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An Efficient Multigram Synthesis of Alkannin and Shikonin

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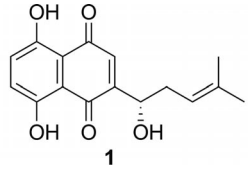
The concise and efficient total syntheses of alkannin (**1**) and shikonin (**2**), based on the resolution of a key acid intermediate, are achieved with excellent enantiomeric excesses and high overall yields (99 % *ee*, 15.6 % for **1** and 99.8 % *ee*, 11.9 % for **2**). The key steps of the synthetic strategy involve the convenient synthesis and separation of a pair of amide diastereoisomers and the mild hydrolysis of the amide to remove the amine chiral auxiliary, together with an efficient deprotection sequence of the methyl protecting groups.

Introduction

Alkannin (**1**) and shikonin (**2**), a pair of enantiomers which are extracted and identified from the roots of *Alkanna tinctoria* in Europe and *Lithospermum erythrorhizon* in the Orient, have been used independently for many centuries as natural red dyes and as crude drugs capable of accelerating wound healing.[1] Over the past few decades, the two natural products and their derivatives have been reported to have a wide variety of biological and pharmacological activities, such as immunostimulatory,[2] antibacterial,[3] anti-inflammatory,[4] antiviral,[5] analgesic,[6] angiostatic,[7] antithrombotic,[8] and antitumor[1,9] properties. Though these natural products can be isolated from many species of Boraginaceae, both as the free alcohols and as ester derivatives, their enantiomeric ratios vary not only with their habitats and species but also with their different derivatives,[10] as has been previously confirmed in our lab.[11] Thus, extraction and purification of **1** and **2** from natural resources proved unsatisfactory, because of inefficiency and providing products with low optical purity, and could not meet the demands. However, the syntheses of **1** and **2** have attracted the attention of many researchers.[10,12] Because of the high chemical reactivity of the naphthazarin moiety,[1] the concise and efficient syntheses of **1** and **2** remained elusive until recently, although their molecular structures are seemingly simple. This, in combination with the excellent biological properties of these natural products, motivated us to investigate new and efficient total syntheses.



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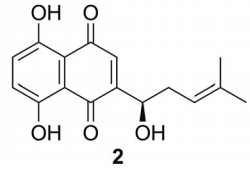

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Results and Discussion

Most successful syntheses reported for **1** and **2** involved using 1,4,5,8-tetramethoxynaphthalene derivatives[12a–12f] and were based on asymmetric syntheses[10,12d,12f,12i,12k,13] from over the past thirty years. The final deprotection sequences to reveal the naphthazarin moiety had poor yields, and the reagents were costly. The chiral reagents and intermediates were either expensive or difficult to obtain, and the enantioselectivity was very disappointing. One of the shortest and most elegant syntheses, which adopted a new protecting system (i.e., the methylene protecting group), was reported by Nicolaou. However, the final deprotection step, proceeding by electrolysis, resulted in low yields and was difficult to scale up, to say nothing of the possibilities for large-scale preparation.[10] Furthermore, the Weinreb amide used in this route was difficult to synthesize.

A practical and efficient synthetic route for alkannin (**1**) and shikonin (**2**) had to overcome several obstacles, such as: (1) to apply a resolution method without using an expensive chiral reagent, so that it would be more suitable for large-scale preparation and (2) to obtain the product with high optical purity, providing the possibility for new drug development in the future.

According to the retrosynthetic analysis in Scheme 1, we designed and obtained a racemic acid, whose structure is very similar to α-hydroxyphenylacetic acid (mandelic acid). The resolution of mandelic acid has already been fully explored and may provide some ideas for our resolution. We then expected to achieve a pair of chiral acids through a

