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Structural Revision of Thelephantin G by Total Synthesis and the Inhibitory Activity against TNF-α Production

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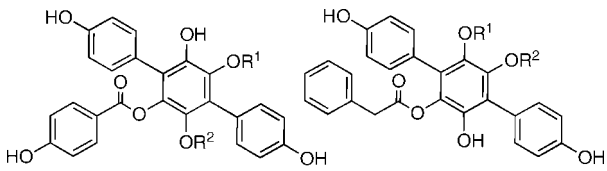

1: R^1 = *p*-HOC_6H_4CO, R^2 = H **3**: R^1 = $COCH_2Ph$, R^2 = H
2: R^1 = H, R^2 = *p*-HOC_6H_4CO **4**: R^1 = H, R^2 = $COCH_2Ph$

This paper describes the total synthesis of thelephantin G, thus revising the proposed structure **1** to **2**. The key steps involved a double Suzuki−Miyaura coupling and an esterification reaction. By a similar strategy, ganbajunins D and E (**3** and **4**) were also prepared. Compound **2** strongly inhibited TNF (tumor necrosis factor)-α production in rat basophilic leukemia (RBL-2H3) cells: IC_{50} = 3.5 nM, while a mixture of **1** and its regioisomer **15** showed no such activity.

Highly substituted phenolic compounds such as certain antibiotics and pigments contain many quaternary carbon atoms, and they lack hydrogens suitable for long-range correlation HMBC experiments if hydroxyl proton does not give a sharp signal in the ^1H NMR spectrum. Therefore it is not easy to determine the hydroxyl group position and connectivity in these molecules. Actually, there are several reports on structural revision of aromatic compounds in the past few years, especially focused on positional isomers of aromatic substituents including phenolic hydroxyl groups.[1] Thelephantin G is a natural terphenyl that was isolated from the mushroom *Thelephora aurantiotincta* by Asakawa et al. in 2003, and the structure was assigned as **1** having a unique *p*-hydroquinone moiety by spectroscopic analyses.[2] A natural terphenyl with a similar structure, ganbajunin E (**4**), has been reported in the literature.[3] However, the natural product was isolated as an inseparable mixture with ganbajunin D (**3**). This result suggested that rearrangement of the hydroxybenzoyl group did not proceed easily. In general, the tendency for benzoate migration to adjacent hydroxyls, in contrast to acetates, is known to be modest.[4] In connection with our studies on natural terphenyls,[5] we were interested in the unique reactivity hidden in **1** and its inhibitory activity against tumor necrosis factor (TNF)-α production in rat basophilic leukemia cells. TNF-α is a potent multifunctional cytokine that mediates a variety of biological actions with a central role in the pathogenesis of many inflammatory diseases.[6] Thus, inhibitors of TNF-α production in activated mast cells and basophils are promising candidates for a new type of antiallergic agent. Described herein is the total synthesis of thelephantin G that dictates revision of the formula to **2**. In addition, biological activities of **1** and **2**, as well as synthesis of a mixture of ganbajunins D and E (**3** and **4**) from the key intermediate, are also discussed.

Our synthetic strategy toward **1** involved reduction of **11** followed by benzoylation and debenzylation to install the *p*-hydroquinone diester moiety. To construct the *p*-terphenyl skeleton of these molecules, we planned to utilize the Suzuki−Miyaura coupling reaction[7] using the highly functionalized aryl halide **6** and benzyl boronic acid **7** as shown in Scheme 1.[8] Bromanilic acid (**5**) was reduced with sodium dithionite and the resulting compound was immediately subjected to *O*-alkylation, giving tetramethoxymethyl (MOM) derivative **6**. Suzuki−Miyaura coupling of **6** with **7** was performed under several conditions (Table 1). The best result was obtained by the use of palladium acetate (0.05 mol equiv) and triphenylphosphine (0.15 mol equiv) in the presence of sodium carbonate in aqueous 1-propanol[9] at 100 °C to afford *p*-terphenyl derivative **8** in high yield (Table 1, entry 4).

