-catalyzed cross-coupling reactions,[2] or as building blocks for the construction of chiral supramolecular and polymeric materials.[3] In nature, however, binaphthalenes or related glucosides have only rarely been discovered, e.g., in plants belonging to the Ebenaceae (*Diospyros* species[4−10]) or the Liliaceae (*Hemerocallis*,[4,11] *Dianella*,[4,12,13] or *Stypandra*[4,13,14] taxa) and in the mold fungus *Chrysosporium meridarium*.[4,15] Dimeric naphthoquinones and "mixed dimers" consisting of a naphthoquinone and a naphthalene portion were isolated from several *Diospyros* species.[4,5,7,16,17] Some of the Ebenaceae and Liliaceae plants are used in folk medicine for the treatment of parasitic diseases (e.g., schistosomiasis), but their application is accompanied by severe toxic side effects.[4−6,10,11,13,15,16] Surprisingly, in contrast to the many investigations on binaphthalenes of synthetic origin, in the reports on naturally occurring binaphthalenes,[5−14] the phenomenon of axial chirality was taken into consideration only for some of these biaryls;[18] for others of those compounds, no ECD investigations were performed, and frequently not even optical rotation values were measured.[4]

In this paper, we describe the isolation and structural elucidation of seven natural products with naphthalene basic structures from the root cultures of the West African liana *Triphyophyllum peltatum*, among them new axially chiral binaphthalenes and binaphthoquinones as well as related (bi)naphthalene glucosides. Due to their occurrence in *T. peltatum* (Dioncophyllaceae), they were named dioncoquinoside A (**1**), triphyoquinols $A_1$ (**3**), $A_2$ (**4**), and B (**5**), triphyoquinone A (**7**), and triphyoquinoside A (**6**). Only plumbaside A (**2**) had already been known from previous isolation work on various plant genera (Figure 1).[19−24] These mono- and dimeric naphthalenes were not identified in the plant itself, which is, rather, a rich source of naphthylisoquinoline alkaloids.[25] Some of the isolated alkaloids, e.g., dioncophylline A (**8**),[25,26] dioncopeltine A (**10**),[25,27] and 5′-*O*-methyldioncophylline D (**12a**/**b**)[28] (Figure 2), had previously also been detected in the root cultures of *T. peltatum*. Naphthylisoquinolines are exclusively produced by Dioncophyllaceae and Ancistrocladaceae plants, which are indigenous to tropical rain forests in West, Central, and East Africa and

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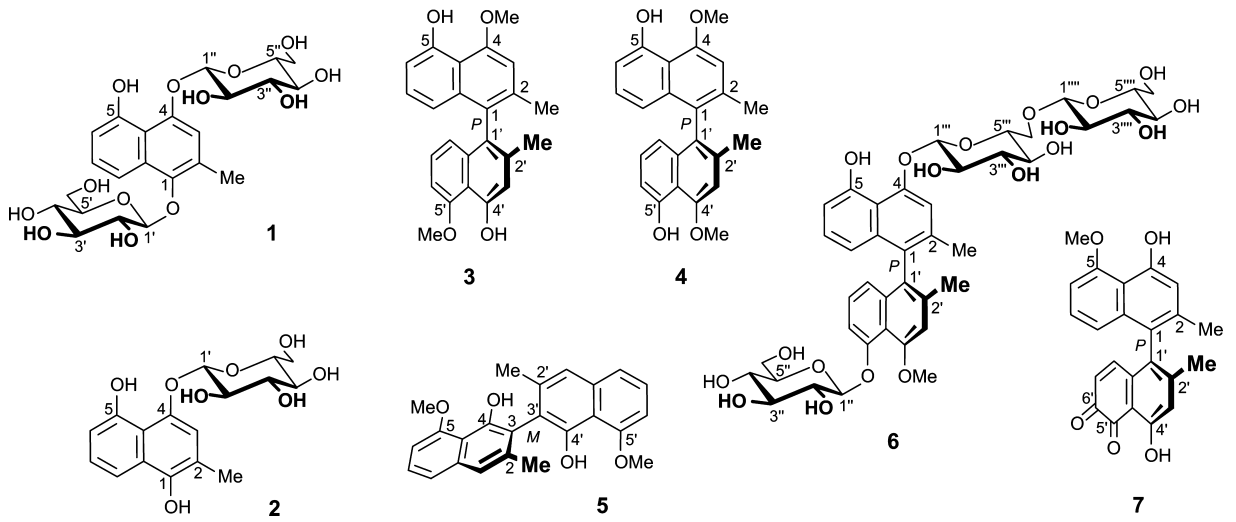

**Figure 1.** Mono- and dimeric naphthalene derivatives (**1**–**7**) from root cultures of *T. peltatum*.[30]

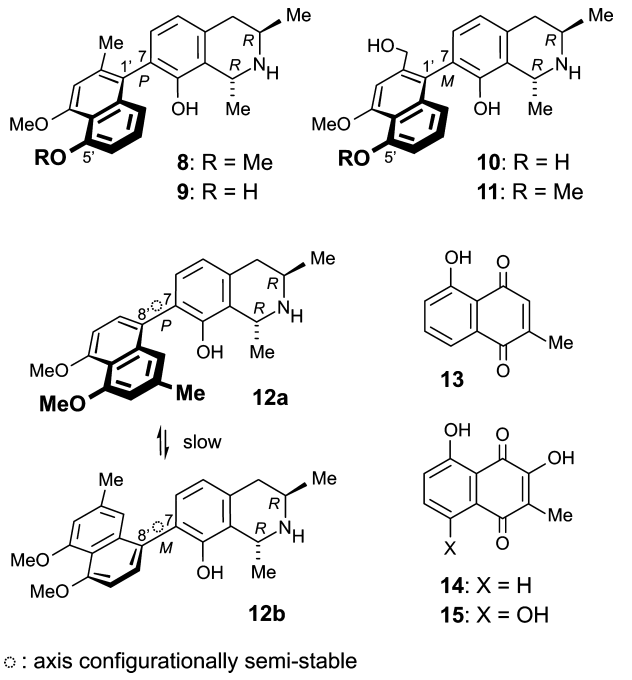


**Figure 2.** Naphthylisoquinoline alkaloids (**8**–**12**) and naphthoquinones (**13**–**15**) identified in the root cultures of *T. peltatum*.

Southeast Asia.[25] In the plants themselves, metabolites structurally related to the naphthalene moieties of the naphthylisoquinolines, e.g., ancistronaphthoic acid B,[29] had so far been identified quite rarely; only three representatives had as yet been discovered in two Congolese *Ancistrocladus* lianas.[29] Far more frequently, naphthalene-derived tetralones such as *cis*-isoshinanolone or naphthoquinones such as plumbagin (**13**) were found to be present in these tropical lianas, and even naphthoquinone dimers such as 3,3′-biplumbagin were isolated.[25] Here, we describe the elucidation of the metabolic pattern of root cultures of *T. peltatum*, with particular emphasis on the chiroptical analysis of the axially chiral constituents triphyoquinol $A_1$ (**3**), triphyoquinone A (**7**), and triphyoquinoside A (**6**).

## RESULTS AND DISCUSSION

Root cultures of *T. peltatum* were initiated from stem explants of in vitro cultivated shoots[31] on a modified Gamborg B5 (G5S2) medium (Supporting Information).[32] Adventitious roots were cut and transferred to medium of the same composition, but without gelling agent. The roots were kept in a submerged state with aeration brought about by continuous shaking. The shake cultures showed a marked acceleration in growth as compared to the corresponding stationary cultures, the maximum dry weight of the root material being attained after about 4 weeks. The roots were then removed from the medium, lyophilized, ground, and exhaustively extracted with $CH_2Cl_2$/MeOH (1:1). The resulting extracts were filtered and subjected to cation-exchange chromatography using the resin Amberlyst 15. The fractions thus obtained were finally purified by chromatography on a semipreparative RP-18 HPLC column.