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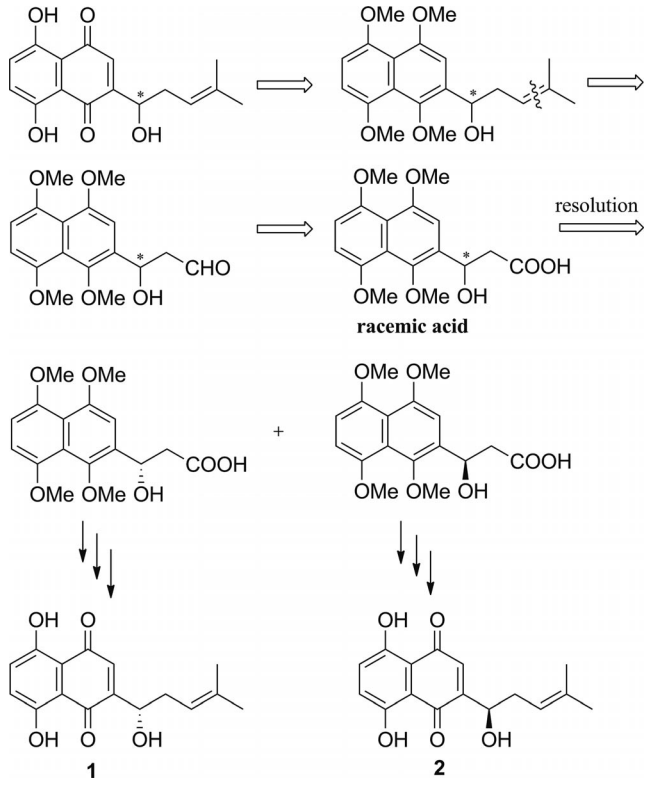
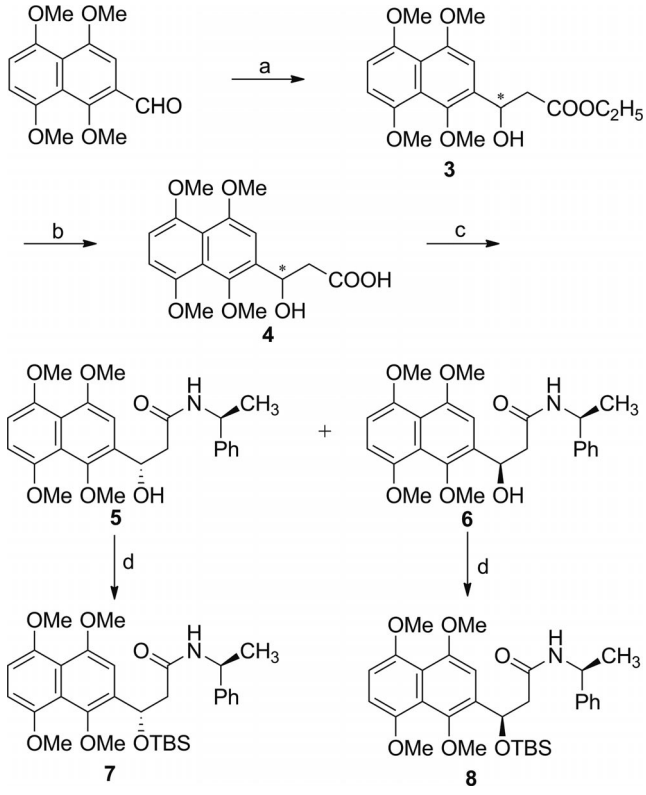
three-step protocol, which includes salt formation with a chiral amine, recrystallization, and dissociation. However, some chiral amines, such as (*S*)-1-phenylethylamine, 10,11-dimethoxystrychnine, chinine, and cinchonine, have proved impracticable for the formation of salts with the racemic acid.



Scheme 1. The retrosynthetic analysis of alkannin (**1**) and shikonin (**2**) to achieve a racemic acid.

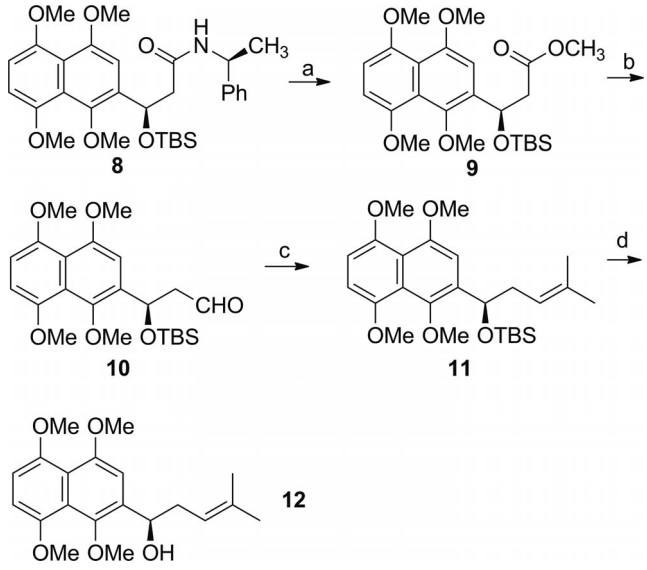


Scheme 2. The synthesis of key diastereomers **5**, **6** and **7**, **8**. Reagents and conditions: (a) Zn, $BrCH_2CO_2C_2H_5$, dry THF (tetrahydrofuran), room temp., 1 h, then 1,4,5,8-tetramethoxy-2-naphthaldehyde, room temp., 1 h, 92%; (b) NaOH (2 M solution), room temp., 1 h, then HCl (6 M solution), 99%; (c) (*S*)-1-phenylethylamine, BOP [bis(2-oxo-3-oxazolidinyl)phosphane], TEA (triethylamine), dry DMF (dimethylformamide), room temp., 3 h, **5** (54%), **6** (41%); (d) TBDPSCl, imidazole, DMAP [4-(dimethylamino)pyridine], room temp., 24 h, 96%.

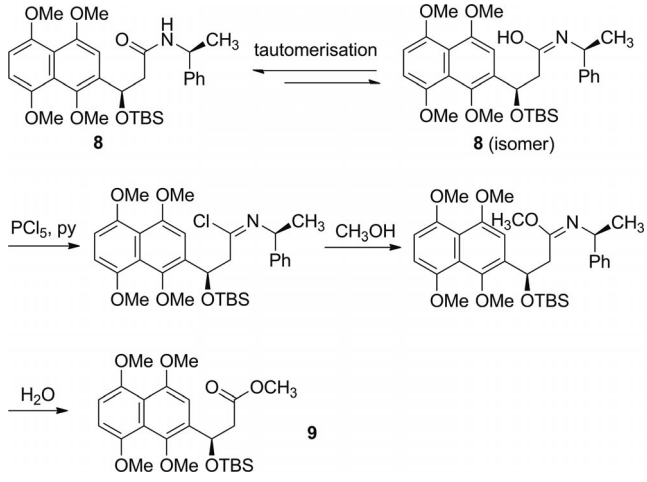
Luckily, the condensation of racemic acid **4** and (*S*)-1-phenylethylamine gave rise to two diastereomers (i.e., **5** and **6**), which were easily separated by one-step column chromatography on silica gel (petroleum ether/ethyl acetate, 3:2), because of the approximate double gap in their polarities (Scheme 2). The secondary hydroxy groups in the two diastereomers (i.e., **5** and **6**) were protected using *tert*-butyldiphenylsilyl chloride (TBDPSCl) to produce **7** and **8**, which could easily be purified further by recrystallization to ensure the optical purity. The starting material 1,4,5,8-tetramethoxy-2-naphthaldehyde was synthesized in good yield according to our reported procedures.[14] Racemic acid **4** was obtained by a Reformatsky reaction and subsequent hydrolysis.