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(1) (a) Williamson, R. T.; McDonald, L. A.; Barbieri, L. R.; Carter, G. T. *Org. Lett.* **2002**, *4*, 4659–4662. (b) Bergeron, R. J.; Huang, G.; Smith, R. E.; Bharti, N.; McManis, J. S.; Butler, A. *Tetrahedron* **2003**, *59*, 2007–2014. (c) Srikrishna, A.; Ravikumar, P. C. *Tetrahedron Lett.* **2005**, *46*, 6105–6109. (d) Ye, Y. H.; Zhu, H. L.; Song, Y. C.; Liu, J. Y.; Tan, R. X. *J. Nat. Prod.* **2005**, *68*, 1106–1108. (e) Chudík, S.; Marek, R.; Sečekářová, P.; Nečeas, M.; Dostál, J.; Slavík, J. *J. Nat. Prod.* **2006**, *69*, 954–956. (f) Siddaiah, V.; Maheswara, M.; Rao, C. V.; Venkateswarlu, S.; Subbaraju, G. V. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1288–1290.

(2) Quang, D. N.; Hashimoto, T.; Hitaka, Y.; Tanaka, M.; Nukada, M.; Yamamoto, I.; Asakawa, Y. *Phytochemistry* **2003**, *63*, 919–924.

(3) Hu, L.; Gao, J.-M.; Liu, J.-K. *Helv. Chim. Acta* **2001**, *84*, 3342–3349.

(4) Haines, A. H. In *Advances in Carbohydrate Chemistry and Biochemistry*; Tipson, S.; Horton, D., Ed.; Academic Press, New York, 1976; Vol. 33, pp 11−110.

(5) (a) Xie, C.; Koshino, H.; Esumi, Y.; Takahashi, S.; Yoshikawa, K.; Abe, N. *Biosci. Biotechnol. Biochem.* **2005**, *69*, 2326–2332. (b) Ye, Y.-Q.; Koshino, H.; Onose, J.; Yoshikawa, K.; Abe, N.; Takahashi, S. *Org. Lett.* **2007**, *9*, 4131–4134. (c) Onose, J.; Xie, C.; Ye, Y.-Q.; Takahashi, S.; Koshino, H.; Yasunaga, K.; Abe, N.; Yoshikawa, K. *Biol. Pharm. Bull.* **2008**, *31*, 831–833.

(6) (a) Vassalli, P. *Annu. Rev. Immunol.* **1992**, *10*, 411–452. (b) Sieper, J.; Braun, J. *Expert Opin. Emerging Drugs* **2002**, *2*, 235–246. (c) Holgate, S. T. *Cytokine* **2004**, *28*, 152–157.

(7) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.

(8) For examples of the coupling of electron-rich arylbromide, see: (a) Narayan, S.; Roush, W. R. *Org. Lett.* **2004**, *6*, 3789–3792. (b) Takase, M.; Nakajima, A.; Takeuchi, T. *Tetrahedron Lett.* **2005**, *46*, 1739–1742. (c) Yonezawa, S.; Komurasaki, T.; Kawada, K.; Tsuri, T.; Fuji, M.; Kugimiya, A.; Haga, N.; Mitsumori, S.; Inagaki, M.; Nakatani, T.; Tamura, Y.; Takechi, S.; Taishi, T.; Ohtani, M. *J. Org. Chem.* **1998**, *63*, 5831–5837.

(9) Huff, B. E.; Koenig, T. M.; Mitchell, D.; Staszak, M. A. *Organic Syntheses*; Wiley & Sons: NewYork, 2004; Collect. Vol. X, pp 102−107.

