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Syntheses of Naturally Occurring Terphenyls and Related Compounds

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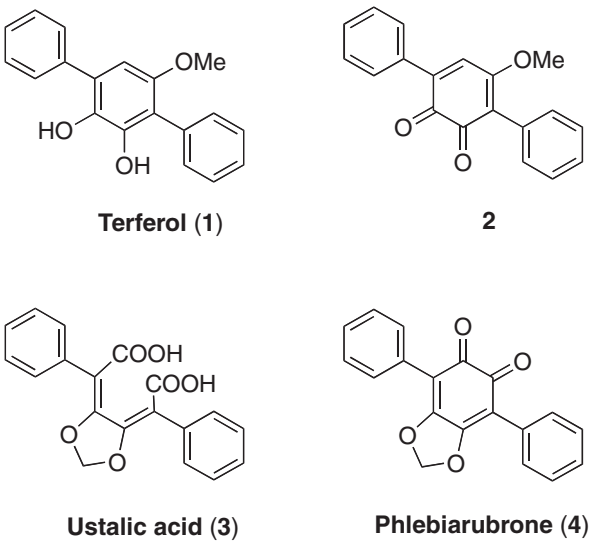
Naturally occurring terphenyls and related compounds such as terferol and its corresponding quinone and phlebiarubrone were synthesized from 2,5-diphenyl-1,4-benzoquinone. According to the proposed biosynthetic pathway, chemical conversion of phlebiarubrone to ustalic acid, a toxic compound isolated from the poisonous mushroom, *Tricholoma ustale*, was examined to find a low-yield conversion to the ustalic acid dimethyl ester.

Key words: terphenyl; quinone; ustalic acid; phlebiarubrone; terferol

Terphenyl is a common structural motif found in various natural products, largely isolated from microorganisms and mushrooms.[1)] Because of the diverse structure as well as its wide variety of biological activities, including antioxidative, neurotoxicity, immunosuppressive, plant growth regulation, antibacterial and insecticidal, these natural products have attracted great attention.[2)] Although many highly oxygenated terphenyl compounds with hydroxyl groups in the aromatic rings have been isolated, relatively simple terphenyl compounds also exhibit interesting biological activities. Terferol (**1**) isolated from *Streptomyces showdoensis* SANK65080 is an inhibitor of cyclic AMP- and cyclic GMP-phosphodiesterase (Fig. 1).[3,4),*] Recently, corresponding *o*-quinone **2** was isolated from a *Phoma* sp. as an inhibitor of parasite cyclic GMP-dependent protein kinase.[6)] Ustalic acid (**3**) was isolated as a toxic principle of mushroom poisoning by *Tricholoma ustale* (Kakishimeji in Japanese), and inhibited Na^+, K^+-ATPase.[7)] The unique structure of **3** is assumed to be biosynthesized by oxidative cleavage of phlebiarubrone (**4**), a well-known red pigment, originally isolated from cultured mycelia of the toadstool, *Phlebia strigosozonata*.[8)] We have been interested in the chemical relationship among these structurally unique natural products with significant biological activities. We describe herein an efficient and expeditious synthetic route for the simple terphenyl and related compound,[**] and attempts at the chemical conversion of phlebiarubrone to ustalic acid according to the biosynthetic hypothesis.[7)]



Terferol (1) **2** **Ustalic acid (3)** **Phlebiarubrone (4)**

Fig. 1. Structures of Naturally Occurring Terphenyl Compounds.

Results and Discussion

Key compounds **7** and **10** for the synthetic studies were synthesized from commercially available 2,5-diphenyl-1,4-benzoquinone (**5**) according to modified procedures of Nozaki and co-workers.[10)] Thiele-Winter acetoxylation of 2,5-diphenyl-1,4-benzoquinone (**5**) with perchloric acid in acetic anhydride gave triacetate **6** (Scheme 1).[11)] Upon treatment of product **6** with K_2CO_3 in methanol, the acetyl group at the 5′ position was selectively removed to give **7** in a 90% yield. Phenol **7** was methylated with CH_3I in the presence of K_2CO_3, and the remaining two acetates of **8** were hydrolyzed under acidic conditions to afford terferol (**1**) in a good yield. On the other hand, oxidation of **1** with