The other synthetic steps starting from **7** to produce **1** are the same as those from **8** to produce **2**. We used the synthesis of **2** as our example. The hydrolysis of amide **8** to obtain ester derivative **9** was one of the most difficult steps (Scheme 3). After a series of experiments, we found the best hydrolysis method, occurring in 80% yield and using a one-pot three-step procedure which included chlorination [PCl_5, py (pyridine)], etherification (CH_3OH), and hydrolysis (H_2O, see Scheme 4). The optimum reaction conditions for each step, such as temperature, time, and ratio of the reagents, were explored. Compound **9** was reduced to corresponding aldehyde **10** with DIBALH (diisobutylaluminum hydride). A Wittig-type elongation of the resulting aldehyde using the ylide of 2-bromopropane afforded fully protected **11**. The deprotection of the side-chain hydroxy group provided key chiral intermediate **12** with a high enantioselectivity (≥99.8% *ee*). Many derivatives of **2** have been synthesized based on **12**.

After **12** was obtained, target molecule **2** could be produced in two steps by the reported literature procedures[12c,12d,12f,12g,12i] in 20% yield. This included oxidation by ammonium cerium(IV) nitrate (CAN) followed by deprotection of the second pair of methyl protecting groups with harsh and costly reagents ($Ag^{II}O$, HNO_3) that were impractical for large-scale preparation. However, the monosubstitution derivatives of naphthazarin (isomers **A** and **B**) have been reported to rapidly tautomerize and favor **A** by virtue of the stabilizing effect of the electron-donating alkyl group[10,15] (Scheme 5). Based on Couladouros' report,[12k] the synthesis of **2** was achieved according to three chemical operations in high yield (65%) with an excellent

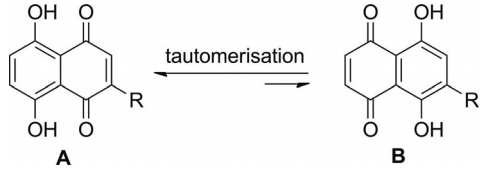


Scheme 3. The synthesis of key chiral intermediate **12**. Reagents and conditions: (a) PCl_5, pyridine, dry CH_2Cl_2, 0 °C, 8 h, then dry CH_3OH, –20 °C, 1 h, then H_2O, room temp., 12 h, 80%; (b) DIBALH, dry CH_2Cl_2, –78 °C, 12 h, 90%; (c) $Ph_3PCH(CH_3)_2Br$, *n*BuLi, dry Et_2O, 0 °C, 30 min, then **10**, room temp., 2 h, 75%; (d) TBAF (tetra-*n*-butylammonium fluoride), dry THF, room temp., 3 h, 95%.

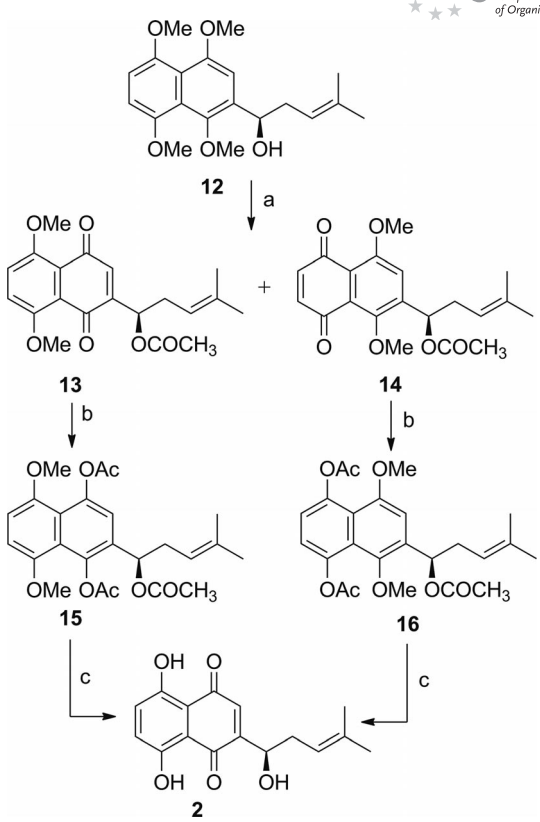


Scheme 4. The plausible hydrolysis mechanism of amide **8**.

enantioselectivity (≥99.8% *ee*) (Scheme 6). The preparation included acetylation–oxidation, reduction–acetylation, and oxidation–hydrolysis–neutralization–tautomerization reactions.



Scheme 5. Tautomerization of isomers **A** and **B**.



