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POLYPHOSPHORIC ACID–MEDIATED, ONE-POT, NOVEL REACTIONS TO BUILD POLYMETHOXYARYLNAPHTHALENE LIGNANS

Guilong Zhao,[1] Fuxu Zhan,[2] Zhifeng Wang,[3] Weiren Xu,[1] Yuli Wang,[1] Wei Liu,[1] Lida Tang,[4] and Jianwu Wang[2]

[1]*Tianjin Key Laboratory of Molecular Design and Drug Discovery, Tianjin Institute of Pharmaceutical Research, Tianjin, China*

[2]*School of Chemistry and Chemical Engineering, Shandong University, Jinan, China*

[3]*School of Chemistry and Chemical Engineering, Qufu Normal University, Jining, China*

[4]*Tianjin State Key Laboratory of Pharmacokinetics and Pharmacodynamics, Tianjin Institute of Pharmaceutical Research, Tianjin, China*

The one-pot reaction of succinic anhydride with 1,2-dimethoxybenzene furnished two structurally complicated polymethoxyarylnaphthalene lignans, polymethoxyarylnaphthol* 1 *as the minor product and polymethoxynaphtho[1,2-*b*]oxacycloheptatrienone* 2 *as the major product, in the presence of a small amount of polyphosphoric acid (PPA) as catalyst at 140°C and yielded* 2 *as a single product in good yield when a large amount of PPA as solvent was employed at 60–80°C. The novel structures of* 1 *and* 2 *were elucidated from* ^{1}H *NMR,* ^{13}C *NMR, infrared (IR), and Electrospray ionization–mass spectrometry (ESI-MS) and further confirmed by x-ray diffractions. The possible mechanisms for the formation of* 1 *and* 2 *were also proposed.

Keywords: Arylnaphthalene lignan; Friedel–Crafts acylation; one pot; polyphosphoric acid; synthesis; x-ray diffraction

INTRODUCTION

Polymethoxyarylnaphthalene lignans belong structurally to arylnaphthalene lignans, and the latter often possess two kinds of strongly electron-donating groups, such as methoxy groups and methylenedioxy groups. Polymethoxyarylnaphthalene lignans constitute an important class of naturally occurring bioactive products that possess hypocholesterolemic,[1] antirheumatic,[2] anti-HIV,[3] and antitumor[4] activities and can also be employed as apical sodium codependent bile acid transporter

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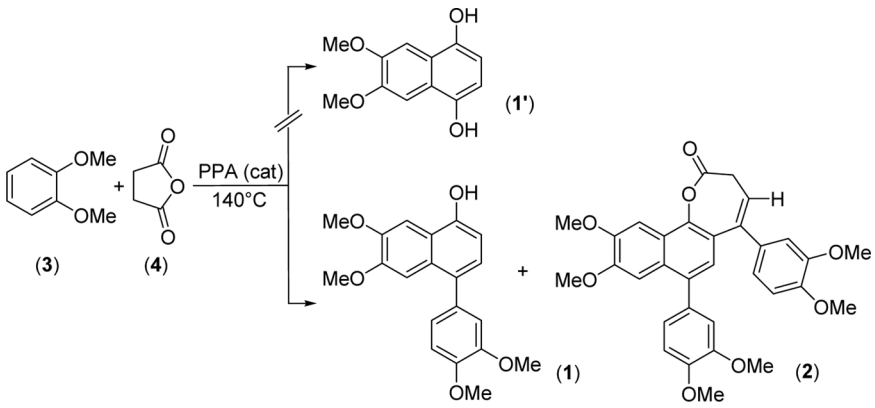
Address correspondence to Guilong Zhao, Tianjin Key Laboratory of Molecular Design and Drug Discovery, Tianjin Institute of Pharmaceutical Research, Tianjin 300193, China. E-mail: zhao_guilong@126.com and Professor Jianwu Wang, School of Chemistry and Chemical Engineering, Shandong University, Jinan 250100, China. E-mail: jwwang@sdu.edu.cn