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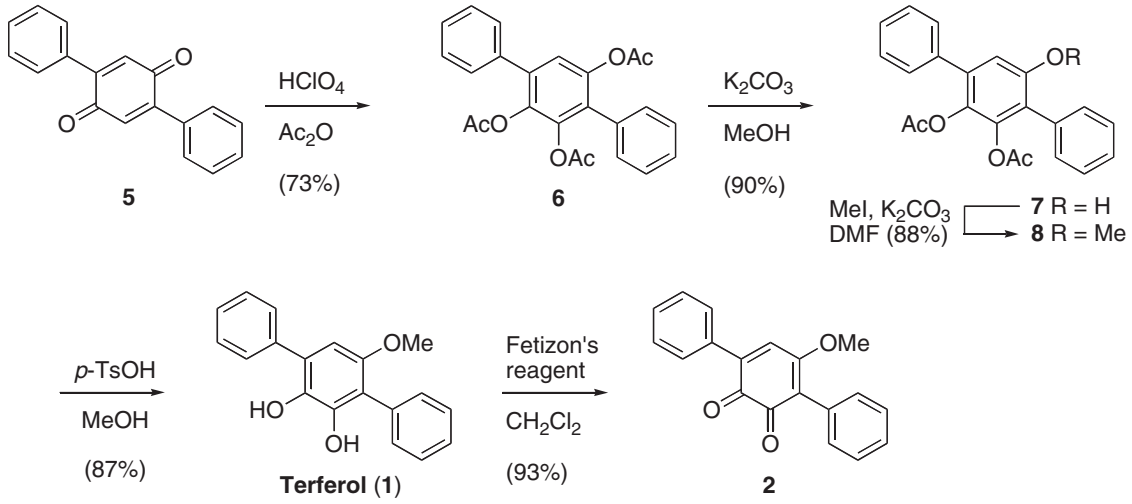
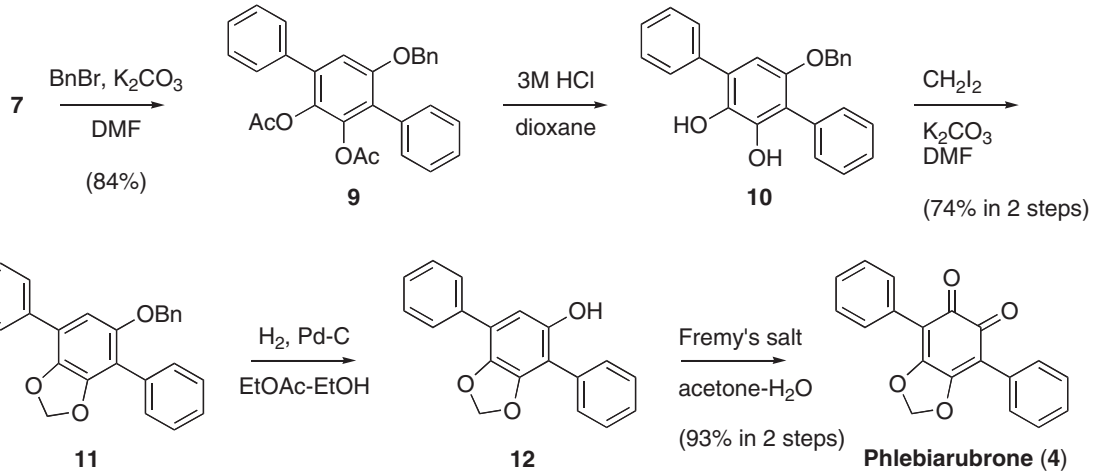


Scheme 1. Synthesis of Terferol (**1**) and Its *o*-Quinone Compound **2**.



Scheme 2. Synthesis of Phlebiarubrone (**4**).

Fetizon's reagent[12] gave corresponding *o*-quinone **2** in a high yield. However, the NMR spectra of synthetic **2** were not identical to those of the literature.[6],***