Scheme 6. The deprotection of the methyl protecting groups on naphthazarin moiety. Reagents and conditions: (a) Ac_2O, Et_3N, DMAP, dry CH_2Cl_2, room temp., 20 min, then CAN, CH_2Cl_2, room temp., 15 min, **13** (25%), **14** (67%); (b) Zn, Ac_2O, Et_3N, DMAP, 2 h, room temp., **15** (76%), **16** (86%); (c) CAN, CH_3CN, room temp., 10 min, then NaOH (1 M solution), 6 h, then HCl (10% solution), 85%.

Conclusions

Based on the practical synthesis and separation of a pair of amide diastereomers and their successful hydrolysis, we have demonstrated a new method of resolution to synthesize alkannin (**1**) and shikonin (**2**) in excellent enantiomeric excesses and high yields (99% *ee*, 15.6% for **1** and 99.8% *ee*, 11.9% for **2**) under mild conditions. (*S*)-1-phenylethylamine, the chiral reagent used for the resolution, is inexpensive and, therefore, practical for use in large-scale preparation. This groundbreaking development, together with the valuable approach for the deprotection of the methyl protecting groups on the naphthazarin core, has allowed us to complete the concise and practical syntheses of the two enantiomers alkannin (**1**) and shikonin (**2**). This research not only marks a breakthrough in the history of alkannin and shikonin syntheses, but also is of great benefit to the research and development of alkannin and shikonin and their analogs as new drugs.

Experimental Section

General Methods: All solvents and reagents were purified by standard techniques. Crude products were purified by column chromatography on silica gel of 100–200 mesh. NMR spectroscopic

data were recorded with a Mercury 300 (Varian) or AVANCE 400 (Bruker) spectrometers. Chemical shifts in ^1H and ^{13}C spectra were recorded with tetramethylsilane as an internal standard. Mass spectra were recorded with a Shimadzu LCMS-2010EV mass spectrometer. HRMS were recorded with a Waters Q-TOF Premier mass spectrometer. The HPLC system was equipped with a UV/Vis detector (G1315C/D), an Agillent 1200 series G1322A IV pump, and software for process control and data handling (Agilent ChemStation for LC 3D Systems). The chiral HPLC column used was a Sino-chiral OD column, no. 0A02014-C [packed with cellulose-tris(3,5-dimethylphenyl carbamate)], purchased from FunSea Beijing Technology Co. Ltd. (Beijing, China), 150 × 4.6 mm. The separations were also conducted at ambient temperature. The mobile phase was degassed before application.

Ethyl 3-Hydroxy-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanoate (3): Ethyl bromoacetate (167.0 g, 1.0 mol) was added dropwise to the solution of zinc powder (117.0 g, 1.8 mol) in dry THF (300 mL) over a period of 1 h, as the solution gently heated to reflux under a nitrogen atmosphere. The mixture was stirred for an additional 1 h at room temperature. Then, a solution of 1,4,5,8-tetramethoxynaphthalene-2-carbaldehyde (138.1 g, 0.5 mol) in THF (300 mL) was added to the mixture over 10 min at room temperature. After being stirred for 1 h, the reaction mixture was quenched with cold HCl (5% solution, 200 mL), and the resulting mixture was extracted with ethyl acetate (3 × 400 mL). The combined organic layers were washed with $NaHCO_3$ (2 × 200 mL) and brine (300 mL), dried with Na_2SO_4, and then evaporated under reduced pressure. Thus, the obtained crude residue was purified over silica gel [PE (petroleum ether)/EtOAc, 1:2) to give **3** (167.5 g, 0.46 mol, 92%) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.04 (s, 1 H, Ar), 6.75 (s, 2 H, Ar), 5.58 (dd, J = 9.6, 2.7 Hz, 1 H, C*H*OHCH$_2$), 4.13 (dd, J = 14.4, 7.2 Hz, 2 H, C*H*$_2$CH$_3$), 3.89 (s, 3 H, ArOC*H*$_3$), 3.86 (s, 3 H, ArOC*H*$_3$), 3.83 (s, 3 H, ArOC*H*$_3$), 3.70 (s, 3 H, ArOC*H*$_3$), 2.85–2.63 (m, 2 H, C*H*$_2$CO$_2$CH$_2$), 1.21 (t, J = 7.2 Hz, 3 H, CH$_2$C*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6 (*C*=O), 153.3 (C_{naph}OCH$_3$), 151.1 (C_{naph}OCH$_3$), 149.9 (C_{naph}OCH$_3$), 145.7 (C_{naph}OCH$_3$), 132.4 (C_{naph}CH), 122.3 (C_{naph}), 119.9 (C_{naph}), 108.0 (C_{naph}H), 107.3 (C_{naph}H), 105.0 (C_{naph}H), 65.0 (*C*HOH), 62.4 (OCH$_3$), 60.5 (*C*H$_2$CH$_3$), 57.5 (OCH$_3$), 56.7 (OCH$_3$), 56.6 (OCH$_3$), 42.4 (*C*H$_2$COOCH$_2$CH$_3$), 13.9 (*C*H$_3$) ppm. MS (ESI): m/z = 397 [M + Na]$^+$.