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SCHEME 1. Suzuki−Miyaura Coupling of 6 with 7

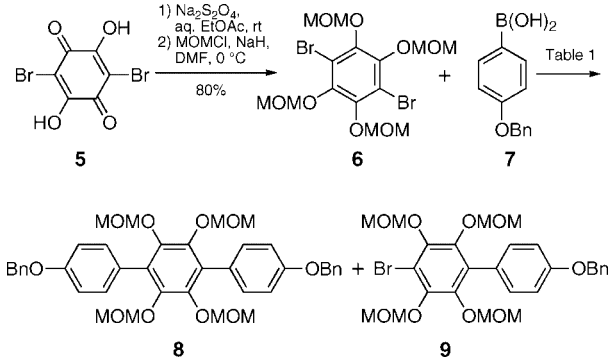
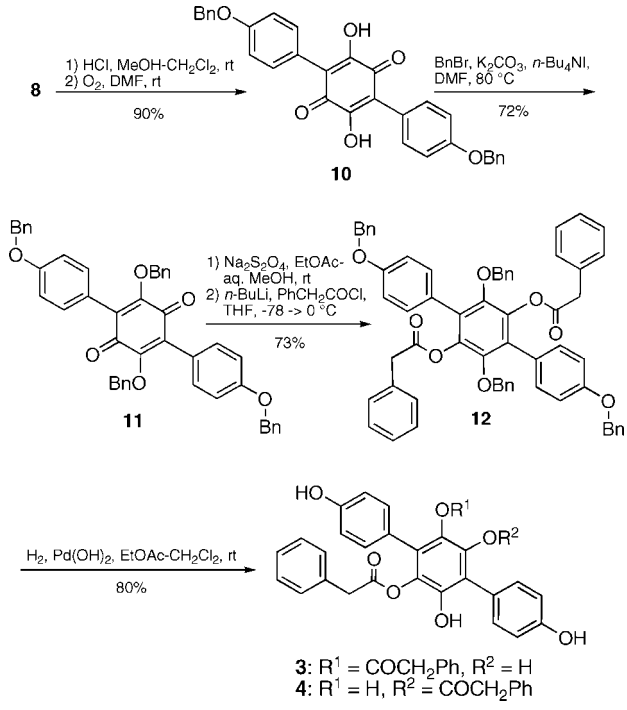


TABLE 1. Suzuki−Miyaura Coupling of Bromide 6 with Benzyl Boronic Acid 7

entry	conditions	terphenyl	biphenyl
1	**7** (2.3 mol equiv), $Pd(PPh_3)_4$ (0.05 mol equiv), K_3PO_4, DMF, 100 °C, 8 h	**8** (15%)	**9** (40%)
2	**7** (2.3 mol equiv), $Pd(PPh_3)_4$ (0.05 mol equiv), Cs_2CO_3, toluene, 100 °C, 8 h	**8** (27%)	**9** (61%)
3	**7** (2.3 mol equiv), $Pd(PPh_3)_4$ (0.05 mol equiv), Na_2CO_3, DME−EtOH−H_2O, 100 °C, 8 h	**8** (75%)	
4	**7** (2.3 mol equiv), $Pd(OAc)_2$ (0.05 mol equiv), Ph_3P (0.15 mol equiv), Na_2CO_3, aq 1-propanol, 100 °C, 4 h	**8** (91%)	

SCHEME 2. Synthesis of Ganbajunins D and E (3 and 4)



Prior to the synthesis of **1**, ganbajunins D and E (**3** and **4**) were prepared for confirmation of a facile rearrangement of the phenylacetyl groups. Acidic hydrolysis of **8**, followed by air oxidation provided *p*-quinone **10** (Scheme 2). Benzylation of **10** proceeded cleanly by heating it in DMF at 80 °C, furnishing tetrabenzyl *p*-quinone **11**. After reduction of **11** with sodium dithionite, the resulting compound was treated successively with *n*-butyllithium at −78 °C and then phenylacetyl chloride, giving **12** in good yield. As anticipated, hydrogenolysis of **12** was accompanied by acyl migration, resulting in an inseparable mixture of **3** and **4**.[10]