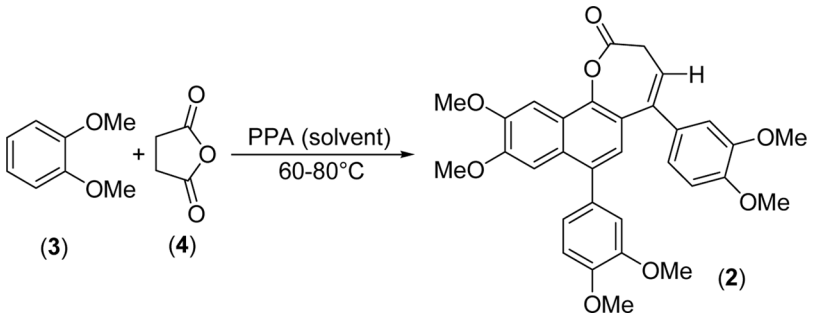
Scheme 1. Reaction of **3** and **4** in the presence of PPA as catalyst at 140°C to yield polymethoxyarylnaphthalene lignans **1** and **2**.

inhibitors.[5] However, because of their nonconventional structures and the presence of a number of sterically congested, strongly electron-donating groups in one molecule, such as methoxy groups and/or methylenedioxy groups, the synthesis of polymethoxyarylnaphthalene lignans and their methylenedioxy counterparts were considerably challenging.[1–9]

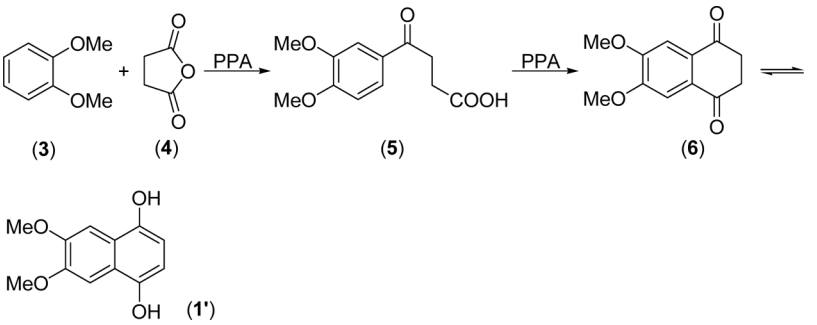
During the total synthesis of 4″-*O*-acetylmananthoside B,[10–13] unexpectedly we found a polyphosphoric acid–mediated novel reaction of succinic anhydride **3** with 1,2-dimethoxybenzene **4** to produce two polymethoxyarylnaphthalene lignans, polymethoxyarylnaphthol **1** as the minor product and polymethoxynaphtho[1,2-*b*]oxacycloheptatrienone **2** as the major product (Scheme 1). An optimized reaction of **3** with **4** could provide **2** specifically in good yield (Scheme 2). These two reactions and the novel lignans **1** and **2** could find applications in the synthesis of lignans and in the pharmaceutical field, respectively.

RESULTS AND DISCUSSION

During the total synthesis of 4″-*O*-acetylmananthoside B, we initially designed an intermediate **1′** and envisioned that this intermediate could be prepared from



Scheme 2. Reaction of **3** and **4** with PPA as solvent at 60–80°C to furnish **2** as a single product.



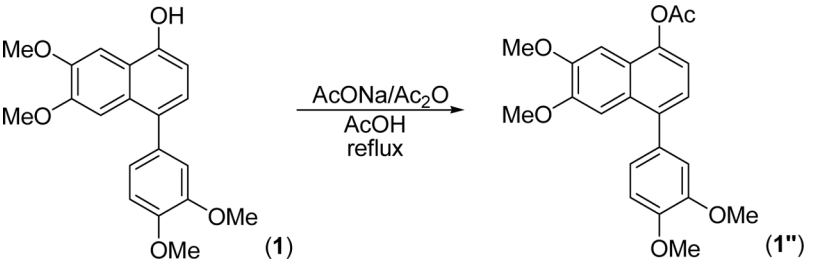
Scheme 3. Initially envisioned mechanism for the formation of **1′** from **3** and **4**.

1,2-dimethoxybenzene **3** and succinic anhydride **4** through two sequential Friedel–Crafts acylation reactions followed by tautomerization (Scheme 3).

It was found experimentally that the reaction of **3** with **4** in the presence of a number of Lewis acids or Brønsted acids in a variety of solvents at various temperatures did not occur at all, and therefore we devised a neat reaction of them in the presence of polyphoric acid (PPA) as catalyst. However, the reaction of **3** and **4** in the presence of PPA at 140°C furnished two products, which were isolated and identified as **1** (minor product) and **2** (major product), instead of the initially envisioned **1′** (Scheme 1).

To unequivocally elucidate the structure of the two products, product **1** was acetylated to its acetate **1″** by acetic anhydride (Scheme 4). The structure of **1** was elucidated from ^{1}H NMR,^{13}C NMR, infrared (IR), and Electrospray ionization–mass spectrometry (ESI-MS) of both **1** and **1″** and further confirmed by the x-ray diffractions of **1″** (Fig. 1), and the structure of **2** was determined from the spectroscopic methods aforementioned and also further confirmed by the x-ray diffraction of **2** as a cocrystal of **2** and ethyl acetate (Fig. 2).