3-Hydroxy-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanoic Acid (4): To a solution of **3** (72.9 g, 0.2 mol) in methanol (400 mL) was added NaOH (2 M solution, 400 mL) dropwise, and the mixture was stirred for 2 h at room temperature. After completion of the reaction, most of the methanol was evaporated under reduced pressure. Then, the obtained crude residue was extracted with CH_2Cl_2 (3 × 150 mL). The aqueous phase was carefully acidified with HCl (6 M solution) to pH = 5 at 0–5 °C, and the nearly white solid precipitated out of the reaction mixture. Simple filtration and drying afforded **4** (66.5 g, 0.2 mol, 99%) as an off-white solid; m.p. 50–54 °C; ref.[12d] m.p. 51–52 °C. ^1H NMR [300 MHz, DMSO (dimethyl sulfoxide)]: δ = 7.10 (s, 1 H, Ar), 6.86 (dd, J = 18.9, 8.7 Hz, 2 H, Ar), 5.53 (t, J = 7.2 Hz, 1 H, C*H*OHCH$_2$), 3.84 (s, 3 H, ArOC*H*$_3$), 3.82 (s, 3 H, ArOC*H*$_3$), 3.76 (s, 3 H, ArOC*H*$_3$), 3.67 (s, 3 H, ArOC*H*$_3$), 2.76 (d, J = 6.3 Hz, 2 H, C*H*$_2$) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 172.5 (*C*=O), 152.9 (C_{naph}OCH$_3$), 151.0 (C_{naph}OCH$_3$), 149.8 (C_{naph}OCH$_3$), 145.2 (C_{naph}OCH$_3$), 134.7 (C_{naph}CH), 122.1 (C_{naph}), 119.3 (C_{naph}), 108.2 (C_{naph}H), 108.0 (C_{naph}H), 105.9 (C_{naph}H), 63.8 (*C*HOH), 62.1 (OCH$_3$), 57.1 (OCH$_3$), 56.8 (OCH$_3$), 56.6 (OCH$_3$), 44.0 (*C*H$_2$) ppm. MS (ESI): m/z = 359 [M + Na]$^+$.

(*S*)-3-Hydroxy-*N*-[(*S*)-1-phenylethyl]-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanamide (5) and (*R*)-3-Hydroxy-*N*-[(*S*)-1-phenylethyl]-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanamide (6): To a solution of **4** (50.4 g, 0.15 mol), BOP (66.4 g, 0.15 mol), TEA (16.7 g, 0.165 mol), and DMAP (0.015 mol) in dry DMF (200 mL) was added (*S*)-1-phenylethylamine (18.2 g, 0.15 mol) dropwise, and the mixture was stirred for 3 h at room temperature. After the completion of reaction, the reaction mixture was diluted with cold water (200 mL), and the resulting solution was extracted with EtOAc (3 × 300 mL). The combined organic layers were washed with brine (300 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the residue which was purified by silica gel column chromatography (PE/EtOAc, 3:2) to give **5** (33.8 g, 54%) and **6** (27.5 g, 41%) as light yellow foamy solids. Data for diastereomer **5**: IR (KBr): $\tilde{\nu}_{max}$ = 3468, 3066, 2929, 2835, 1643, 1600, 1543, 1454, 1362, 1257, 1074, 832, 802, 757, 701 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 5 H, Ar), 7.12 (s, 1 H, Ar), 6.82 (s, 2 H, Ar), 6.01 (d, J = 4.5 Hz, 1 H, CHOHCON*H*), 5.52 (dd, J = 8.7, 2.7 Hz, 1 H, NHC*H*CH$_3$), 5.14–5.02 (m, 1 H, C*H*OHCONH), 3.95 (s, 3 H, ArOC*H*$_3$), 3.94 (s, 3 H, ArOC*H*$_3$), 3.89 (s, 3 H, ArOC*H*$_3$), 3.74 (s, 3 H, ArOC*H*$_3$), 2.77–2.57 (m, 2 H, C*H*$_2$), 1.39 (d, J = 6.9 Hz, 3 H, NHCHC*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5 (*C*=O), 153.5 (C_{naph}OCH$_3$), 151.3 (C_{naph}OCH$_3$), 150.1 (C_{naph}OCH$_3$), 145.7 (C_{naph}OCH$_3$), 143.0 (C_{Ar}), 133.2 (C_{Ar}H), 128.6 (C_{Ar}H), 127.2 (C_{Ar}H), 126.0 (C_{naph}CH), 122.4 (C_{naph}), 120.1 (C_{naph}), 108.3 (C_{naph}H), 107.1 (C_{naph}H), 105.6 (C_{naph}H), 65.9 (*C*OH), 62.5 (OCH$_3$), 57.8 (OCH$_3$), 57.0 (OCH$_3$), 56.5 (OCH$_3$), 48.8 (*C*HCH$_3$), 43.4 (*C*H$_2$CO), 21.8 (*C*H$_3$) ppm. HRMS: calcd. for $C_{25}H_{29}NO_6$ 439.1995; found 439.1990. Data for diastereoisomer **6**: IR (KBr): $\tilde{\nu}_{max}$ = 3468, 3066, 2928, 2834, 1627, 1600, 1543, 1454, 1362, 1256, 1074, 834, 800, 757, 701 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.20–7.08 (m, 6 H, Ar), 6.82 (s, 2 H, Ar), 6.08 (d, J = 7.5 Hz, 1 H, CHOHCON*H*), 5.54 (d, J = 6.0 Hz, 1 H, NHC*H*CH$_3$), 5.12–5.03 (m, 1 H, C*H*OHCONH), 3.94 (s, 3 H, ArOC*H*$_3$), 3.90 (s, 3 H, ArOC*H*$_3$), 3.88 (s, 3 H, ArOC*H*$_3$), 3.76 (s, 3 H, ArOC*H*$_3$), 2.77–2.57 (m, 2 H, C*H*$_2$), 1.45 (d, J = 6.9 Hz, 3 H, NHCHC*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.7 (*C*=O), 153.5 (C_{naph}OCH$_3$), 151.4 (C_{naph}OCH$_3$), 150.1 (C_{naph}OCH$_3$), 145.6 (C_{naph}OCH$_3$), 143.0 (C_{Ar}), 133.3 (C_{Ar}H), 128.5 (C_{Ar}H), 127.1 (C_{Ar}H), 125.8 (C_{naph}CH), 122.4 (C_{naph}), 120.2 (C_{naph}), 108.3 (C_{naph}H), 107.2 (C_{naph}H), 105.6 (C_{naph}H), 66.0 (*C*OH), 62.5 (OCH$_3$), 57.9 (OCH$_3$), 56.9 (OCH$_3$), 56.6 (OCH$_3$), 48.8 (*C*HCH$_3$), 43.3 (*C*H$_2$CO), 21.9 (*C*H$_3$) ppm. HRMS: calcd. for $C_{25}H_{29}NO_6$ 439.1995; found 439.1990.