SCHEME 3. Synthesis of the Proposed Structure 1 of Thelephantin G

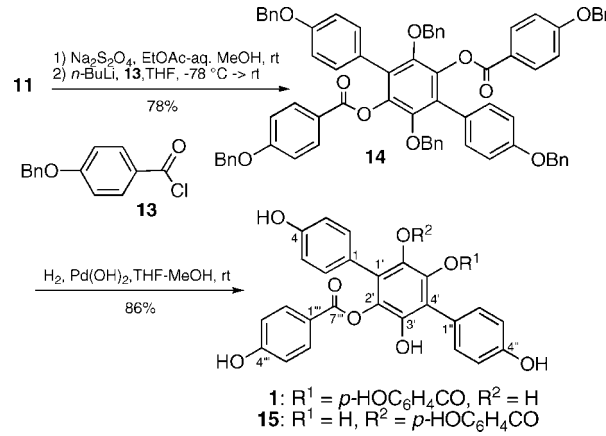


TABLE 2. ^{1}H NMR (600 MHz) Data (δ) for Natural Thelephantin G, 1, and 2 in MeOH-d_4

position	thelephantin G[ab]	**1**[b]	**2**[b]
2 (2″)	7.26 d (8.8)	7.22 d (8.8)	7.26 d (8.8)
3 (3″)	6.75 d (8.8)	6.73 d (8.8)	6.75 d (8.8)
5 (5″)	6.75 d (8.8)	6.73 d (8.8)	6.75 d (8.8)
6 (6″)	7.26 d (8.8)	7.22 d (8.8)	7.26 d (8.8)
2‴	7.62 d (8.8)	7.80 d (8.8)	7.62 d (8.8)
3‴	6.62 d (8.8)	6.77 d (8.8)	6.62 d (8.8)
5‴	6.62 d (8.8)	6.77 d (8.8)	6.62 d (8.8)
6‴	7.62 d (8.8)	7.80 d (8.8)	7.62 d (8.8)

[a] Reference 2 [b] Numbers in parentheses are *J* values.

TABLE 3. ^{13}C NMR (150 MHz) Data (δ) for Natural Thelephantin G, 1, and 2 in MeOH−d_4

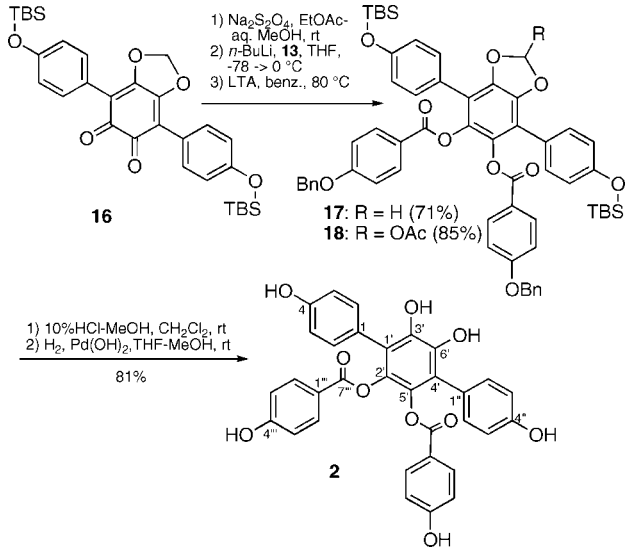
position	thelephantin G[a]	**1**	**2**
1 (1″)	125.1	125.3	125.1
2, 6 (2″, 6″)	132.6	132.7	132.6
3, 5 (3″, 5″)	115.9	115.9	115.9
4 (4″)	157.9	157.9	157.9
1′ (4′)	124.1	125.7	124.1
2′	135.3	137.2	135.3
3′	142.5	141.3	142.4
5′	135.3	137.2	135.3
6′	142.5	141.3	142.4
1‴	120.9	121.6	120.9
2‴, 6‴	133.2	133.4	133.1
3‴, 5‴	116.0	116.0	116.0
4‴	163.8	163.8	163.8
7‴	166.6	166.6	166.5

[a] Reference 2.