Encouraged by this interesting one-pot reaction and the novel structures of **1** and **2**, in particular the potential applications of these two lignans in the pharmaceutical field, we then optimized this reaction. After considerable experimentation, the optimal reaction conditions for this reaction were as follows: (1) the molar ratio of **3**/**4** ranges from 0.5–2.0, (2) the ratio of **3**/**4** by weight of PPA to total amounts of **3** and **4** is 5/20, and (3) reaction temperature is 140°C.



Scheme 4. Acetylation of **1** with acetic anhydride to give rise to its acetate **1″**.

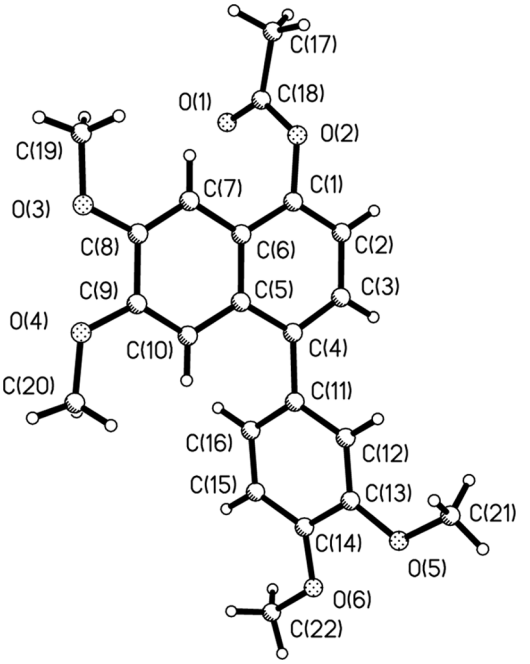


Figure 1. Crystal structure of **1**″.

Given that the reaction of **3** and **4** under the reaction condition described produced two products (**1** and **2)** simultaneously and that the separation of them required column chromatography, we therefore continued the optimization of this reaction with an expectation to produce both of them specifically. After a lot of

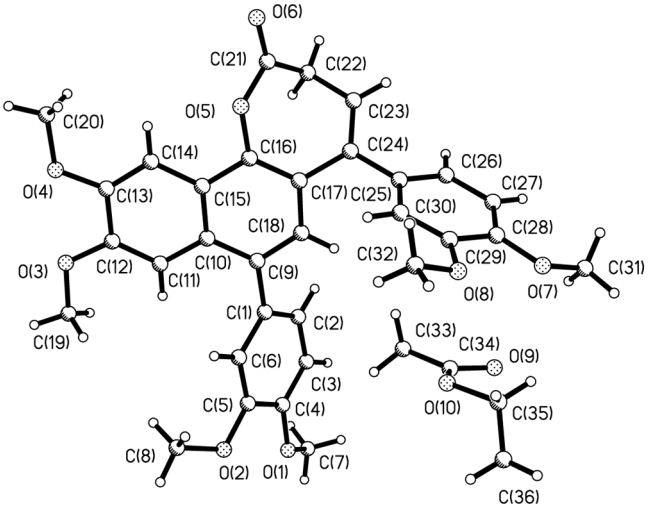
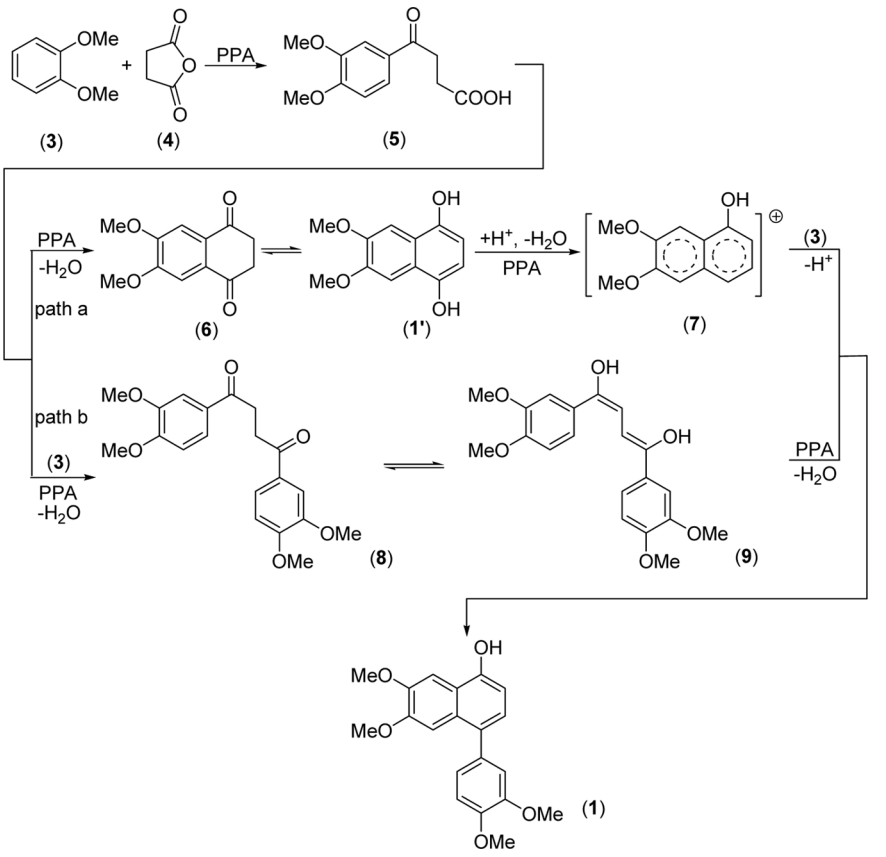