(*S*)-3-(*tert*-Butyldimethylsilyloxy)-*N*-[(*S*)-1-phenylethyl]-3-(1,4,5,8 tetramethoxynaphthalen-2-yl)propanamide (7): To a cooled (0 °C) solution of **5** (22 g, 0.05 mol), DMAP (1.22 g, 0.01 mol), and imidazole (6.80 g, 0.1 mmol) in dry CH_2Cl_2 (300 mL) was added dropwise a solution of *tert*-butyldiphenylsilyl chloride (9.04 g, 0.06 mol) in dry CH_2Cl_2 (50 mL), and the mixture was stirred for 24 h. After the completion of reaction, the mixture was diluted with water (200 mL), and the resulting solution was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were washed with brine (3 × 200 mL), dried with anhydrous Na_2SO_4, and evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (PE/EtOAc, 5:1) to give **7** which was purified further by recrystallization (PE/EtOAc, 4:1) to afford sufficiently pure **7** (26.5 g, 96%) as off-white crystals; m.p. 135–137 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3374, 2929, 2855, 1670, 1603, 1529, 1461, 1360, 1259, 1216, 1072, 1013, 951, 834, 777, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.09 (m, 5 H, Ar), 6.89 (s, 1 H, Ar), 6.70 (dd, J = 10.5, 9 Hz, 2 H, Ar), 6.06 (d, J = 7.2 Hz, 1 H, CHOHCON*H*), 5.57 (dd, J = 7.8, 3.3 Hz, 1 H, NHC*H*CH$_3$), 5.06–

4.97 (m, 1 H, C*H*OHCONH), 3.80 (s, 3 H, ArOCH_3), 3.78 (s, 3 H, ArOCH_3), 3.72 (s, 3 H, ArOCH_3), 3.66 (s, 3 H, ArOCH_3), 2.59–2.41 (m, 2 H, CH_2), 1.38 (d, J = 6.9 Hz, 3 H, NHCHCH_3), 0.78 (s, 9 H, *t*Bu*H*Si), –0.04 (s, 3 H, CH_3Si), –0.25 (s, 3 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4 (*C*=O), 153.2 (C_{naph}OCH$_3$), 151.4 (C_{naph}OCH$_3$), 150.3 (C_{naph}OCH$_3$), 145.4 (C_{naph}OCH$_3$), 143.4 (C_{Ar}), 134.2 (C_{Ar}H), 128.5 (C_{Ar}H), 127.2 (C_{Ar}H), 126.2 (C_{naph}CH), 122.7 (C_{naph}), 120.1 (C_{naph}), 108.0 (C_{naph}H) 107.9 (C_{naph}H), 106.0 (C_{naph}H), 66.7 (*C*H), 62.4 (O*C*H$_3$), 57.6 (O*C*H$_3$), 57.1 (O*C*H$_3$), 56.8 (O*C*H$_3$), 48.8 (*C*H$_2$), 47.3 (*C*HCH$_3$), 25.8 [C(*C*H$_3$)$_3$], 21.9 (CH*C*H$_3$), 18.0 [*C*(CH$_3$)$_3$], –4.78 (*C*Si), –5.07 (*C*Si) ppm. HRMS: calcd. for $C_{31}H_{43}NO_6Si$ 553.2860; found 553.2856.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-*N*-[(*S*)-1-phenylethyl]-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanamide (8): Following the same procedure as described for **7**, **8** was obtained as white crystals; m.p. 124–125.5 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3371, 2927, 2849, 1640, 1597, 1538, 1456, 1361, 1257, 1196, 1077, 1012, 946, 834, 780, 697 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.17 (m, 5 H, Ar), 6.98 (s, 1 H, Ar), 6.74 (s, J = 9.0, 2.1 Hz, 2 H, Ar), 6.13 (d, J = 6.9 Hz, 1 H, CHOHCON*H*), 5.60 (dd, J = 7.8, 3.0 Hz, 1 H, NHC*H*CH$_3$), 5.08–4.99 (m, 1 H, C*H*OHCONH), 3.84 (s, 3 H, 2 ArOCH_3), 3.82 (s, 6 H, ArOCH_3), 3.73 (s, 3 H, ArOCH_3), 2.65–2.47 (m, 2 H, CH_2), 1.40 (d, J = 6.9 Hz, 3 H, NHCHCH_3), 0.75 (s, 9 H, *t*Bu*H*Si), –0.08 (s, 3 H, CH_3Si), –0.22 (s, 3 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3 (*C*=O), 153.2 (C_{naph}OCH$_3$), 151.4 (C_{naph}OCH$_3$), 150.3 (C_{naph}OCH$_3$), 145.4 (C_{naph}OCH$_3$), 143.2 (C_{Ar}), 134.1 (C_{Ar}H), 128.5 (C_{Ar}H), 127.2 (C_{Ar}H), 126.4 (C_{naph}CH), 122.7 (C_{naph}), 120.1 (C_{naph}), 107.9 (C_{naph}H), 106.1 (C_{naph}H), 66.6 (*C*H), 62.4 (O*C*H$_3$), 57.5 (O*C*H$_3$), 57.0 (O*C*H$_3$), 56.9 (O*C*H$_3$), 48.8 (*C*H$_2$), 47.1 (*C*HCH$_3$), 25.7 [C(*C*H$_3$)$_3$], 21.7 (CH*C*H$_3$), 18.0 [*C*(CH$_3$)$_3$], –4.86 (*C*Si), –5.20 (*C*Si) ppm. HRMS: calcd. for $C_{31}H_{43}NO_6Si$ 553.2860; found 553.2858.