LC hyphenation with UV and ESIMS/MS analysis permitted rapid dereplication of five known naphthylisoquinoline alkaloids, viz., dioncophylline A (**8**),[26] 5′-*O*-demethyldioncophylline A (**9**),[33] dioncopeltine A (**10**),[27] habropetaline A (**11**),[34] and 5′-*O*-methyldioncophylline D (**12a**/**b**).[28] The latter had recently been identified as the first 7,8′-coupled (D-type) naphthylisoquinoline alkaloid from a Dioncophyllaceae plant.[28] Moreover, similar to the callus cultures,[35,36] the root cultures were found to also produce the naphthoquinones plumbagin (**13**), droserone (**14**), and 8-hydroxydroserone (**15**). The identity of metabolites **8**–**15** was confirmed by coelution with authentic reference compounds;[26−28,33−36] in the case of 5′-*O*-methyldioncophylline D (**12**), an ultimate structural proof was achieved by preparative isolation of this alkaloid, which is a 1:1 mixture of its two slowly interconverting atropo-diastereomers, **12a** and **12b**.[28]

The most polar substance among the metabolites of the root cultures of *T. peltatum* exhibiting a UV spectrum typical of naphthalenes was found to possess a molecular formula of $C_{23}H_{30}O_{13}$ (*m*/*z* 537.1579, $[M + Na]^+$) as evidenced by HRESIMS. $^1H$ and $^{13}C$ NMR investigations indicated the presence of a 1,4,5-trioxy-substituted 2-methylnaphthalene derivative: Its $^1H$ NMR spectrum (Experimental Section) revealed resonances corresponding to a methyl group ($\delta$ 2.42) and four aromatic protons ($\delta$ 6.88, 7.12, 7.41, and 7.82), among them the signals (two doublets, one multiplet) of three


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contiguous hydrogens. The $^{13}C$ NMR spectrum (Experimental Section) showed three low-field-shifted quaternary aromatic carbons resonating at 147.2, 152.6, and 154.8 ppm, suggesting the presence of three oxygen functions, two of them being located at C-1 and C-4 in the "eastern" ring system. The third one, a hydroxy function, was deduced to be located at C-5, which was in agreement with HMBC couplings to C-5 (154.8 ppm) observed from the proton signals of both H-6 and H-7. That the oxygen functions at C-1 and C-4 were each linked to a glucopyranosyl residue became evident from the characteristic signals in the $^{1}H$ and $^{13}C$ NMR spectra, from $^{1}H,^{1}H$−COSY and HMBC interactions, and in particular from ROESY correlations between 2-Me and H-1′ and between H-3 and H-1″ (Figure 3). The $\beta$-configurations at the anomeric C-1′ and C-1″ centers (and hence also the attachment to the aglycone) were assigned by the large coupling constants ($^{3}J$ = 7.9 Hz) from H-1′ to H-2′ and from H-1″ to H-2″. Thus, the structure of the new compound was assigned as 1,4-di-$\beta$-D-glucopyranosyloxy-5-hydroxy-2-methylnaphthalene (**1**) and named dioncoquinoside A (Figure 3).

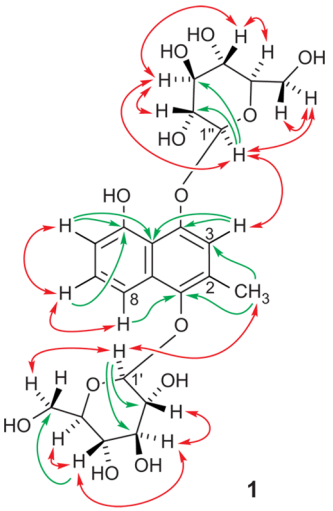

**Figure 3.** Key HMBC (single arrows) and $^{1}H,^{1}H$-COSY and ROESY (double arrows) interactions of dioncoquinoside A (**1**).

Treatment of **1** with a commercial $\beta$-glucosidase at room temperature or with methanolic HCl at 60 °C led to its complete deglucosidation, providing D-glucose (identical to an authentic sample by cochromatography on TLC, $^{1}H$ NMR, and $[\alpha]_D$), along with the respective naphthalenetriol, which underwent immediate spontaneous oxidation to give the naphthoquinone plumbagin (**13**), identical in all respects with a reference sample of **13**.

A second, likewise polar and water-soluble naphthalene glucoside isolated from the root cultures showed a behavior similar to that of dioncoquinoside A (**1**), chromatographically and also spectroscopically, according to its $^{1}H$ and $^{13}C$ NMR data. With a molecular formula of $C_{17}H_{20}O_8$ (*m/z* 375.1050 [M + Na]$^+$), as determined by HRESIMS, its structure differed from that of **1** by the absence of one of the glucopyranosyl residues. This compound, called plumbaside A (**2**) (Figure 1),[19,20,24] is a well-known metabolite, previously isolated from various plant genera such as *Plumbago*,[19,20] *Nepenthes*,[21] *Drosophyllum*,[22] *Drosera*,[23] and *Dionaea*,[24] among them some carnivorous species, which are the closest phylogenetic neighbors of the likewise carnivorous Dioncophyllaceae.[31,37]

Similar to dioncoquinoside A (**1**), plumbaside A (**2**) was also found to undergo a spontaneous oxidation reaction, giving rise to plumbagin (**13**) after cleavage of the glucopyranosyl residue. In the case of **2**, this reaction was observed to proceed readily, even without enzymatic assistance.

The two naphthalene glucosides, dioncoquinoside A (**1**) and plumbaside (**2**), presumably serve as storage products in the roots (like pro-drugs), releasing the toxic plumbagin (**13**) as a phytoalexin for protection of the plants, e.g., when attacked by herbivores.

Further isolation work provided three new naphthalene dimers with substitution patterns similar to those of the isocyclic parts of naphthylisoquinoline alkaloids. They were named triphyoquinols $A_1$ (**3**), $A_2$ (**4**), and B (**5**).

Triphyoquinol $A_1$ (**3**) (Figure 4) had a molecular formula of $C_{24}H_{23}O_4$ (*m/z* 375.1591, [M + H]$^+$), as deduced from HRESIMS and from the number of signals in the $^{13}C$ NMR spectrum (Table 1). Similar to the results of the monomeric dioncoquinoside A (**1**), the binaphthalene **3** displayed $^{1}H$ NMR signals (Table 1) for eight aromatic protons, viz., two sets of three contiguous hydrogens and two one-proton singlets, together with signals for two methoxy and two methyl groups. Furthermore, the appearance of two signals at 153.6 and 154.5 ppm in the $^{13}C$ NMR spectrum hinted at the additional presence of two phenolic functions (Figure 4A). Specific NOESY correlations from H-8 to Me-2′ and from H-8′ to Me-2