The structural difference between **1** and **4** lies in the ester moiety of the central ring. Therefore, acylation of **11** was done with **13**[11] instead of phenylacetyl chloride (Scheme 3). The fully protected terphenyl **14** thus obtained was subjected to hydrogenolysis, giving a single product as judged by TLC analysis. However, ^{1}H NMR analyses revealed it as an inseparable mixture of **1** and **15** not a single isomer **1**.[10] The result suggested that the benzoyl groups also migrated during hydrogenolysis. The NMR data of **1** did not match with that of natural thelephantin G reported, showing that the proposed structure **1** was incorrect (Tables 2 and 3). Compound **15** also showed different NMR spectra compared with that of natural thelephantin G.

(10) These structures were determined by extensive 2D-NMR analyses.
(11) Cavallito, C. J.; Buck, J. S. *J. Am. Chem. Soc.* **1943**, *65*, 2140–2142.

SCHEME 4. Synthesis of the Revised Structure 2 of Thelephantin G



In re-examining the NMR data reported, we considered that natural thelephantin G should have a symmetrical structure, and proposed two possible structures: one was the originally proposed ganbajunin C type[3,12] with tetrahydroxy groups on the central ring and the other vialinin A type **2**. But the former was precluded because of instability toward oxygen.[5b] Consequently, we proposed **2** as the real structure of natural thelephantin G. The synthesis began from a key intermediate **16**[5b] in our total synthesis of vialinin A (Scheme 4). Acylation of the catechol obtained from **16** with **13** afforded the corresponding benzoate **17**. This underwent oxidation with lead tetraacetate, giving **18** in good yield. Finally, acid treatment of **18** followed by hydrogenolysis under the same conditions that were used on **14** afforded **2**. The ^{1}H and ^{13}C NMR data of **2**[13] were identical with those of natural thelephantin G, establishing the structure of the natural product as **2**.[14]

The inhibitory activities of **2** and the mixture of **1** and **15** against TNF-α production from RBL-2H3 cells were evaluated.[15] Compound **2** showed potent inhibition of TNF-α production (IC_{50} = 3.5 nM vs. 0.25 nM for FK-506) while the regioisomeric mixture was not effective. These results are similar to those of vialinin A and ganbajunins D and E (**3** and **4**).[16] The fact that displacement of the phenylacetyl group in vialinin A by a hydroxybenzoyl group retained most of the inhibitory activity is of interest. These results would be useful for designing new antiallergic drugs.

In conclusion, *p*-terphenyl **1** and its regioisomer **2** were synthesized from **5** and **16**, respectively, thus revising the originally proposed structure of thelephantin G to **2**. Compound **2** was shown to be a potent inhibitor of TNF-α production from RBL-2H3 cells (IC_{50} = 3.5 nM).

Experimental Section

3,6-Di(*p*-(benzyloxy)phenyl)-1,2,4,5-tetrakis((methoxy)methoxy)-benzene (8). A mixture of **6** (299 mg, 0.63 mmol) and **7** (329 mg, 1.44 mmol) in 1-propanol (6.0 mL) was stirred at rt for 30 min, allowing the solids to dissolve. The resulting solution was treated with palladium acetate (7.1 mg, 31.6 μmol), triphenylphosphine (24.8 mg, 94.5 μmol), 2 M sodium carbonate (0.95 mL), and water (0.55 mL) then heated at 100 °C with stirring for 4 h and cooled to rt. After addition of water, the resulting mixture was stirred at rt for 1 h, and then extracted with ethyl acetate. The extracts were washed successively with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 100:1 → 25:1) to give **8** (390 mg, 91%) as a colorless solid: mp 146.5−147 °C (ethanol); IR (ZnSe) 2901, 2826, 1518, 1430, 1376, 1244, 1156, 1044, 993, 917 cm^{-1}; UV λ_{max} (CH_3CN) nm (log ε) 214 (4.43), 228 (4.44), 265 (4.42); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.45 (14H, m), 7.03 (4H, d, *J* = 8.3 Hz), 5.13 (4H, s), 4.81 (8H, s), 2.87 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 144.3, 136.9, 132.5, 130.9, 128.5, 127.9, 127.4, 126.8, 114.3, 98.9, 69.9, 56.8; HRMS (ESI) calcd for $C_{40}H_{42}O_{10}Na$ [M + Na]$^+$ 705.2676, found 705.2690. Anal. Found: C, 70.39; H, 6.22. Calcd for $C_{40}H_{42}O_{10}$: C, 70.37; H, 6.20.