(*R*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanoate (9): To a cooled (0 °C) solution of phosphorus pentachloride (33.3 g, 0.16 mol) in dry CH_2Cl_2 (250 mL) was added pyridine (12.64 g, 0.32 mol) dropwise. After stirring for 30 min, **8** (22.1 g, 0.04 mol) was added, and the mixture was stirred for 8 h at 0 °C. Then, the reaction temperature was cooled to –30 °C, and dry methanol (200 mL) was added slowly keeping the reaction temperature below –20 °C. The solution turned dark red and was stirred for 1 h at –20 °C. Then, water (300 mL) was added, and the mixture was stirred at room temperature and was monitored by TLC. After completion of the reaction (12 h), the mixture was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were washed with brine (3 × 200 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the residue which was purified by silica gel column chromatography (PE/EtOAc, 5:1) to afford **9** (14.8 g, 80%) as a yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 2953, 2929, 2855, 1742, 1601, 1463, 1363, 1256, 1165, 1079, 1015, 954, 833, 779 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (s, 1 H, Ar), 6.82 (s, 2 H, Ar), 5.75–5.71 (m, 1 H, C*H*OHCH$_2$), 3.94 (s, 6 H, 2 ArOCH_3), 3.90 (s, 3 H, ArOCH_3), 3.81 (s, 3 H, ArOCH_3), 3.72 (s, 3 H, CH$_2$CO$_2$CH_3), 2.77–2.61 (m, 2 H, CH_2), 0.88 (s, 9 H, *t*Bu*H*Si), 0.07 (s, 3 H, CH_3Si), –0.11 (s, 3 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4 (*C*=O), 153.3 (C_{naph}OCH$_3$), 151.4 (C_{naph}OCH$_3$), 150.2 (C_{naph}OCH$_3$), 145.1 (C_{naph}OCH$_3$), 134.1 (C_{naph}CH), 122.5 (C_{naph}), 120.0 (C_{naph}), 107.9 (C_{naph}H), 107.8 (C_{naph}H), 105.6 (C_{naph}H), 66.4 (*C*OH), 62.4 (O*C*H$_3$), 57.5 (O*C*H$_3$), 56.9 (O*C*H$_3$), 56.7 (O*C*H$_3$), 51.4 (O*C*H$_3$), 45.3 (*C*H$_2$), 25.6 [C(*C*H$_3$)$_3$], 18.0 [*C*(CH$_3$)$_3$], –4.75 (*C*Si), –5.34 (*C*Si) ppm. HRMS: calcd. for $C_{24}H_{36}Si$ 464.2230; found 464.2226.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-3-(1,4,5,8-tetramethoxynaphthalen-2-yl)propanal (10): To a cooled (–78 °C) solution of **9** (4.39 g, 0.01 mmol) in dry CH_2Cl_2 (60 mL) was added DIBALH (20% in toluene, 10 mL, 0.012 mol), and the reaction mixture was stirred at –78 °C for 12 h. Then, the reaction mixture was quenched with a saturated solution of ammonium chloride (10 mL), and the resulting mixture was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (200 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the residue which was purified by silica gel column chromatography (PE/EtOAc, 5:1) to afford **10** (3.9 g, 90%) as a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.84 (s, 1 H, CH$_2$C*H*O), 7.10 (s, 1 H, Ar), 6.83 (s, 2 H, Ar), 5.80–5.76 (m, 1 H, C*H*OHCH$_2$), 3.94 (s, 6 H, 2 ArOCH_3), 3.90 (s, 3 H, ArOCH_3), 3.79 (s, 3 H, ArOCH_3), 2.84–2.70 (m, 2 H, CH_2), 0.90 (s, 9 H, *t*Bu*H*Si), 0.11 (s, 3 H, CH_3Si), –0.09 (s, 3 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.9 (*C*HO), 153.3 (C_{naph}OCH$_3$), 151.3 (C_{naph}OCH$_3$), 150.0 (C_{naph}OCH$_3$), 144.8 (C_{naph}OCH$_3$), 133.6 (C_{naph}CH), 120.0 (C_{naph}), 107.8 (C_{naph}H), 107.6 (C_{naph}H), 105.3 (C_{naph}H), 64.8 (*C*OH), 62.2 (O*C*H$_3$), 57.3 (O*C*H$_3$), 56.7 (O*C*H$_3$), 56.6 (O*C*H$_3$), 53.1 (*C*H$_2$), 25.5 [C(*C*H$_3$)$_3$], 17.9 [*C*(CH$_3$)$_3$], –4.83 (*C*Si), –5.28 (*C*Si) ppm. MS (ESI): m/z = 435 [M + H]$^+$.