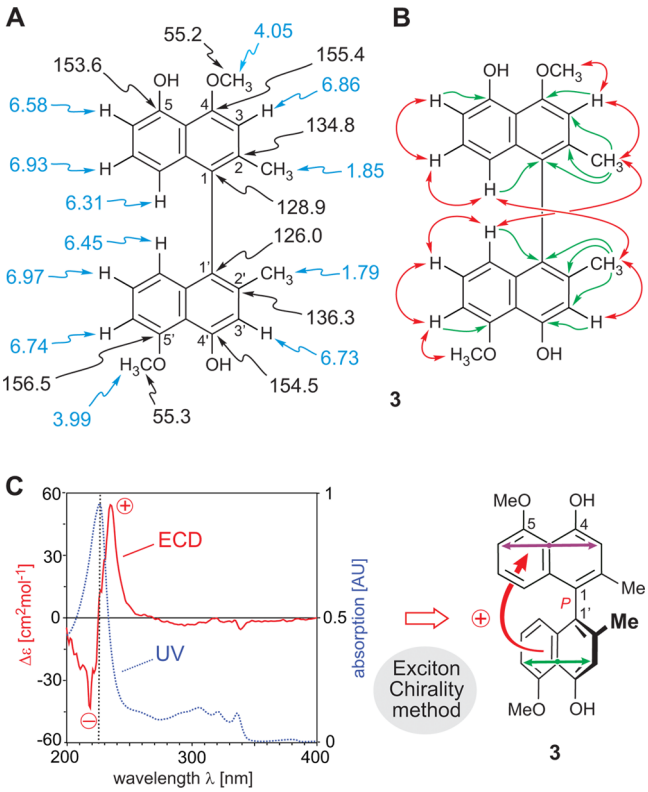


**Figure 4.** Triphyoquinol $A_1$ (**3**): (A) Selected $^{1}H$ and $^{13}C$ NMR shifts (methanol-$d_4$, $\delta$ values in ppm), (B) key HMBC (single arrows) and $^{1}H,^{1}H$-COSY and NOESY (double arrows) interactions, and (C) assignment of the absolute configuration at the biaryl axis by ECD spectroscopy in combination with the exciton chirality method[38] (double arrows mark relevant electronic transition dipole moments; the red arrow shows the clockwise array responsible for the positive exciton couplet).



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Table 1. $^{1}H$ (600 MHz) and $^{13}C$ (150 MHz) NMR Data of 3−5 and 7 in Methanol-$d_4$ ($\delta$ in ppm, $J$ in Hz)

| | triphyoquinol $A_1$ (3) | | triphyoquinol $A_2$ (4) | | triphyoquinol B (5) | | triphyoquinone A (7) | |
|---|---|---|---|---|---|---|---|---|
| no. | $\delta_H$ ($J$ in Hz) | $\delta_C$, type | $\delta_H$ ($J$ in Hz) | $\delta_C$, type | $\delta_H$ ($J$ in Hz) | $\delta_C$, type | $\delta_H$ ($J$ in Hz) | $\delta_C$, type |
| 1 | | 128.9, C | | 129.9, C | 7.26, s | 120.3, CH | | 123.7, C |
| 2 | | 134.8, C | | 136.1, C | | 139.2, C | | 138.3, C |
| 3 | 6.86, s | 106.4, CH | 6.96, s | 107.9, CH | | 121.5, C | 6.84, s | 113.4, CH |
| 4 | | 155.4, C | | 156.9, C | | 152.0, C | | 156.1, C |
| 5 | | 153.6, C | | 156.0, C | | 157.5, C | | 158.1, C |
| 6 | 6.58, dd (7.6, 1.1) | 108.9, CH | 6.69, dd (7.6, 1.0) | 110.4, CH | 6.73, d (7.6) | 104.5, CH | 6.93, d (7.5) | 105.2, CH |
| 7 | 6.93, dd (7.7, 8.9) | 127.1, CH | 7.03, dd (7.6, 8.4) | 128.6, CH | 7.29, dd (7.6, 8.4) | 126.7, CH | 7.26, dd (7.5, 8.3) | 128.3, CH |
| 8 | 6.31, dd (8.4, 1.1) | 116.3, CH | 6.41, dd (8.5, 1.1) | 117.7, CH | 7.39, d (8.4) | 122.6, CH | 6.73, d (8.4) | 119.6, CH |
| 9 | | 136.2, C | | 137.4, C | | 137.5, C | | 137.1, C |
| 10 | | 113.5, C | | 115.0, C | | 115.0, C | | 114.9, C |
| 1′ | | 126.0, C | | | | | | 127.9, C |
| 2′ | | 136.3, C | | | | | | 135.8, C |
| 3′ | 6.73, s | 112.0, CH | | | | | 7.12, s | 123.2, CH |
| 4′ | | 154.5, C | | | | | | 153.4, C |
| 5′ | | 156.5, C | | | | | | 183.3, C |
| 6′ | 6.74, d (7.8) | 103.1, CH | | | | | | 182.1, C |
| 7′ | 6.97, s | 125.7, CH | | | | | 6.16, d (10.3) | 128.4, CH |
| 8′ | 6.45, dd (8.5, 0.9) | 118.9, CH | | | | | 6.80, d (10.4) | 144.0, CH |
| 9′ | | 135.7, C | | | | | | 134.8, C |
| 10′ | | 113.3, C | | | | | | 115.1, C |
| 2-$CH_3$ | 1.85, s | 18.9, $CH_3$ | 1.95, s | 20.3, $CH_3$ | 2.16, s | 21.7, $CH_3$ | 2.06, s | 20.5, $CH_3$ |
| 2′-$CH_3$ | 1.79, s | 18.7, $CH_3$ | | | | | 1.86, s | 21.1, $CH_3$ |
| 4-$OCH_3$ | 4.05, s | 55.2, $CH_3$ | 4.15, s | 56.7, $CH_3$ | | | | |
| 5-$OCH_3$ | | | | | 4.00, s | 57.3, $CH_3$ | 4.10, s | 56.9, $CH_3$ |
| 5′-$OCH_3$ | 3.99, s | 55.3, $CH_3$ | | | | | | |

indicated that the biaryl axis was located at C-1 in both naphthalene moieties. The position of the methoxy group at C-4 was deduced from its NOESY interaction with H-3, while the other methoxy function was established to be at C-5′ by a NOESY correlation with H-6′ (Figure 4B). According to these findings, triphyoquinol $A_1$ was assigned to possess the constitution of the unsymmetric binaphthalene **3**, as presented in Figure 4A,B.

With its high steric hindrance at the central biaryl axis, **3** should show the phenomenon of axial chirality. HPLC analysis of **3** on a chiral phase (Phenomenex Lux Cellulose-1) gave only one peak, suggesting a high enantiomeric purity of the compound. This 1,1′-linked[30] binaphthalene **3** should be a classic case of a molecule where the exciton chirality method[38] is applicable due to the fact that it contains two electronically very similar, nearly identical chromophores. The ECD spectrum of **3** exhibited sequential positive and negative Cotton effects at 235 and 219 nm, i.e., a positive couplet (Figure 4C, left). Application of the exciton chirality method led to the conclusion that the electronic transition dipole moments defined a "positive chirality", and, thus, the absolute axial configuration of triphyoquinol $A_1$ (**3**) was attributed to be *P* (Figure 4C, right).

The second dimer, triphyoquinol $A_2$ (**4**) (Figure 1), was found to be $C_2$-symmetric. From $^{1}H$ and $^{13}C$ NMR measurements (Table 1) it became evident that this binaphthalene was a regioisomer of triphyoquinol $A_1$ (**3**), consisting of two structurally identical naphthalene portions, which are connected via a 1,1′-linkage[30] as deduced from the low-field-shifted quaternary aromatic carbons (C-1/C-1′) resonating at 129.9 ppm. The positions of the methoxy groups were established from its HMBC correlations with C-4 (and thus also with C-4′) and from the specific NOESY interactions with H-3 (and H-3′) (Supporting Information). As in the case of **3**, the ECD spectrum of **4** displayed a strong positive couplet, with sequential positive and negative Cotton effects at 234 ($\Delta\varepsilon$, +56.6) and 218 nm ($\Delta\varepsilon$, −44.6); thus, according to the exciton chirality method[38] its biaryl axis was *P*-configured, like that of **3**.