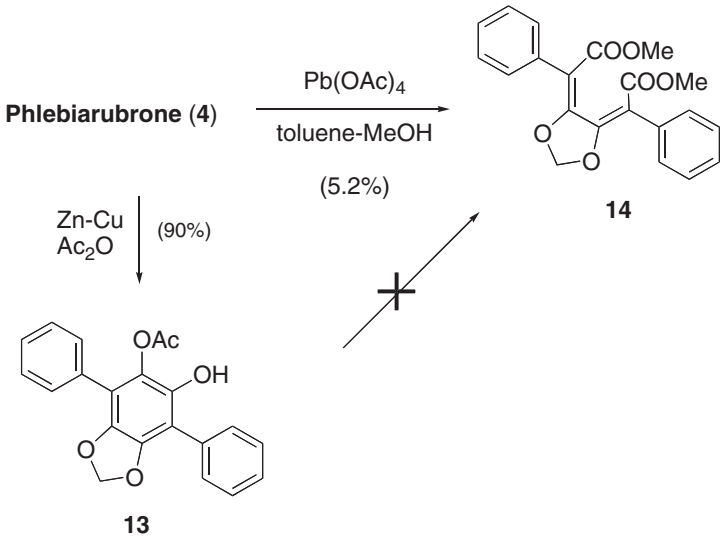
Phlebiarubrone (**4**) was synthesized from **7** as shown in Scheme 2. Protection of phenol **7** with a benzyl group under conventional conditions gave **9**, in which two acetates were hydrolyzed with hydrochloric acid in dioxane to give catechol **10**. In the transformation of **10** to methylene ketal **11** with diiodomethane in the presence of K_2CO_3, we found that dissolved oxygen caused the decomposition of substrate **10** and product **11** during the reaction, resulting in low yields (up to *ca.* 30%). Thus, when the reaction was conducted under oxygen-free conditions (see the experimental section), ketal **11** could be obtained reproducibly in a good overall yield from **9**. Deprotection of the benzyl group under hydrogenolytic conditions was followed by oxidation with Fremy's salt[13] to afford phlebiarubrone (**4**) in a high yield. NMR data for the synthetic material were good agreement with those of the literature.[14]

Since the scalable synthesis of phlebiarubrone had been established, chemical conversion of phlebiarubrone (**4**) to ustalic acid (**3**) was next examined. Many reactions for the oxidative cleavage of *o*-quinones or their *o*-dihydroquinones (catechols) to dicarboxylic acids have been reported: Baeyer-Villiger type of oxidation with peracids,[15,16] oxidation with potassium superoxide,[17] oxygen with copper-pyridine complex,[18] potassium permanganate[19] and lead tetraacetate,[20] and a photo-induced reaction.[21] However, the dihydroquinone obtained by reduction of **4** could not be isolated because of its extreme instability. Instead, hydroquinone monoacetate **13** was prepared by a brief treatment of **4**

* Terferol (**1**) was synthesized before its isolation from a natural source.[5]

** Phlebiarubrone (**4**) was synthesized from polyporic acid.[9]

*** Direct comparison between synthetic **2** and the natural compound indicated clear differences. Reexamination of the structure of natural **2** is currently underway by Dr. S. B. Singh (personal communication).



Scheme 3. Attempted Transformation of **4** to Ustalic Acid Dimethyl Ester **14**.

with Zn–Cu in acetic anhydride (Scheme 3), while the prolonged reaction time gave the corresponding diacetate.[8)] We then examined the conversion of **4** and **13** to ustalic acid. Many experiments under the above-mentioned conditions led us to find that phlebiarubrone was treated with a large excess of lead tetraacetate in methanol and toluene to give ustalic acid dimethyl ester **14** in a poor yield. Unfortunately, all attempts to improve this yield failed. Thus, it has been the sole condition for the transformation, while all the other conditions have never yielded ustalic acid (**3**) and its ester or anhydride. Spectroscopic data for synthetic **14** were identical to those derived from the methylation of natural ustalic acid with TMS-diazomethane.[22)] Because of the limited amount of dimethyl ester **14**, hydrolysis of the ester has not yet been examined.

In conclusion, we developed a new practical route for the synthesis of terferol, its *o*-quinone, and phlebiarubrone from the same starting material. Chemical conversion of phlebiarubrone (**4**) to ustalic acid derivative **14** was achieved for the first time by oxidative cleavage with lead tetraacetate, although the yield was poor.