3,6-Di(*p*-(benzyloxy)phenyl)-2,5-dibenzyloxy-1,4-di(*p*-(benzyloxy)-benzoyloxy)benzene (14). To a stirred solution of **11** (101 mg, 0.15 mmol) in ethyl acetate−methanol (15:1, 32 mL) was added dropwise a solution of sodium dithionite (105 mg, 0.60 mmol) in water (4.0 mL) at rt. The resulting mixture was stirred for 4 h, and then extracted with ethyl acetate. The extracts were washed successively with cold aqueous HCl, water, and brine, dried, then concentrated to give hydroquinone (106 mg), which was employed in the next step without further purification. To a stirred solution of the above hydroquinone (106 mg, ca. 0.15 mmol) in THF (8.0 mL) was added dropwise 1.59 M *n*-butyllithium (0.20 mL, 0.32 mmol) in hexane at −78 °C. After 15 min, **13** (86.7 mg, 0.33 mmol) in THF (1.5 mL) was added, and the mixture was stirred at −78 °C for 30 min and at 0 °C → rt for 13 h. After being quenched with the addition of saturated aqueous NH_4Cl, the resulting mixture was extracted with ethyl acetate. The extracts were washed successively with water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was treated with ether to afford **14** (126 mg, 78% from **11**) as a colorless solid: IR (ZnSe) 3030, 2926, 1725, 1604, 1508, 1438, 1233, 1161, 1074 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (4H, d, *J* = 8.8 Hz), 7.30−7.46 (24H, m), 7.08 (2H, t, *J* = 7.4 Hz), 6.99 (4H, t, *J* = 7.7 Hz), 6.95 (4H, d, *J* = 8.8 Hz), 6.94 (4H, d, *J* = 8.8 Hz), 6.75 (4H, d, *J* = 7.1 Hz), 5.13 (4H, s), 5.04 (4H, s), 4.44 (4H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.8, 158.3, 145.6, 140.6, 136.9, 136.5, 136.2, 132.3, 131.4, 129.6, 128.7, 128.52, 128.46, 128.2, 127.9, 127.7, 127.5, 127.4, 125.1, 121.7, 114.5, 114.4, 75.2, 70.1, 69.9; HRMS (ESI) calcd for $C_{74}H_{58}O_{10}Na$ [M + Na]$^+$ 1129.3928, found 1129.3938.

3,6-Di(*p*-(hydroxy)phenyl)-2,5-dihydroxy-1,4-di(*p*-(hydroxy)benzoyloxy)benzene (1) and 3,6-Di(*p*-(hydroxy)phenyl)-2,4-dihydroxy-1,5-di(*p*-(hydroxy)benzoyloxy) benzene (15). To a stirred solution of **14** (40.0 mg, 36.1 μmol) in THF−methanol (4:1, 2.5 mL) was