$^{1}H$ and $^{13}C$ NMR investigations (Table 1) in combination with HRESIMS measurements suggested the third binaphthalene, triphyoquinol B (**5**) (Figures 1 and 5), again to be $C_2$-

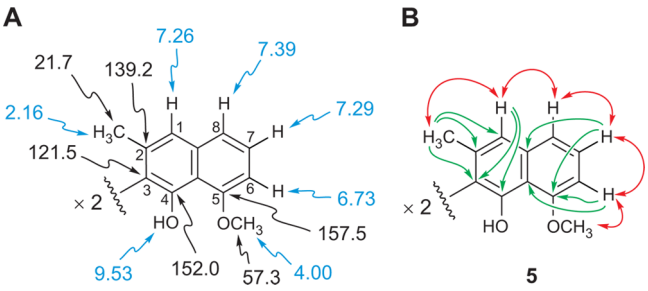


**Figure 5.** Selected NMR data of triphyoquinol B (**5**): (A) $^{1}H$ and $^{13}C$ NMR shifts (methanol-$d_4$, $\delta$ values in ppm) and (B) HMBC (single arrows) and $^{1}H,^{1}H$-COSY and NOESY (double arrows) interactions.

symmetric, like **4**. Its constitution was evidenced from a series of NOESY correlations {Me-2 ↔ H-1 ↔ H-8 ↔ H-7 ↔ H-6 ↔ 5-OMe ↔ 4-OH} and from an NOE interaction between 4-OH and 2′-Me and the low-field shift of C-3 (120 ppm). The latter suggested the biaryl linkage[30] to be located between C-3 and C-3′ of the constitutionally identical naphthalene halves. The ECD spectrum of this binaphthalene dimer **5** displayed a negative first Cotton effect at 242 nm ($\Delta\varepsilon$, −25.1) and a second positive one at 224 nm ($\Delta\varepsilon$, +39.0), i.e., a negative couplet; thus, in contrast to the *P*-configured dimers **3** and **4**,


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the absolute configuration at the biaryl axis of triphyoquinol B (**5**) was assigned to be *M*.

A further new metabolite, triphyoquinone A (**7**) (Figure 6), exhibited a UV profile similar to those of the three

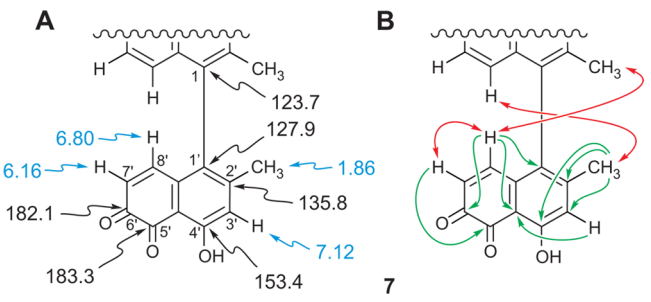


**Figure 6.** (A) Selected $^{1}H$ and $^{13}C$ NMR shifts (methanol-$d_4$, $\delta$ values in ppm) and (B) HMBC (single arrows) and $^{1}H,^{1}H$-COSY and NOESY (double arrows) interactions of the "southern", quinoid molecular moiety of triphyoquinone A (**7**).

binaphthalenes described above, but with an additional maximum at 440 nm, hinting at the presence of a quinoid compound. This assumption was confirmed by $^{13}C$ NMR measurements exhibiting two downfield-shifted signals at 182.1 and 183.3 ppm typical of carbonyl functions (Figure 6A). The two quinoid carbonyl groups were located *ortho* to each other, at C-5′ and C-6′, as established by HMBC interactions between H-7′ and H-8′ and by NOE correlations between H-8′ and Me-2 (Figure 6B), likewise evidencing this binaphthoquinone **7** to possess a 1,1′-biaryl linkage. All other NMR data of this new dimer were similar to those reported above for the two structurally closely related 1,1′-coupled triphyoquinols $A_1$ (**3**) and $A_2$ (**4**).

Although triphyoquinone A (**7**) thus consisted of two structurally and electronically different molecular portions, the exciton chirality method was still applicable to the assignment of the absolute configuration at the biaryl axis provided that the dihedral angle at the configurationally stable axis was known either from an X-ray structure analysis or from quantum-chemical calculations. A conformational analysis of **7** (B3LYP/TZVP), arbitrarily for the *P*-atropisomer, indicated a dihedral angle of 92° between the planes of the two chromophores. In addition, the electronic transition dipole moments of the naphthalene and the *ortho*-quinone portions were calculated, showing that the relevant transitions for the exciton coupling were polarized along the long axes of the chromophores. According to the exciton chirality method, the coupling of the electronic transition dipole moments led to a positive first and negative second Cotton effect and, thus, to a positive ECD couplet (Figure 7A). Since the experimental ECD spectrum of triphyoquinone A (**7**) showed a positive couplet, **7** was assigned to have the absolute *P*-configuration. This result was confirmed by the unambiguous match of the experimental ECD curve of triphyoquinone A with the spectrum calculated for the *P*-atropisomer of **7**. As expected, the curve predicted for the *M*-configured atropisomer of **7** was opposite compared to the experimental ECD spectrum of **7**, thus giving rise to mirror-image-like curves (see Figure 7B).

Finally, triphyoquinoside A (**6**), a structurally more complex binaphthalene, possessing a molecular formula of $C_{40}H_{48}O_{19}$ (*m/z* 855.2699 $[M + Na]^+$), was isolated from the root cultures of *T. peltatum*. The 1D and 2D NMR spectra exhibited signals

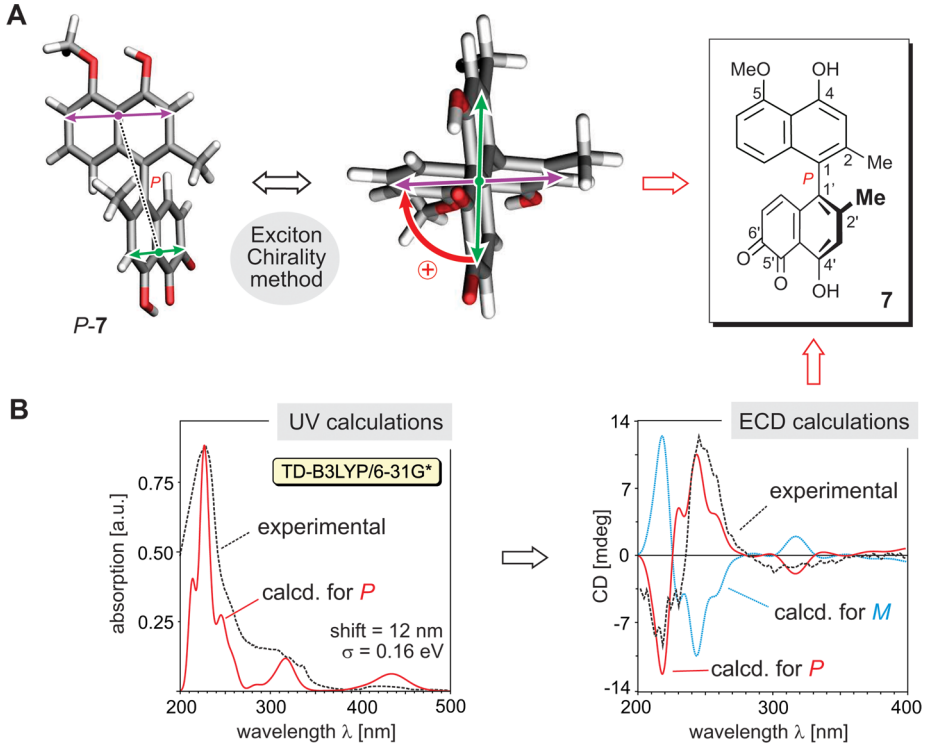


**Figure 7.** Assignment of the absolute axial configuration of triphyoquinone A (**7**) (A) by applying the exciton chirality method (double arrows mark the relevant electronic transition dipole moments; the red arrow shows the clockwise array responsible for the positive exciton couplet) and (B) by comparison of the experimental ECD curve of isolated **7** with the ECD spectra of *P*-**7** and *M*-**7** predicted by ECD calculations with TD-B3LYP/6-31G* based on the B3LYP/TZVP optimizations.