Figure 2. Cocrystal structure of **2** with ethyl acetate.

experimentation, compound **2** could be produced individually. Thus, **3** and **4** were heated at 60–80°C with PPA as solvent to provide **2** as a single product in good yield (Scheme 2). Nonetheless, attempts to optimize the reaction condition to furnish **1** as a single product were unsuccessful. Parenthetically, **1** and **2** were always produced as a mixture if a catalytic amount of PPA was employed and the reaction was carried out at high temperatures, and the proportion of **1** in the product mixture reached up to maximum under the optimized reaction conditions.

After structures of **1** and **2** were determined unambiguously, we commenced to investigate the mechanisms for the formation of the two novel products and herein propose the possible mechanisms for their formations.

Two possible mechanisms for the formation of **1**, each involving two Friedel–Crafts acylations and one Friedel–Crafts alkylation, were proposed, as represented by path a and path b in Scheme 5. Compound **3** underwent Friedel–Crafts acylation with **4** in the presence of PPA as catalyst to give β-benzoylpropionic acid **5**. Following path a, **5** underwent intramolecular Friedel–Crafts acylation catalyzed by PPA to afford diketone **6**, which tautomerized to form naphthalene-1,4-diol **1′**. In the

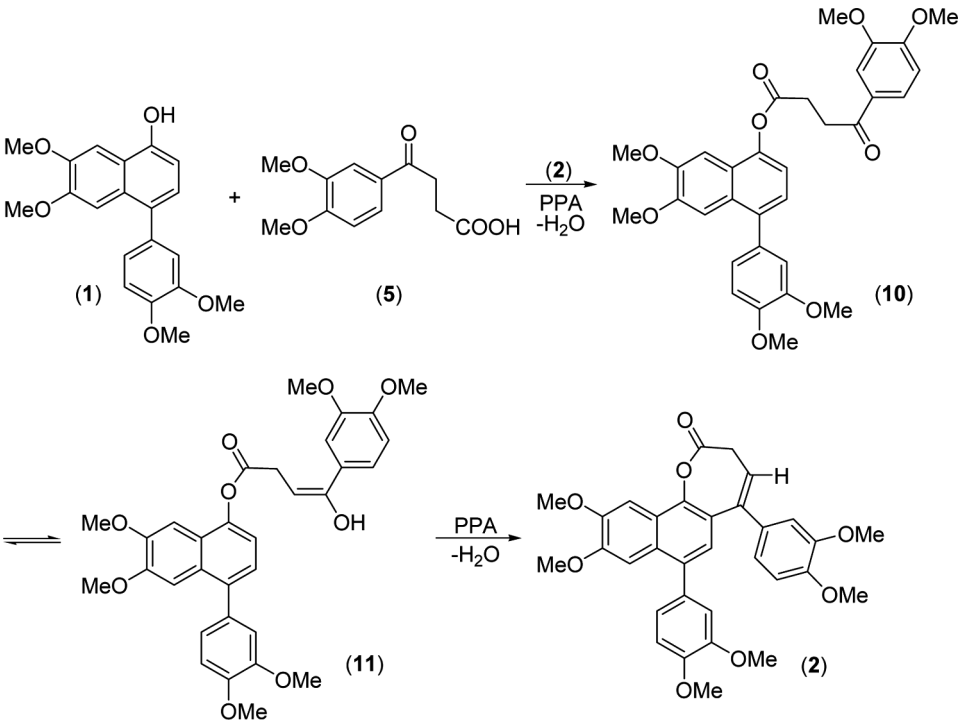


Scheme 5. Two possible mechanisms for the formation of **1**.