Experimental

Melting point (Mp) data were recorded by a Yanaco MP-S3 melting point apparatus and are not corrected. Infrared spectra (IR) were recorded by a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded by a Bruker ARX-400 (400 MHz), Avance-400 (400 MHz) or Varian Gemini-2000 (300 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm from tetramethylsilane ($\delta = 0.00$ ppm) or acetone ($\delta = 2.04$ ppm) as internal standards. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, br = broadened, m = multiplet), and assignment. Carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded by a Bruker ARX-400 (100 MHz), Avance-400 (100 MHz) or Varian Gemini-2000 (75 MHz) spectrometer. Chemical shifts are reported in ppm from chloroform-d_1 ($\delta = 77.0$ ppm) or acetone-d_6 ($\delta = 206.0$ ppm). Electron ionization mass spectra (EI-MS) were recorded by a JEOL JMS-700 instrument and are reported in m/z. High resolution mass spectra (HR-MS FAB) in fast atom bombardment ionization (FAB) mode were recorded by a JEOL LCMATE mass spectrometer. Elemental analyses were performed by the analytical laboratory at Graduate School of Bioagricultural Sciences of Nagoya University.

*2′,3′,5′-Triacetoxy-p-terphenyl (**6**).* To a stirred suspension of 2,5-diphenyl-1,4-benzoquinone **5** (5.20 g, 20.0 mmol) in Ac_2O (52 ml) was added 70% $HClO_4$ (1.2 ml, 20.0 mmol) under an argon atmosphere. After being stirred at 70 °C for 2 h, the mixture was cooled to room temperature, and then poured into ice-cold water (100 ml). The mixture was extracted with EtOAc (50 ml × 4). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give a crude product which was crystallized from MeOH to give triacetate **6** (5.81 g, 73%) as colorless crystals. Mp 193–194 °C, (lit.[11)] 189.7 °C); IR (KBr) ν_{max} (cm^{-1}): 3062, 1772, 1469, 1415, 1370, 1189, 1096, 1042, 916; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 1.97 (6H, s, Ac × 2), 2.08 (3H, s, Ac), 7.13 (1H, s, Ar), 7.31 (2H, dd, J = 7.5, 2 Hz, Ar), 7.35–7.49 (8H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 20.0, 20.3, 20.4, 122.0, 128.1, 128.5, 128.8, 129.6, 131.9, 136.0, 136.2, 138.4, 141.6, 146.2, 167.9, 168.1, 169.0, *Anal.* Calcd. for $C_{24}H_{20}O_6$: C, 71.28; H, 4.98%. Found: C, 71.28; H, 4.98%.

*2′,3′-Diacetoxy-5′-hydroxy-p-terphenyl (**7**).* A suspension of **6** (14.0 g, 34.5 mmol) and K_2CO_3 (5.67 g, 41.4 mmol) in MeOH (475 ml) was stirred at 0 °C for 3 h. The reaction mixture was quenched with a sat. aqueous NH_4Cl solution and extracted with EtOAc (×3). The combined organic layers were successively washed with water (×2) and brine (×1), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (300 g of silica gel, EtOAc/hexane = 1:3 to 1:1) to afford **7** (11.3 g, 90%) as a pale yellow amorphous solid. IR (film) ν_{max} (cm^{-1}): 3428, 3023, 1771, 1419, 1371, 1212, 1094, 1045; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 1.96 (3H, s, Ac), 2.05 (3H, s, Ac), 5.15 (1H, s, –OH), 6.97 (1H, s, Ar), 7.31–7.53 (10H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 20.0, 20.2, 114.7, 122.2, 127.9, 128.4, 128.8, 128.9, 129.4, 130.2, 131.0, 133.8, 136.4, 136.7, 141.0, 151.1, 168.3, 168.8; HRMS (FAB, negative): calcd. for $C_{22}H_{17}O_5$ (M − H), 361.10760; found. 361.10757, *Anal.* Calcd. for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01%. Found: C, 72.92; H, 5.07%.

*2′,3′-Diacetoxy-5′-methoxy-p-terphenyl (**8**).* To a stirred solution of diacetate **7** (1.30 g, 3.59 mmol) in DMF (40 ml) were added CH_3I (1.0 ml, 16 mmol) and K_2CO_3 (700 mg, 5.07 mmol) at 0 °C. The resulting purple mixture was stirred at room temperature for 2 h, cooled back to 0 °C, and then diluted with Et_2O (40 ml). The mixture was successively washed with a sat. aqueous NH_4Cl solution, sat. aqueous $NaHCO_3$ solution (50 ml), and brine (50 ml). The organic layer was dried over anhydrous Na_2SO_4, filtered through a cotton pad, and concentrated *in vacuo*. The residue was purified by crystallization from Et_2O to afford methyl ether **8** (1.18 g, 88%) as colorless crystals. Mp 164–167 °C; IR (KBr) ν_{max} (cm^{-1}): 3062, 1772, 1618, 1476, 1370, 1205, 1103, 1082, 1011, 929, 886; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 1.96 (3H, s, Ac), 2.06 (3H, s, Ac), 3.78 (3H, s, –OMe), 6.90 (1H, s, Ar), 7.30–7.52 (10H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 20.1, 20.3, 56.1, 110.3, 124.8, 127.7, 128.0, 128.5, 128.8, 130.2, 132.6, 135.5, 137.2, 155.0, 168.3, 168.8; *Anal.* Calcd. for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36%. Found: C, 73.39; H, 5.44%.