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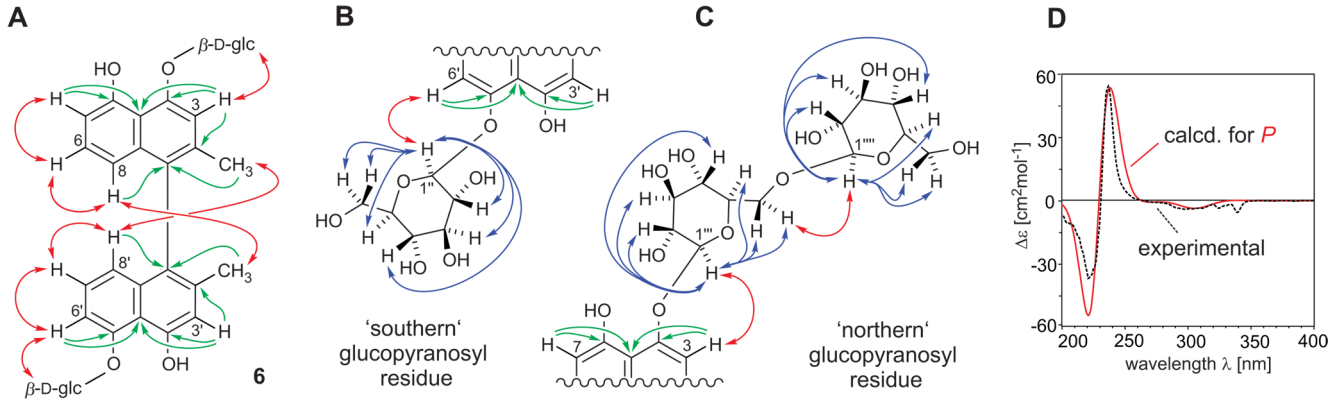


**Figure 8.** HMBC (single green arrows), $^{1}$H,$^{1}$H–COSY/ROESY (double red arrows), and TOCSY (double blue arrows) interactions relevant for the constitution of triphyoquinoside A (**6**): (A) the binaphthalene core and (B) the "southern" and (C) "northern" glucopyranosyl residues; (D) assignment of the absolute axial configuration by comparison of the experimental ECD spectrum of **6** with that calculated for *P* using ZINDO/S-Cl (PM3 geometries).

typical of a 1,1′-coupled naphthalene dimer suggesting the presence of three glucopyranosyl residues (Figures 1 and 8). From HMBC and ROESY correlations (Figure 8A–C) it became evident that the two oxygen groups at C-4 and C-5′ of the binaphthalene core were attached to sugar moieties, each with a *β*-configuration at the anomeric sugar carbon atoms, C-1″ and C-1‴, as deduced from the large coupling constants ($^{3}J$ = 7.8 and 7.9 Hz), from H-1″ to H-2″ and from H-1‴ to H-2‴, respectively. Furthermore, the $^{1}$H NMR spectrum showed signals suggesting the presence of a third anomeric proton, which displayed no interactions with the binaphthalene core according to HMBC and ROESY investigations, but showed strong correlations with a $CH_2$ group of one of the glucopyranosyl residues. Complete attribution of the sugar signals was finally achieved by TOCSY measurements, which permitted clear assignment of geminal, vicinal, and long-range couplings within one spin system, here, for example, within a glucopyranosyl subunit (Figure 8B,C). Treatment of **6** with methanolic HCl at 60 °C afforded D-glucose (identical to an authentic sample by cochromatography on TLC, $^{1}$H NMR, and $[\alpha]_D$), as the only carbohydrate, while the air-sensitive aglycone got decomposed immediately.

The experimental ECD spectrum of **6** showed a positive first and a negative second Cotton effect. As expected for these types of structures, the ECD behavior of **6** was dominated by the exciton coupling of the long-axis-polarized transitions of the naphthalene chromophores.[38] Semiempirical calculations on the *P*-atropo-diastereomer of **6** predicted a dihedral angle of 92° at the biaryl axis. Within this geometry, the naphthalene moieties constituted a clockwise array. According to the exciton chirality method, the experimentally observed positive ECD couplet around 235 nm thus indicated a "positive chirality" in triphyoquinoside A (**6**), here corresponding to the *P*-configuration. ZINDO/S-Cl calculations of the ECD spectrum of the PM3 minimum of **6** corroborated the assignment of the absolute configuration at the biaryl axis of **6** to be *P* (Figure 8D).

Summarizing, like the intact West African liana *T. peltatum* itself, its root cultures have become a promising new source of naphthylisoquinoline alkaloids, among them dioncophylline A (**8**),[25,26] habropetaline A (**11**),[34] and 5′-*O*-methyldioncophylline D (**12a/b**)[28] (Figure 2). Furthermore, these cultures, representing differentiated tissues of a complete organ, furnished a series of structurally new axially chiral binaphthalenes, the triphyoquinols $A_1$ (**3**), $A_2$ (**4**), and B (**5**), along with the binaphthoquinone triphyoquinone A (**7**), and the glucosides dioncoquinoside A (**1**) and triphyoquinoside A (**6**) (Figure 1). The substitution patterns of these compounds resemble those of the isocyclic parts of the biosynthetically related naphthylisoquinoline alkaloids. The mono- and dimeric naphthalenes were not identified in the plant itself and—except for triphyoquinol B (**5**)—not even in callus cultures of *T. peltatum*. On the other hand, some highly oxygenated naphthoquinones, the dioncoquinones A–E,[35] were detected exclusively in solidified callus cultures, but not in the root cultures, thus showing that the availability of different systems (plants, callus cultures, root cultures) of the same species, here *T. peltatum*, provides a valuable extension of the chemodiversity of this productive plant species.

The discovery of new (bi)naphthalenes and related glucosides demonstrates the remarkable ability of *T. peltatum* to produce a broad variety of structurally interesting secondary metabolites. Similar to the naphthylisoquinoline alkaloids[25−28,33,34] and dioncoquinones,[35] the naphthalenes and binaphthalenes identified in the root cultures are likely to be formed from acetate/malonate units. The basic structures of the metabolites previously isolated from Ebenaceae and Liliaceae plants are assumed to arise from heptaketide precursors, too.[4,15,39] The unique biosynthesis of naphthylisoquinoline alkaloids,[25,28,36] which are the first (and as yet only!) acetogenic di- and tetrahydroisoquinoline alkaloids found in nature, is known to be extremely susceptible to all sorts of chemical, physical, or biotic stress.[25,35,40] As a reaction to stress, the introduction of nitrogen by the postulated transamination step[40] is easily blocked. As a consequence, the formation of the tetrahydroisoquinoline portion of the alkaloids is inhibited, thus leading to a predominant production of naphthoquinones and (bi)naphthalenes in the root cultures of *T. peltatum*, instead.