presence of PPA, one hydroxyl group of **1′** was protonated followed by dehydration to give rise to a transient carbocation **7**, which was stabilized by two fused phenyl rings, one hydroxyl group, and two methoxy groups, and therefore was considerably more stable than conventional aromatic carbocations. Carbocation **7** was trapped by another molecule of **3** to furnish **1** through Friedel–Crafts alkylation. Alternatively, following path b, compound **3** underwent Friedel–Crafts acylation with β-benzoylpropionic acid **5** in the presence of PPA as catalyst to yield diacetophenone **8**, which tautomerized to give dienol **9**. One hydroxyl group in **9** was protonated by PPA followed by intramolecular dehydration to produce **1** via intramolecular Friedel–Crafts alkylation.

The possible mechanism for the formation of **2** is proposed in Scheme 6. The esterification of β-benzoylpropionic acid **5** with **1**, both of which were already presented in Scheme 4, was effected in the presence of PPA as catalyst to deliver ester **10**, which tautomerized to give enol **11**. Finally, enol **11** yielded **2** after the protonation of its hydroxyl group by PPA followed by dehydration through intramolecular Friedel–Crafts alkylation.

These two reactions may find applications in the synthesis of arylnaphthalene lignans. The two polymethoxyarylnaphthalene lignans **1** and **2** may also find applications in the pharmaceutical field. The investigation of the pharmacodynamic properties of **1** and **2**, along with their derivatives, is in progress.



Scheme 6. Possible mechanism for the formation of **2**.

EXPERIMENTAL

Melting points were determined with an XT-4 microscopic melting-point apparatus and are uncorrected. IR spectra were recorded on a Thermo Nicolet Avtar Fourier transform (FT)–IR spectrophotometer as KBr discs. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC300 or AC400 spectrometer at 300 MHz or 400 MHz for ^{1}H NMR and at 75 MHz or 100 MHz for ^{13}C NMR, with dimethyl sulfoxide (DMSO-d_6) or $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. The ESI-MS spectra were taken on an ABI API4000 system. Elemental analyses were performed with an Elementar EI Vario EL III CHN analyzer.

6,7-Dimethoxy-1-(3,4-dimethoxyphenyl)naphth-4-ol (1) and 5,7-Di(3,4-dimethoxyphenyl)-2,3-dihydro-9,10-dimethoxy-1-oxanaphtho[1,2-*b*]-cycloheptatrien-2-one (2)

A 250-mL, round-bottomed flask was charged with 10.0 g (72.5 mmol) of 1,2-dimethoxybenzene **3** and 10.0 g (100 mmol) of succinic anhydride **4**, and the flask was heated in an oil bath held at 140°C until all the starting materials were melted to a clear solution. In a 25-mL beaker, 3.0 g of phosphorus pentaoxide were carefully added to 2.0 g of 85% phosphoric acid portionwise while stirring to produce freshly prepared PPA as a viscous, colorless oil. The prepared PPA was added in one portion to the molten materials, and the resultant mixture was stirred at 140°C for 3 h.

On slight cooling, 50 mL of acetone was added with care to the reaction flask and the stirring was continued for 15 min to give a purple solution. This solution was poured into 300 mL of ice water, and the aqueous mixture thus obtained was brought to pH 14 with concentrated aqueous sodium hydroxide, warmed on a hot-water bath until a clear purple solution formed, and then brought back to pH 4–5 with concentrated hydrochloric acid. This aqueous solution was exacted with three 50-mL portions of DCM, and the combined exacts were washed with saturated brine, dried over sodium sulfate, and evaporated on a rotary evaporator to afford a residue, which was separated and purified by column chromatography to furnish **1** and **2** as white solids.