(12) Hu, L.; Liu, J.-K. *Z. Naturforsch.* **2003**, *58c*, 452–454.
(13) As shown in Scheme 4, a numbering system different from that of **1** in Scheme 3 was used for comparison of NMR data.
(14) Many natural *p*-terphenyls with a *p*-hydroquinone diester moiety like ganbajunin E (**4**) have been described. However, terphenyls such as thelephorin A,[17] thelephantins A−C,[18] D−F,[2] and J and N[19] curtisian M−Q[20] were reported to be isolated as a single isomer although the reported ^{13}C NMR data of their central ring were similar to those of the revised thelephantin G (**2**). We would like to suggest that reinvestigation of the structures of such terphenyls are necessary. Actually, reported NMR data of thelephantin D and terrestrin C were almost identical and the true structure should be terrestrin C.[21]
(15) The bioassay was performed by the method[5c] previously reported.
(16) Vialinin A is an extremely potent inhibitor of TNF-α production from RBL-2H3 cells (IC_{50} = 90 pM vs. 0.25 nM for FK-506).[5c] On the other hand, the positional isomers **3** and **4** showed no such activity.
(17) Tsukamoto, S.; Macabalang, A. D.; Abe, T.; Hirota, H.; Ohta, T. *Tetrahedron* **2002**, *58*, 1103–1105.
(18) Quang, D. N.; Hashimoto, T.; Nukada, M.; Yamamoto, I.; Hitaka, Y.; Tanaka, M.; Asakawa, Y. *Phytochemistry* **2003**, *62*, 109–113.
(19) Quang, D. N.; Hashimoto, T.; Hitaka, Y.; Tanaka, M.; Nukada, M.; Yamamoto, I.; Asakawa, Y. *Phytochemistry* **2004**, *65*, 1179–1184.
(20) Quang, D. N.; Hashimoto, T.; Nukada, M.; Yamamoto, I.; Tanaka, M.; Asakawa, Y. *Chem. Pharm. Bull.* **2003**, *51*, 1064–1067.
(21) Radulovic, N.; Quang, D. N.; Hashimoto, T.; Nukada, M.; Asakawa, Y. *Phytochemistry* **2005**, *66*, 1052–1059.

added palladium hydroxide (10.0 mg). The mixture was stirred vigorously under a hydrogen atmosphere at rt for 1 d, filtered through a filter paper under N_2 atmosphere, and then concentrated. The residue was treated with *n*-hexane−THF to give a ca. 2:1 mixture of **1** and **15** (17.6 mg, 86%) as a powder: IR (ZnSe) 3390, 1702, 1604, 1589, 1511, 1257, 1218, 1161, 1075 cm^{-1}; ^1H NMR for **15** (600 MHz, CD_3OD) δ 7.78 (4H, d, J = 8.8 Hz), 7.32 (2H, d, J = 8.8 Hz), 7.13 (2H, d, J = 8.8 Hz), 6.88 (2H, d, J = 8.8 Hz), 6.75 (4H, d, J = 8.8 Hz), 6.59 (2H, d, J = 8.8 Hz); ^{13}C NMR for **15** (150 MHz, CD_3OD) δ 166.9, 163.7, 158.0, 157.7, 146.3, 133.44, 133.41, 132.0, 131.6, 130.1, 125.3, 125.2, 121.6, 119.9, 116.3, 116.0, 115.7; ^1H NMR for **1** (600 MHz, CD_3OD) δ 7.80 (4H, d, J = 8.8 Hz), 7.22, (4H, d, J = 8.8 Hz), 6.77 (4H, d, J = 8.8 Hz), 6.73 (4H, d, J = 8.8 Hz); ^{13}C NMR for **1** (150 MHz, CD_3OD) δ 166.6, 163.8, 157.9, 141.3, 137.2, 133.4, 132.7, 125.7, 125.3, 121.6, 116.0, 115.9; HRMS (ESI) calcd for $C_{32}H_{22}O_{10}Na$ $[M + Na]^+$ 589.1111, found 589.1129.