## EXPERIMENTAL SECTION

**General Experimental Procedures.** Melting points were obtained on a Reichert Kofler hot-stage microscope and are uncorrected. IR spectra were recorded on a Jasco FT/IR-410 spectrometer, UV spectra on a Varian Cary 50 Conc spectrophotometer, ECD spectra on a Jasco J-715 spectropolarimeter, and optical rotations on a Jasco P-1020 polarimeter. $^{1}$H NMR (600 MHz) and $^{13}$C NMR (150 MHz) were recorded on a Bruker DMX 600 instrument, using $D_2O$ ($\delta$ 4.79) and methanol-$d_4$ ($\delta$ 3.31 and 49.15 ppm) as the solvents and the internal $^{1}$H and $^{13}$C standards. For the ROESY


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experiments the mixing time was set to 1 s. Proton-detected, heteronuclear correlations were analyzed using HMQC (optimized for $^1J_{HC}$ = 145 Hz) and HMBC (optimized for $^nJ_{HC}$ = 7 Hz) experiments. HRESIMS analyses were performed on a Bruker micrOTOF-focus mass instrument. Solvents were either purchased from commercial suppliers or purified by standard techniques. Thin-layer chromatography plates were visualized by exposure to ultraviolet light at 254 and 365 nm. Column chromatography was carried out utilizing silica gel (0.063 mm, Merck). Preparative HPLC was performed on a Jasco System (PU-1580 Plus) in combination with UV/vis detection at 195−650 nm (Jasco MD-2010 Plus diode array detector). For isolation and purification of the root culture extracts a Chromolith Semi-Prep RP-18e HPLC column (100 × 10 mm) from Merck and a Symmetry $RP_{18}$ column (19 × 300 mm, 7 μm) from Waters were used; flow rate 10 mL/min; mobile phase (A) $H_2O$ (0.05% TFA, (B) $CH_3CN$ (0.05% TFA); room temperature.

**Sterile Root Cultures.** Aseptic root cultures of *T. peltatum* were initiated by transferring stem explants of in vitro cultivated shoot cultures of *T. peltatum*[31] to a modified Gamborg B5 (G5S2) medium[32] with full strength of micro- and macroelements, but supplemented with 2% sucrose, 0.1% casein hydrolysate, and 0.3% Gelrite. Adventitious roots were transferred to Erlenmeyer flasks containing liquid medium of the same composition, but without gelling agent. To further increase adventitious root formation, 0.2 mg/L of the phytohormone 1-naphthalene acetic acid was added to the medium. The resulting root cultures were kept in the dark at 24 ± 2 °C, in 300 mL Erlenmeyer flasks (containing 80−100 mL of liquid medium) in a submerged state with aeration brought about by continuous shaking of the cultures (130 rpm). For maintenance and propagation, the root cultures were transferred to fresh medium every 4 weeks over a couple of years.

**Extraction and Isolation.** Lyophilized root material (9.2 g) was ground and repeatedly extracted (3×) with MeOH/$CH_2Cl_2$ (1:1). The combined extracts were filtered and concentrated in vacuo to give 2.65 g of a crude residue. The extract was dissolved in MeOH and directly submitted to cation-exchange chromatography using the resin Amberlyst 15 (Fluka) (column size: 8 × 25 cm). The resin was successively eluted with MeOH (3 × 10 mL) to provide fraction A. Subsequent elution with an aqueous saturated NaCl solution (containing 0.05% TFA) (3 × 5 mL) and finally again with MeOH (3 × 10 mL) afforded fraction B.

Fraction A was concentrated under reduced pressure, macerated with water, and then repeatedly extracted with *n*-hexane to separate polar compounds (water subfraction, A-1) from moderately polar and unpolar metabolites (*n*-hexane subfraction, A-2). Resolution of subfraction A-1 by preparative HPLC on a Chromolith Semi-Prep RP-18e HPLC column, using a linear gradient (0 min 5% B, 10 min 40% B, 16 min 100% B, 18 min 100% B, 19 min 5% B, 25 min 5% B), yielded 13.3 mg of dioncoquinoside A (**1**) (retention time 8.9 min), 5.6 mg of plumbaside (**2**) (retention time 12.5 min), and 10.5 mg of triphyoquinoside A (**6**) (retention time 20.2 min). From subfraction A-2, 1.2 mg of triphyoquinol $A_1$ (**3**) (retention time 14.6 min), 3.0 mg of triphyoquinol $A_2$ (**4**) (retention time 13.5 min), 1.77 mg of triphyoquinol B (**5**) (retention time 12.4 min), and 1.40 mg of triphyoquinone A (retention time 11.3 min) were isolated by preparative HPLC on a Chromolith Semi-Prep RP-18e HPLC column, using a linear gradient (0 min 30% B, 10 min 70% B, 16 min 100% B, 18 min 100% B, 19 min 30% B, 25 min 30% B). Furthermore, subfraction A-2 was found to contain the known metabolites 8-hydroxydroserone (**15**)[35] (retention time 11.8 min), droserone (**14**)[35,40] (retention time 27.5 min), and plumbagin (**13**)[35,40] (retention time 32.3 min), which were purified by preparative HPLC on a Symmetry $RP_{18}$ column, using a linear gradient (0 min 5% B, 30 min 70% B, 35 min 100% B, 40 min 100% B, 41 min 5% B, 46 min 5% B), as described earlier.[35]

After removal of the organic solvent from fraction B, the aqueous solution was repeatedly extracted with $CH_2Cl_2$. The organic phases were evaporated to dryness, then dissolved in MeOH, and directly submitted to preparative HPLC on a Symmetry $RP_{18}$ column, applying the same chromatographic conditions described above for the purification of compounds **13**−**15**, to give the naphthylisoquinoline alkaloids habropetaline A (**11**) (retention time 18.0 min) and dioncopeltine A (**10**) (retention time 20.5 min), along with a mixture of dioncophylline A (**8**), 5′-*O*-demethyldioncophylline A (**9**), and 5′-*O*-methyldioncophylline D (**12a**/**b**) (retention time 22.1 min). Further resolution and purification of the coeluting compounds **8**, **9**, and **12a**/**b** was done as reported previously,[28] by repeatedly performed crystallization and preparative HPLC.

Structural elucidation of the known compounds **2** and **8**−**15** was achieved by coelution with authentic reference material (for **8**−**15**) and by comparison of their physical and spectroscopic data with reported data.[19,20,26−28,33−35]