Compound **1**, white solid, mp 198–200°C, 3.82 g, yield 31%. IR (KBr): ν 3374, 1600, 1513, 1495, 1259, 1171 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55 (s, 1H), 7.24 (s, 1H), 7.11–7.13 (d, 1H, $J = 7.5$ Hz), 6.97–7.02 (m, 3H), 6.74–6.77 (d, 1H, $J = 7.8$ Hz), 3.83, 3.90, 3.97, 4.05 (4 s, 3H each). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.83, 149.81, 148.87, 148.63, 148.02, 133.97, 131.75, 128.77, 125.19, 122.12, 119.79, 113.34, 111.18, 107.03, 105.01, 100.97, 55.95, 55.71. ESI-MS, $m/z = 341.4$ ($[M + H]^+$), 358.4 ($[M + NH_4]^+$), 698.6 ($[2M + NH_4]^+$), 703.5 ($[2M + Na]^+$). Elemental analysis calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.47; H, 5.90.

Compound **2**, white solid, mp 202–204°C, 6.42 g, yield 49%. IR (KBr): ν 1763, 1621, 1510, 1465, 1258, 1246 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.59 (s, 1H), 7.26 (s, 1H), 7.03–7.06 (d, 1H, $J = 8.4$ Hz), 6.99–7.00 (d, 1H, $J = 2.0$ Hz), 6.95–6.97 (d, 1H, $J = 8.4$ Hz), 6.957–6.962 (d, 1H, $J = 2.0$ Hz), 6.90–6.91, 6.92–6.93 (dd, 1H, $J = 2.0$ Hz and 8.0 Hz), 6.92 (s, 1H), 6.858–6.862, 6.878–6.883 (dd, 1H, $J = 2.0$ Hz

and 8.2 Hz), 6.32–6.36 (t, 1H, $J = 7.2$ Hz), 3.97, 3.78, 3.76, 3.75, 3.73, 3.72 (6 s, 3H each), 3.20 (bs, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 168.93, 150.34, 149.87, 148.92, 148.60, 148.48, 148.27, 144.50, 141.33, 134.34, 131.87, 131.57, 127.43, 125.46, 122.23, 121.54, 121.41, 121.00, 119.20, 113.07, 112.01, 111.85, 111.60, 104.87, 101.46, 55.52, 55.48, 55.44, 55.31, 34.44. ESI-MS, m/z = 543.4 ($[M + H]^+$), 560.4 ($[M + NH_4]^+$), 565.4 ($[M + Na]^+$), 581.3 ($[M + K]^+$). Elemental analysis calcd. for $C_{32}H_{30}O_8$: C, 70.84; H, 5.57. Found: C, 70.75; H, 5.59.

Suitable crystals of **2** for x-ray single-crystal diffraction were obtained by slow evaporation of a solution of **2** in DCM/ethyl acetate/petroleum ether at room temperature. A colorless crystal of **2** with dimensions of 0.24 mm × 0.18 mm × 0.10 mm was mounted on a glass fiber in a random orientation at 113(2) K. The determination of unit cell and data collection were performed with Mo$K\alpha$ radiation ($\lambda = 0.71073$ Å) on a Bruker Smart CCD diffractometer with a ψ-ω scan mode. A total of 10476 reflections including 5374 independent ones ($R_{int} = 0.0307$) were collected in the range of $3.24° < \theta < 25.02°$, of which 3843 were observed [$I > 2\sigma(I)$] and used in the structure determination and refinements. The structure was solved by direct methods with SHELXS-97 program.[14] The nonhydrogen atoms were refined anisotropically, and the hydrogen atoms were determined with theoretical calculation. A full-matrix least-squares refinement gave $R_1 = 0.0640$, $wR_2 = 0.1830$ [$w = 1/[\sigma^2(F_o^2) + (0.1138P)^2 + 0.7150P]$, where $P = (F_o^2 + 2F_c^2)/3$], $S = 1.099$, $(\Delta\rho)_{max} = 1.057$, and $(\Delta\rho)_{min} = -0.614$ e · Å^{-3}. The crystal is triclinic, and its space group is P-1, with $a = 11.002(2)$ Å, $b = 12.141(2)$ Å, $c = 12.682(3)$ Å, $\alpha = 79.04(3)°$, $\beta = 72.43(3)°$, $\gamma = 73.90(3)°$, $V = 1541.1(5)$ Å^3, $Z = 2$, $D_c = 1.359$ g · cm^{-3}, $F(000) = 668$, and $\mu = 0.099$ mm^{-1}. The determined empirical formula of this crystal, $C_{36}H_{30}O_{10}$, with formula weight 630.66, is consistent with the cocrystal of **2** and one molecule of ethyl acetate.