*Terferol (**1**).* A suspension of methyl ether **8** (625 mg, 1.66 mmol) and *p*-TsOH·H_2O (48 mg, 0.25 mmol) in MeOH (20 ml) was stirred at 60 °C for 24 h. The mixture was allowed to cool to room temperature and then concentrated under reduced pressure. The residue was purified by column chromatography (40 g of silica gel, CH_2Cl_2) to give terferol **1** (420 mg, 87%) as red crystals. Mp 188–191 °C (lit.[4] 184 °C); IR (KBr) ν_{max} (cm^{-1}): 3544, 3495, 3058, 3017, 2960, 1773, 1594, 1481, 1378, 1319, 1227, 1104, 1071, 823; ^{1}H-NMR (300 MHz, acetone-d_6) δ (ppm): 3.64 (3H, s, OMe), 6.50 (1H, s, Ar), 7.22–7.42 (8H, m, Ar), 7.58–7.64 (2H, m, Ar); ^{13}C-NMR (75 MHz, acetone-d_6) δ (ppm): 55.9, 104.4, 118.5, 127.4, 127.5, 128.4, 128.7, 129.8, 131.7, 134.8, 137.1, 139.4, 144.6, 151.4; HR-MS (FAB, negative): calcd. for $C_{19}H_{15}O_3$ (M − H), 291.1021; found, 291.1025.

*4-Methoxy-3,6-diphenylcyclohexa-3,5-diene-1,2-dione (**2**).* To a stirred solution of terferol (**10**; 8.3 mg, 0.028 mmol) in CH_2Cl_2 (3.0 ml) was added 65 mg of Ag_2CO_3 on Celite (1.75 mmol Ag_2CO_3/1 g). The mixture was stirred at room temperature for 5 min, and then filtered through a pad of Hyflo Super-Cel® (filter aid), the residue being rinsed with CH_2Cl_2. The combined filtrate was concentrated. The crude product was purified by preparative TLC ($CHCl_3/CH_3CN$ = 20:1) to give **2** as a deep-purple solid (7.7 mg, 93%). Mp 179–182 °C; IR (KBr) ν_{max} (cm^{-1}): 3057, 1687, 1637, 1617, 1557, 1493, 1377, 1232, 1058, 955; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 3.84 (3H, s, OMe), 7.27 (1H, s, Ar), 7.30–7.48 (8H, m, Ar), 7.50–7.56 (2H, m, Ar); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 58.6, 120.7, 128.0, 128.1, 128.6, 128.7, 129.7, 130.7, 130.8, 131.5, 133.2, 140.3, 163.4, 178.1, 179.1; HR-MS (FAB, positive): calcd. for $C_{19}H_{16}O_3$ (M + 2H),[23] 291.1100; found, 291.1004.

*2′,3′-Diacetoxy-5′-benzyloxy-p-terphenyl (**9**).* To a stirred solution of **7** (11.2 g, 31.0 mmol) in DMF (343 ml) were added BnBr (7.3 ml, 62 mmol) and K_2CO_3 (6.00 g, 43.4 mmol). The reaction mixture was successively stirred at room temperature for 5 h, and then diluted with EtOAc. The mixture was washed with water (×2), a sat. aqueous $NaHCO_3$ solution (×1) and brine (×1), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was washed with hexane to afford **9** as a white solid (11.8 g, 84%). Mp 143–145 °C; IR (KBr) ν_{max} (cm^{-1}): 3063, 1775, 1475, 1415, 1370, 1207, 1100, 1066; ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 1.97 (3H, s, $COCH_3$), 2.06 (3H, s, $COCH_3$), 5.05 (2H, s, OCH_2Ph), 6.97 (1H, s, Ar), 7.18–7.47 (15H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 20.1, 20.2, 70.9, 112.4, 125.7, 126.8, 127.6, 127.7, 127.9, 128.5, 128.8, 130.3, 132.6, 134.4, 135.5, 136.7, 137.1, 141.6, 154.1, 168.3, 168.7. *Anal.* Calcd for $C_{29}H_{24}O_5$: C, 76.98; H, 5.35%. Found: C, 76.96; H, 5.15%.