*Dioncoquinoside A (**1**):* pale brown solid (MeOH); mp 164 °C; $[\alpha]_D^{20}$ −230.1 (*c* 0.20, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (1.01), 303 (0.18), 319 (0.14), 331 (0.11) nm; IR (ATR) $\nu_{max}$ 3332 (br, m), 2968 (w), 2921 (m), 1617 (m), 1508 (w), 1428 (w), 1365 (m), 1236 (m), 1070 (s), 1039 (s) $cm^{-1}$; $^1H$ NMR ($D_2O$, 600 MHz) $\delta$ 7.82 (1H, d, $^3J$ = 8.40 Hz, 8-H), 7.41 (1H, dd, $^3J$ = 7.8 Hz, $^3J$ = 8.3 Hz, 7-H), 7.12 (1H, s, 3-H), 6.88 (1H, d, $^3J$ = 7.6 Hz, 6-H), 5.24 (1H, d, $^3J$ = 7.9 Hz, 1″-H), 4.88 (1H, d, $^3J$ = 7.9 Hz, 1′-H), 3.92 (1H, dd, $^2J$ = 12.6 Hz, $^3J$ = 2.3 Hz, 6″$\beta$-H), 3.74 (1H, dd, $^2J$ = 12.4 Hz, $^3J$ = 2.4 Hz, 6″$\alpha$-H), 3.79−3.73 (1H, m, 2′-H), 3.71−3.69 (1H, m, 2″-H), 3.66−3.63 (2H, m, 6′-$CH_2$), 3.63−3.61 (1H, m, 5″-H), 3.60−3.58 (1H, m, 3″-H), 3.55−3.48 (1H, m, 3′-H), 3.55−3.48 (1H, m, 4″-H), 3.55−3.48 (1H, m, 4′-H), 3.18−3.16 (1H, m, 5′-H), 2.42 (3H, s, 2-$CH_3$); $^{13}C$ NMR ($D_2O$, 150 MHz) $\delta$ 154.8 (C, C-5), 152.6 (C, C-4), 147.2 (C, C-1), 133.4 (C, C-9), 131.3 (CH, C-3), 131.3 (C, C-2), 130.4 (CH, C-7), 117.1 (C-10), 116.9 (CH, C-8), 113.2 (CH, C-6), 106.5 (CH, C-1′), 104.9 (CH, C-1″), 79.1 (CH, C-5″), 78.5 (CH, C-5′), 78.3 (CH, C-3′), 78.3 (CH, C-3″), 76.4 (CH, C-2′), 75.5 (CH, C-2″), 71.9 (CH, C-4″), 71.8 (CH, C-4′), 63.1 ($CH_2OH$, C-6″), 62.8 ($CH_2OH$, C-6′), 19.2 ($CH_3$, 2-$CH_3$); EIMS *m*/*z* 514 $[M]^+$ (100), 352 $[M - Glc]^+$ (78), 190 $[M - 2Glc]^+$ (29); HRESIMS *m*/*z* 537.1579 $[M + Na]^+$ (calcd for $C_{23}H_{30}NaO_{13}$, 537.1579).

*Triphyoquinol $A_1$ (**3**):* brown, amorphous solid (MeOH); mp 155 °C; $[\alpha]_D^{20}$ +27.1 (*c* 0.05, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (1.39), 307 (0.35), 323 (0.24), 335 (0.22) nm; ECD (*c* 0.1, MeOH) $\Delta\varepsilon_{219}$ −44.6, $\Delta\varepsilon_{235}$ +56.6, $\Delta\varepsilon_{294}$ −3.6, $\Delta\varepsilon_{320}$ +0.2, $\Delta\varepsilon_{339}$ −5.4 $cm^2$ $mol^{-1}$; IR (ATR) $\nu_{max}$ 3399 (br, w), 2973 (w), 2927 (w), 2512 (br, m), 2159 (s), 2026 (s), 1974 (s), 1683 (w), 1610 (w), 1511 (w), 1428 (w), 1361 (w), 1180 (w), 1124 (w), 1085 (w), 833 (w), 802 (w), 742 (m), 617 (w) $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR see Table 1; EIMS *m*/*z* 374 $[M]^+$ (100), 359 $[M - CH_3]^+$ (12), 187 $[M/2]^+$ (23), 172 $[M/2 - CH_3]^+$ (9); HRESIMS *m*/*z* 375.1596 $[M + H]^+$ (calcd for $C_{24}H_{23}O_4$, 375.1591).

*Triphyoquinol $A_2$ (**4**):* white, crystalline solid (MeOH); mp 152 °C; $[\alpha]_D^{20}$ +64.4 (*c* 0.05, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (1.29), 307 (0.28), 323 (0.26), 255 (0.24) nm; ECD (*c* 0.1, MeOH) $\Delta\varepsilon_{218}$ −44.6, $\Delta\varepsilon_{234}$ +56.6, $\Delta\varepsilon_{294}$ −3.6 $cm^2$ $mol^{-1}$; IR (ATR) $\nu_{max}$ 3659 (br, w), 3409 (br, w), 2979 (s), 2361 (m), 2161 (br, w), 2029 (br, w), 1716 (w), 1656 (w), 1607 (s), 1457 (m), 1425 (m), 1379 (s), 1361 (s), 1245 (s), 1228 (s), 1118 (s), 1083 (s), 953 (m), 827 (m), 812 (m), 755 (s), 700 (w), 667 (w), 621 (w), 607 (m) $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR see Table 1; EIMS *m*/*z* 374 $[M]^+$ (100), 359 $[M - CH_3]^+$ (9), 187 $[M/2]^+$ (21), 172 $[M/2 - CH_3]^+$ (5); HRESIMS *m*/*z* 373.1440 $[M - H]^+$ (calcd for $C_{24}H_{21}O_4$, 373.1440).

*Triphyoquinol B (**5**):* brown, amorphous solid (MeOH); mp 106 °C; $[\alpha]_D^{20}$ −30.4 (*c* 0.05, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (0.89), 307 (0.15), 319 (0.13), 331 (0.10), 443 (0.08) nm; ECD (*c* 0.1, MeOH) $\Delta\varepsilon_{244}$ +13.22, $\Delta\varepsilon_{217}$ −10.04 $cm^2$ $mol^{-1}$; IR (ATR) $\nu_{max}$ 3401 (br, w), 2975 (w), 2925 (w), 2854 (w), 2524 (br, m), 2159 (s), 2026 (s), 1974 (s), 1718 (w), 1671 (w), 1631 (w), 1430 (w), 1386 (w), 1353 (w), 1267 (w), 1178 (w), 1081 (w), 871 (w), 806 (w), 742 (m), 613 (w) $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR see Table 1; EIMS *m*/*z* 374 $[M]^+$ (100), 187 $[M/2]^+$ (14), 172 $[M/2 - CH_3]^+$ (6); HRESIMS *m*/*z* 397.1410 $[M + Na]^+$ (calcd for $C_{24}H_{22}NaO_4$, 397.1410).

*Triphyoquinone A (**7**):* pale brown, amorphous solid (MeOH); mp 163 °C; $[\alpha]_D^{20}$ −324.5 (*c* 0.02, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (0.89), 307 (0.15), 319 (0.13), 331 (0.10), 443 (0.08) nm; ECD (*c*


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0.1, MeOH) $\Delta\varepsilon_{244}$ +13.22, $\Delta\varepsilon_{217}$ −10.04 mdeg; IR (ATR) $\nu_{max}$ 3401 (br, w), 2975 (w), 2925 (w), 2854 (w), 2524 (br, m), 2159 (s), 2026 (s), 1974 (s), 1718 (w), 1671 (w), 1631 (w), 1430 (w), 1386 (w), 1353 (w), 1267 (w), 1178 (w), 1081 (w), 871 (w), 806 (w), 742 (m), 613 (w) $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR see Table 1; EIMS *m/z* 374 $[M]^+$ (100), 359 $[M - CH_3]^+$ (53), 190 [M − naphthalene]$^+$ (5), 188 [M − naphthoquinone]$^+$ (5); HRESIMS *m/z* 397.1047 $[M + Na]^+$ (calcd for $C_{23}H_{18}NaO_5$, 397.1052).