6,7-Dimethoxy-1-(3,4-dimethoxyphenyl)naphth-4-ol Acetate (1″)

Into a 100-mL, round-bottomed flask, 3.40 g (10 mmol) of **1**, 1.00 g (12.2 mmol) of anhydrous sodium acetate, 20 mL of acetic anhydride, and 10 mL of glacial acetic acid were introduced, and the resulting mixture was stirred at reflux for 1 h.

On cooling, the reaction mixture was poured into 200 mL of cooled water, and the resulting mixture was stirred at room temperature for 3 h until the complete hydrolysis of acetic anhydride. The acidic aqueous solution thus obtained was exacted with three 50-mL portions of DCM, and the combined extracts were washed with saturated brine, dried over sodium sulfate, and evaporated on a rotary evaporator to afford the crude product as a residue, which was purified by column chromatography to yield the pure product **1″** as colorless crystals. Mp 168–170°C, 3.71 g, yield 97%. IR (KBr): ν 1756, 1485, 1512, 1605 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.25–7.29 (m, 2H), 7.14–7.16 (m, 2H), 6.99–7.07 (m, 3H), 3.82, 3.90, 3.97, 4.02 (4 s, 3H each). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.61, 149.79, 148.61, 148.25, 144.83, 136.70, 133.33, 128.81, 124.95, 122.55, 122.02, 116.14, 113.11, 111.06, 105.33, 99.85, 55.92, 55.80, 55.76, 21.15. Elemental analysis calcd. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 69.04; H, 5.81.

Crystals of **1″** suitable for x-ray single-crystal diffraction were obtained by slow evaporation of a solution of **1″** in DCM/ethyl acetate/petroleum ether at room

temperature. A colorless crystal of **1″** with dimensions of 0.24 mm × 0.18 mm × 0.10 mm was mounted on a glass fiber in a random orientation at 273(2) K. The determination of unit cell and data collection were performed with Mo$K\alpha$ radiation ($\lambda = 0.71073$ Å) on a Bruker Smart CCD diffractometer with a ψ-ω scan mode. A total of 14060 reflections including 3271 independent ones ($R_{int} = 0.0485$) were collected in the range of $1.61° < \theta < 24.80°$, of which 2049 were observed [$I > 2\sigma(I)$] and used in the structure determination and refinements. The structure was solved by direct methods with SHELXS-97 program.[14] The nonhydrogen atoms were refined anisotropically, and the hydrogen atoms were determined with theoretical calculation. A full-matrix least-squares refinement gave $R_1 = 0.0447$, $wR_2 = 0.1071$ [$w = 1/[\sigma^2(F_o^2) + (0.0624P)^2 + 0.3251P]$, where $P = (F_o^2 + 2F_c^2)/3$], $S = 1.010$, $(\Delta\rho)_{max} = 0.261$, and $(\Delta\rho)_{min} = -0.210\ e \cdot Å^{-3}$. The crystal is monoclinic, and its space group is $P2_1/c$, with $a = 12.8203(3)$ Å, $b = 8.3471(2)$ Å, $c = 18.1518(4)$ Å, $\alpha = 90°$, $\beta = 99.270(2)°$, $\gamma = 90°$, $V = 1917.10(8)$ Å^3, $Z = 4$, $D_c = 1.325\ g \cdot cm^{-3}$, $F(000) = 808$, and $\mu = 0.096\ mm^{-1}$. The determined empirical formula of this crystal, $C_{22}H_{22}O_6$, with formula weight 382.40, is consistent with the acetate of **1**.

5,7-Di(3,4-dimethoxyphenyl)-2,3-dihydro-9,10-dimethoxy-1-oxanaphtho-[1,2-*b*]cycloheptatrien-2-one (2)

In a 250-mL, round-bottomed flask, 20 g of 85% phosphoric acid and 30 g of phosphorus pentaoxide were carefully added portionwise while stirring. The resulting mixture was stirred to give 50 g of freshly prepared PPA as a viscous colorless oil. Subsequently, 5.0 g (36.2 mmol) of 1,2-dimethoxybenzene **3** and 5.0 g (50 mmol) of succinic anhydride **4** were added in one portion, and the resultant mixture was stirred at 60–80°C for 3 h.

On slight cooling, the reaction mixture was slowly poured into 400 mL of ice water, and the mixture thus obtained was stirred for 1 h. Concentrated sodium hydroxide was slowly added to neutralize the aqueous mixture to pH 5–7, and the precipitate was collected via filtration with suction. The filtrate was back-exacted with three 50-mL portions of DCM, and the combined exacted were mixed with the collected precipitate to afford a solution, which was washed with brine, dried over sodium sulfate, and evaporated on a rotary evaporator to furnish the product **2** as a residue. The crude product was purified by column chromatography to yield the pure product as a white solid (5.62 g, yield 86%).