*2′,3′-Dihydroxy-5′-benzyloxy-p-terphenyl (**10**).* To a stirred suspension of **9** (3.02 g, 6.68 mmol) in 1,4-dioxane (55 ml) was added 3*N* HCl (55 ml) at rt. After being stirred at 80 °C for 24 h, the reaction mixture was extracted with Et_2O (×3). The combined organic layers were washed with brine (×2), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was washed with hexane to afford **10** (2.40 g), which was used in the next reaction without further purification. An analytical sample was prepared by recrystallization from EtOAc–hexane. Mp 132.5–135 °C; IR (KBr) ν_{max} (cm^{-1}): 3531, 3501, 3061, 1481, 1455, 1428, 1375, 1273, 1235, 1101,

1065; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 4.94 (2H, s, OCH_2Ph), 5.26 (1H, s, O*H*), 5.39 (1H, s, O*H*), 6.61 (1H, s, Ar), 7.15–7.31 (4H, m, Ar), 7.34–7.61 (11H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 71.4, 107.2, 127.0, 127.56, 127.64, 128.0, 128.4, 128.8, 128.9, 129.0, 130.7, 132.7, 135.8, 137.4, 137.5, 141.5, 150.0. *Anal.* Calcd. for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47%. Found: C, 81.49; H, 5.57%.

*4,7-Diphenyl-5-benzyloxybenzo[d]-1,3-dioxole (**11**).* Into a flask were placed catechol **10** (2.00 g, 5.43 mmol), K_2CO_3 (3.20 g, 23.1 mmol), DMF (60 ml) and CH_2I_2 (1.2 ml, 15 mmol), the whole mixture being degassed through freeze-thaw cycles. The mixture was stirred for 1 h at 60 °C, cooled to room temperature, and then diluted with Et_2O. The mixture was washed with a sat. aqueous NH_4Cl solution, and the aqueous layer was extracted with Et_2O (×3). The combined organic extract was successively washed with water, a sat. aqueous Na_2SO_3 solution and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered through a cotton pad, and concentrated *in vacuo*. The residue was purified by column chromatography (70 g of the silica gel, hexane/CH_2Cl_2 = 1:3 to 1:2) to afford methylene ketal **11** (1.86 g, 74% in 2 steps) as a colorless powder. Mp 126.5–128 °C; IR (KBr): ν_{max} (cm^{-1}) 3032, 2886, 1952, 1405, 1068, 952; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 5.01 (2H, s, OCH_2Ph), 6.01 (2H, s, OCH_2O), 6.73 (1H, s, Ar), 7.26–7.49 (11H, m, Ar), 7.62–7.73 (4H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 71.9, 101.1, 106.1, 114.4, 121.0, 127.1, 127.6, 127.7, 127.8, 128.0, 128.4, 128.7, 130.3, 132.2, 135.9, 137.2, 139.5, 146.4, 151.5. *Anal.* Calcd. for $C_{26}H_{20}O_3$: C, 82.08; H, 5.30%. Found: C, 82.08; H, 5.36%.

*4,7-Diphenylbenzo[d][1,3]dioxol-5-ol (**12**).* Compound **11** (1.50 g, 4.00 mmol), EtOAc (80 ml), EtOH (40 ml), and 10% Pd/C (1.5 g, wet water content = 55 wt %, purchased from Kawaken Fine Chemicals Co., Ltd.) were placed in a round-shaped flask (200 ml) connected to a three-way cock. The atmosphere in the reaction vessel was replaced with nitrogen, and then filled with hydrogen (1 atm). After stirring for 5 h at room temperature, the catalyst was filtered off through a pad of Hyflo Super-Cel® (rinsed with EtOAc). The combined filtrate was concentrated under reduced pressure to afford **12** (1.10 g), which was used in the next reaction without further purification. IR (KBr) ν_{max} (cm^{-1}): 3529, 3020, 2888, 1404, 1057; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 4.97 (1H, brs, O*H*), 5.98 (2H, s, OCH_2O), 6.72 (1H, s, Ar), 7.31–7.59 (8H, m, Ar), 7.71–7.77 (2H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm): 101.2, 106.6, 111.4, 122.1, 127.7, 127.8, 128.5, 128.7, 129.3, 129.8, 131.1, 135.6, 138.6, 145.9, 148.0; HR-MS (FAB, negative): calcd. For $C_{19}H_{13}O_3$ (M − H), 289.0865; found, 289.0869.