*Triphyoquinoside A (**6**):* pale brown, amorphous solid (MeOH); mp 215 °C; $[\alpha]_D^{20}$ −206.7 (*c* 0.2, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 227 (0.85), 307 (0.16), 335 (0.11) nm; ECD (*c* 0.1, MeOH) $\Delta\varepsilon_{236}$ +60.81, $\Delta\varepsilon_{221}$ −41.2 $cm^2$ $mol^{-1}$; IR (ATR) $\nu_{max}$ 3370 (br, m), 2973 (w), 2518 (s, br), 2159 (s), 2026 (s), 1974 (s), 1673 (w), 1427 (w), 1357 (w), 1178 (m), 1139 (w), 1056 (m), 829 (w), 759 (w), 607 (w) $cm^{-1}$; $^1H$ NMR ($D_2O$, 600 MHz) $\delta$ 7.40 (1H, s, 3-H), 7.25 (1H, d, $^3J$ = 7.8 Hz, 6′-H), 7.05 (1H, dd, $^3J$ = 8.5 Hz, $^3J$ = 7.8 Hz, 7′-H), 7.03 (1H, dd, $^3J$ = 8.3 Hz, $^3J$ = 7.7 Hz, 7-H), 6.88 (1H, s, 3′-H), 6.72 (1H, d, $^3J$ = 7.7 Hz, 6-H), 6.62 (1H, d, $^3J$ = 8.8 Hz, 8′-H), 6.45 (1H, d, $^3J$ = 8.5 Hz, 8-H), 5.24 (1H, d, $^3J$ = 7.8 Hz, 1‴-H), 5.13 (1H, d, $^3J$ = 7.9 Hz, 1″-H), 4.39 (1H, d, $^3J$ = 7.7 Hz, 1⁗-H), 4.23 (1H, dd, $^2J$ = 11.7 Hz, $^3J$ = 2.0 Hz, 6‴-H), 3.94 (1H, m, 6″-H), 3.91 (1H, m, 6‴-H), 3.86 (1H, m, 5‴-H), 3.85 (1H, m, 6⁗-H), 3.75 (1H, dd, $^2J$ = 12.2 Hz, $^3J$ = 6.4 Hz, 6″-H), 3.63 (1H, m, 2‴-H), 3.63 (1H, m, 6⁗-H), 3.61 (1H, m, 2″-H), 3.56 (1H, m, 3‴-H), 3.52 (1H, m, 5⁗-H), 3.52 (1H, m, 5″-H), 3.51 (1H, m, 3″-H), 3.50 (1H, m, 4‴-H), 3.46 (1H, m, 4″-H), 3.33 (1H, m, 3⁗-H), 3.29 (1H, m, 4⁗-H), 3.25 (1H, m, 2⁗-H), 1.94 (3H, s, 2-$CH_3$), 1.91 (3H, s, 2′-$CH_3$); $^{13}C$ NMR ($D_2O$, 150 MHz) $\delta$ 156.1 (C, C-5′), 155.3 (C, C-5), 155.0 (C, C-4), 154.4 (C, C-4′), 137.6 (C, C-2′), 137.5 (C, C-9), 137.1 (C, C-9′), 136.6 (C, C-2), 132.0 (C, C-1), 128.5 (CH, C-7), 127.7 (C, C-1′), 127.2 (CH, C-7′), 122.2 (CH, C-8′), 118.0 (CH, C-8), 115.7 (C, C-10′), 115.6 (C, C-10), 114.3 (CH, C-3), 114.1 (CH, C-3′), 111.0 (CH, C-6′), 111.0 (CH, C-6), 105.2 (CH, C-1‴), 104.5 (CH, C-1″), 104.3 (CH, C-1‴), 78.8 (CH, C-5″), 78.2 (CH, C-3″), 78.1 (CH, C-5⁗), 78.1 (CH, C-3⁗), 78.1 (CH, C-3‴), 78.0 (CH, C-4⁗), 77.7 (CH, C-5‴), 75.2 (CH, C-2⁗), 75.1 (CH, C-2‴), 75.1 (C, C-2″), 71.5 (CH, C-4‴), 71.3 (C, C-4″), 70.5 ($CH_2$, C-6‴), 62.8 ($CH_2OH$, C-6⁗), 62.5 ($CH_2OH$, C-6″), 20.5 ($CH_3$, 2-$CH_3$), 20.2 ($CH_3$, 2′-$CH_3$); EIMS *m/z* 832 $[M]^+$ (100), 670 [M − Glc]$^+$ (56), 508 [M − 2Glc]$^+$ (37), 346 [M − 3Glc]$^+$ (25); HRESIMS *m/z* 855.2699 $[M + Na]^+$ (calcd for $C_{40}H_{48}NaO_{19}$, 855.2682).

**Hydrolysis of the Glucosides 1, 2, and 6.** Treatment of the glucoside dioncoquinoside A (**1**), plumbaside (**2**), or triphyoquinoside A (**6**) (ca. 1.5 mg) with methanolic HCl or with a commercial $\beta$-glucosidase from almonds (Sigma) led to a complete deglucosidation of the compounds. For this purpose, the compounds were dissolved in HCl/MeOH (3 mL, 1:1) at 60 °C for 2 h and cooled to room temperature, or stirred in 2 mL of DMSO/$H_2O$ (1:1) and incubated with the enzyme at room temperature for 90 min. Ethyl acetate (2 × 5 mL) was added, and the phases were separated. In each case, evaporation of the aqueous phase gave D-glucose, which was identical with an authentic sample (Aldrich) by TLC comparison (silica gel, $CHCl_3$/MeOH/$H_2O$, 9:6:1, detection by spraying with 10% vanillin in concentrated $H_2SO_4$, followed by heating) and by $^1H$ NMR and optical rotation, $[\alpha]_D^{20}$ +49.0 (*c* 0.05, $H_2O$), lit.[41] $[\alpha]_D^{20}$ +52.2 (*c* 0.05, $H_2O$). For dioncoquinoside A (**1**) and plumbaside (**2**), evaporation of the organic phases afforded plumbagin (**13**) as the aglycone. Its chromatographic (HPLC) and spectroscopic ($^1H$ NMR) properties were in accordance with those of a sample isolated from callus cultures of *T. peltatum*.[35,40] The aglycone of triphyoquinoside A (**6**) was not detectable; it was found to decompose during deglucosidation and workup.

**Computational Details.** The conformational analysis of the *P*-configured dimer triphyoquinone A (**7**) and the optimization of the naphthalene and *ortho*-quinone building blocks, in which the free binding site of the former biaryl axis was substituted by a hydrogen atom, were performed with B3LYP/TZVP[42,43] using ORCA.[44] The excited-state properties of the three compounds were simulated with TD-B3LYP/6-31G*[42,45] using the Gaussian 03[46] software package. For the dimer, a total number of 40 vertical excitations were taken into account, while 20 excitations were calculated for each of the monomeric halves. The excitations of the monomers were then compared in order to identify the relevant excited states along with their electronic transition dipole moments. Comparison of the calculated UV and ECD spectra with the experimental ones was performed with SpecDis.[47] A UV correction of 12 nm in combination with a spectral bandwidth $\sigma$ of 0.16 eV was applied to the calculated curves.

The *P*-atropo-diastereomer of triphyoquinoside A (**6**) was investigated with an automated conformational search using the modified-Dreiding[48] force field implemented in the Vconf[49] program, which was followed by the optimization of the thus identified conformations, with PM3.[50] The PM3 minimum geometry was taken as a starting point for the calculation of the UV and ECD spectra of *P*-**6** using ZINDO/S-CI[51] (40 excited states). The calculated ECD spectra were compared with the experimental ones by using SpecDis.[47] For the calculation of the curves, a UV correction[52] of −18 nm in combination with a spectral bandwidth $\sigma$ of 0.20 eV was used.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jnatprod.6b00439.

NMR ($^1H$, $^{13}C$, $^1H$,$^1H$-COSY, HSQC, HMBC, NOESY, and ROESY), HRESIMS, and IR spectra of compounds **1** and **3**−**7** (PDF)

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### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

We dedicate this paper to Professor Ulrike Holzgrabe, Chair of Pharmaceutical and Medicinal Chemistry of the University of Würzburg, on the occasion of her 60th birthday.

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