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REFERENCES

1. Mori, S.; Takechi, S. T.; Shimizu, S.; Kida, S.; Iwakura, H.; Hajima, M. Convergent synthesis of S-8921, a new potent hypocholesterolemic arylnaphthalene lignan analog. *Tetrahedron Lett.* **1999**, *40*, 1165–1168.

2. Baba, A.; Oda, T.; Taketomi, S.; Notoya, K.; Nishimura, A.; Makino, H.; Sohda, T. Studies on disease-modifying antirheumatic drugs, III: Bone resorption inhibitory effects of ethyl 4-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2-(1,2,4-triazol-1-ylmethyl)quinoline-3-carboxylate (TAK-603) and related compounds. *Chem. Pharm. Bull.* **1999**, *47*, 369–374.
3. Sagar, K. S.; Chang, C. C.; Wang, W. K.; Lin, J. Y.; Lee, S. S. Preparation and anti-HIV activities of retrojusticidin B analogs and azalignans. *Bioorg. Med. Chem.* **2004**, *12*, 4045–4054.
4. Ding, H. X.; Lu, W.; Li, H. B.; Yang, L. X.; Zhang, Q. J.; Zhou, C. X.; Wu, X. M.; Baudoin, O.; Cai, J. C.; Guéritte, F.; Zhao, Y. Synthesis and biological evaluation of novel compounds related to 1-arylnaphthalene lignans and isoquinolines. *Chem. Biodiversity* **2005**, *2*, 1217–1231.
5. Tollefson, M. B.; Vernier, W. F.; Huang, H. C.; Chen, F. P.; Reinhard, E. J.; Beaudry, J.; Keller, B. T.; Reitz, D. B. A novel class of apical sodium co-dependent bile acid transporter inhibitors: The 2,3-disubstituted-4-phenylquinolines. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 277–279.
6. Sato, Y.; Tamura, T.; Kinbara, A.; Mori, M. Synthesis of biaryls via palladium-catalyzed [2 + 2 +2] cocyclization of arynes and diynes: Application to the synthesis of arylnaphthalene lignans. *Adv. Synth. Catal.* **2007**, *349*, 647–661.
7. Sato, Y.; Tamura, T.; Kinbara, A.; Mori, M. Arylnaphthalene lignans through Pd-catalyzed [2 + 2 + 2] cocyclization of arynes and diynes: Total synthesis of taiwanins C and E. *Angew. Chem. Int. Ed.* **2004**, *43*, 2436–2440.
8. Zheng, X. F.; Wang, X. L.; Chang, J. B.; Zhao, K. Novel rearrangement of 1H-2,3-benzoxazines to cyclic N-acyl hemiaminals: Application to the synthesis of 1-arylnaphthalene skeletal congeners. *Tetrahedron* **2008**, *64*, 39–44.
9. Harrowven, D. C.; Bradley, M.; Castro, J. L.; Flanagan, S. R. Total syntheses of justicidin B and retrojusticidin B using a tandem Horner–Emmons–Claisen condensation sequence. *Tetrahedron Lett.* **2001**, *42*, 6973–6975.
10. Susplugas, S.; Hung, N. V.; Bignon, J.; Thoison, O.; Kruczynski, A.; Sévenet, T.; Guéritte, F. Cytotoxic arylnaphthalene lignans from a vietnamese acanthaceae, *Justicia patentiflora*. *J. Nat. Prod.* **2005**, *68*, 734–738.
11. Chen, B.; Liu, Y.; Feng, C.; Li, G. B.; Zhang, L. G. Two new arylnaphthalene lignan glycosides from *Mananthes patentiflora*. *Chin. Chem. Lett.* **2002**, *13*, 959–962.
12. Zhao, G. L.; Jia, J.; Liu, J. Z.; Wang, J. W. Total synthesis of 4″-*O*-acetylmananthoside B, part I: Synthesis and tentative ozonolysis of a cyclohexadiene derivative. *Synth. Commun.* **2006**, *36*, 3821–3828.
13. Zhao, G. L.; Yu, Z. Y.; Li, Y.; Pang, L. N.; Wang, J. W. Total synthesis of 4″-*O*-acetylmananthoside B, part II: Synthesis of the disaccharide fragment. *Chin. J. Chem.* **2008**, *26*, 158–164.
14. Sheldrick, G. M. *SHELXL97: Program for the Refinement of Crystal Structure*; University of Göttingen: Germany, 1997.