5,6-Bis-*p*-(benzyloxy)benzoyloxy-4,7-di(*p*-(*tert*-butyldimethylsilyloxy)phenyl)benzo[*d*][1,3]dioxole (17). According to the method for the preparation of **14**, **16** (90 mg, 0.16 mmol) was transformed into **17** (112 mg, 71%) as needles: mp 174−175 °C; IR (ZnSe) 2927, 2886, 2855, 1731, 1604, 1508, 1245, 1165, 1074 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (4H, d, J = 9.0 Hz), 7.43 (4H, d, J = 8.6 Hz), 7.32−7.38 (10H, m), 6.81 (4H, d, J = 9.0 Hz), 6.78 (4H, d, J = 8.6 Hz), 6.06 (2H, s), 5.02 (4H, s), 0.93 (18H, s), 0.13 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 162.8, 155.4, 142.8, 136.0, 135.4, 132.2, 130.7, 128.7, 128.2, 127.4, 124.0, 121.2, 119.8, 117.1, 114.2, 101.5, 70.1, 25.6, 18.1, −4.5; HRMS (ESI) calcd for $C_{59}H_{62}O_{10}Si_2Na$ $[M + Na]^+$ 1009.3779, found 1009.3792.

5,6-Bis-*p*-(benzyloxy)benzoyloxy-4,7-di(*p*-(*tert*-butyldimethylsilyloxy)phenyl)benzo[*d*][1,3]dioxole-2-yl Acetate (18). A mixture of **17** (42.4 mg, 42.9 μmol) and lead tetraacetate (38.1 mg, 85.9 μmol) in benzene (2.0 mL) was stirred at 80 °C for 10 h. Then more lead tetraacetate (8.3 mg, 18.7 μmol) was added and stirring was continued for a further 10 h. After being cooled to rt, the reaction mixture was filtered through a pad of Celite, and then concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 50:1→ 20:1) to give **18** (38.1 mg, 85%) as an amorphous solid: IR (ZnSe) 2953, 2930, 2856, 1780, 1735, 1603, 1508, 1249, 1166, 1003 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (4H, d, J = 8.8 Hz), 7.81 (1H, s), 7.45 (4H, d, J = 8.6 Hz), 7.32−7.38 (10H, m), 6.82 (4H, d, J = 8.8 Hz), 6.78 (4H, d, J = 8.6 Hz), 5.03 (4H, s), 2.14 (3H, s), 0.94 (18H, s), 0.15 (12H, s); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 169.2, 164.2, 163.4, 156.2, 140.5, 136.7, 136.5, 132.4, 131.1, 128.9, 128.5, 127.9, 123.7, 121.2, 120.3, 118.1, 114.8, 113.5, 70.5, 25.7, 21.3, 18.4, −4.4; HRMS (ESI) calcd for $C_{61}H_{64}O_{12}Si_2Na$ $[M + Na]^+$ 1067.3834, found 1067.3859.

Thelephantin G (2). To a stirred solution of **18** (38.1 mg, 36.4 μmol) in dichloromethane (2.0 mL) was added a 10% HCl solution in methanol (0.5 mL), and the mixture was stirred at rt for 14 h, then concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 10:1 → 0:1) to give a solid (25.8 mg), which was dissolved in ethyl acetate (2.0 mL). Palladium hydroxide (10.0 mg) was added and the resulting mixture was stirred vigorously under a hydrogen atmosphere at rt for 15 h, filtered through a filter paper under N_2 atmosphere, and then concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 10:1→ 1:2) under N_2 atmosphere to give **2** (16 mg, 76%) as a white solid: mp 192.5−195 °C; IR (ZnSe) 3307, 1701, 1604, 1588, 1511, 1217, 1161, 1073, 1043 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.62 (4H, d, J = 8.8 Hz), 7.26 (4H, d, J = 8.8 Hz), 6.75 (4H, d, J = 8.8 Hz), 6.62 (4H, d, J = 8.8 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 166.6, 163.8, 157.9, 142.5, 135.3, 133.2, 132.6, 125.1, 124.1, 120.9, 116.0, 115.9; HRMS (ESI) calcd for $C_{32}H_{22}O_{10}Na$ $[M + Na]^+$ 589.1111, found 589.1111.

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Supporting Information Available: Experimental procedures, NMR spectra of **1**−**4**, **6**, **8**−**12**, **14**, **15**, **17**, and **18**. This material is available free of charge via the Internet at http://pubs.acs.org.

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