*Phlebiarubrone (**4**).* Potassium nitrosodisulfonate (4.90 g, 18.1 mmol) was dissolved in H_2O (100 ml). To the resulting purple solution was added a solution of **12** (1.05 g, 3.62 mmol) in acetone (50 ml). The reaction mixture was stirred at room temperature for 3 h, and then extracted with CH_2Cl_2 (×4). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (silica gel 50 g, CH_2Cl_2/MeOH = 1:0 to 10:1) to afford **4** (1.11 g, 93% in 2 steps) as red crystals. Mp 248–250 °C (lit.[8] 248–250 °C) ($CHCl_3$); IR (KBr) ν_{max} (cm^{-1}): 2926, 1646, 1496, 1357, 1060, 963, 812; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 6.13 (2H, s, OCH_2O), 7.34–7.48 (6H, m, Ar), 7.60–7.66 (4H, m, Ar); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 102.9, 113.8, 128.4, 128.8, 128.9, 129.6, 156.4, 176.3. *Anal.* Calcd. for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97%. Found: C, 74.82; H, 4.27%.

*Dihydro-phlebiarubrone monoacetate (**13**).* To a suspension of **4** (102 mg, 0.34 mmol) in Ac_2O (10 ml) was added Zn–Cu (130 mg, 1.01 mmol). After stirring at 40 °C for 20 min, the reaction mixture was cooled to 0 °C and quenched with AcOH (a few drops). The mixture was filtered through the pad of Hyflo Super-Cel® and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5 g of silica gel, CH_2Cl_2/hexane = 2:1 to 3:1) to afford **13** (104 mg, 90%) as a white solid. Mp 168–170 °C; IR (KBr) ν_{max} (cm^{-1}): 3393, 3063, 2900, 1748, 1715, 1415, 1231, 1057; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 2.10 (3H, s, COCH_3), 4.94 (1H, s, O*H*), 5.94 (2H, s, OCH_2O), 7.34–7.46 (4H, m, Ar), 7.47–7.53 (4H, m, Ar), 7.57–7.61 (2H, m, Ar), 7.57–7.61 (2H, m, Ar); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 20.5, 101.3, 112.0, 117.3, 128.1, 128.4, 128.5, 129.0, 129.5, 129.9, 130.8, 131.6, 138.7, 139.8, 142.9, 169.2.

*Ustalic acid dimethyl ester (**14**).* Into a flask was placed phlebiarubrone **4** (40.0 mg, 0132 mmol) and $Pb(OAc)_4$ (1.16 g, 2.62 mmol). The reaction vessel was evacuated and then filled with nitrogen. Toluene (3 ml) and MeOH (2 ml) were added, the mixture was stirred at room temperature for 41 h, and then filtered through a pad of Hyflo Super-Cel®. The filtrate was diluted with water, and ethylene glycol (a few drops) was added. The resulting solution was extracted with Et_2O. The combined organic layers were successively washed with water (×1), a sat. aqueous $NaHCO_3$ solution (×1), and water (×1), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (5 g of silica gel, EtOAc/hexane = 1:5) followed by preparative TLC (EtOAc/hexane = 1:2, then CH_2Cl_2) to afford ustalic acid dimethyl ester **14** (2.5 mg, 5.2%) as a yellow solid. IR (KBr) ν_{max} (cm^{-1}): 2925, 1718, 1636, 1435, 1296, 1220, 1101; ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 3.73 (6H, s, COOCH_3 × 2), 5.42 (2H, s, OCH_2O), 7.31–7.41 (10H, m, Ar); ^{13}C-NMR (75 MHz, $CDCl_3$) δ (ppm):

52.2, 96.1, 115.4, 128.0, 128.1, 130.0, 134.6, 148.8, 167.7; EI-MS m/z 366 (M^+); HR-MS (FAB, positive): calcd. for $C_{21}H_{19}O_6$ (M + H), 367.1182; found, 367.1179.

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