(*R*)-*tert*-Butyldimethyl-[4-methyl-1-(1,4,5,8-tetramethoxynaphthalen-2-yl)pent-3-enyloxy]silane (11): To a cooled (0 °C) solution of $Ph_3PCH(CH_3)_2Br$ (3.85 g, 0.01 mol) in dry Et_2O (100 mL) was added *n*-butyllithium (2.5 M in hexane, 3.2 mL, 8 mmol) dropwise under a nitrogen atmosphere, and the mixture was stirred for 30 min at 0 °C. Then, a solution of **10** (2.17 g, 5 mmol) in dry Et_2O (50 mL) was added dropwise, and the mixture was stirred for 2 h at room temperature. After completion of the reaction, the mixture was quenched by the slow addition of water (50 mL), and the resulting solution was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with brine (200 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the crude residue which was purified by silica gel column chromatography (PE/EtOAc, 5:1) to afford **11** (1.73 g, 75%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (s, 1 H, Ar), 6.79 (dd, J = 11.6, 8.8 Hz, 2 H, Ar), 5.34–5.26 (m, 2 H, C*H*OHCH$_2$ and C*H*=C), 3.96 (s, 3 H, ArOCH_3), 3.91 (s, 3 H, ArOCH_3), 3.89 (s, 3 H, ArOCH_3), 3.79 (s, 3 H, ArOCH_3), 2.50–2.35 (m, 2 H, CH_2), 1.72 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 0.92 (s, 9 H, *t*Bu*H*Si), 0.08 (s, 3 H, CH_3Si), –0.08 (s, 3 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0 (C_{naph}OCH$_3$), 151.6 (C_{naph}OCH$_3$), 150.3 (C_{naph}OCH$_3$), 145.2 (C_{naph}OCH$_3$), 136.0 (*C*=CH), 133.1 (C_{naph}CH), 122.6 (C_{naph}), 121.7 (C=*C*H), 119.9 (C_{naph}), 107.8 (C_{naph}H), 107.6 (C_{naph}H), 106.7 (C_{naph}H), 69.4 (*C*OH), 62.3 (O*C*H$_3$), 57.5 (O*C*H$_3$), 57.1 (O*C*H$_3$), 56.9 (O*C*H$_3$), 38.7 (*C*H$_2$), 25.8 [C(*C*H$_3$)$_3$], 18.2 [*C*(CH$_3$)$_3$], –4.70 (*C*Si), –4.89 (*C*Si) ppm. MS (ESI): m/z = 483 [M + Na]$^+$.

(*R*)-4-Methyl-1-(1,4,5,8-tetramethoxynaphthalen-2-yl)pent-3-en-1-ol (12): To a solution of **11** (2.3 g, 5 mmol) in dry THF (40 mL) was added tetra-*n*-butyl ammonium fluoride (2.61 g, 10 mmol), and the mixture was stirred at room temperature and was monitored by TLC. After completion of the reaction (3 h), the mixture was quenched by the addition of water (50 mL), and the resulting solution was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the residue which was purified by silica gel column chromatography (PE/EtOAc, 2:1) to afford **12** (1.64 g, 95%) as a yellow oil. ^{1}H NMR (300 MHz, DMSO): δ = 7.04 (s, 1 H, Ar), 6.82 (s, J = 8.7, 16.5 Hz, 2 H, Ar), 5.22–5.31 (m, 2 H, C*H*OHCH$_2$ and C*H*=C), 3.82 (s, 3 H, ArOCH_3), 3.80 (s, 3 H, ArOCH_3), 3.76 (s, 3 H, ArOCH_3), 3.61

(s, 3 H, ArOCH_3), 2.41–2.28 (m, 2 H, CH_2), 1.62 (s, 3 H, CH_3),1.50 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 152.5 (C_{naph}OCH$_3$), 150.9 (C_{naph}OCH$_3$), 149.6 (C_{naph}OCH$_3$), 145.3 (C_{naph}OCH$_3$), 135.5 (CH=*C*), 131.7 (C_{naph}CH), 121.9 (C_{naph}), 121.4 (*C*H=C), 119.0 (C_{naph}), 108.2 (C_{naph}H), 107.7 (C_{naph}H), 106.4 (C_{naph}H), 66.2 (*C*OH), 61.9 (OCH$_3$), 57.0 (OCH$_3$), 56.8 (OCH$_3$), 56.5 (OCH$_3$), 37.1 (*C*H$_2$), 25.5 (*C*H$_3$), 17.6 (*C*H$_3$) ppm. MS (ESI): *m*/*z* = 369 [M + Na]$^+$. HPLC (Sino-chiral OD Chiralpak AD-H; hexane/*i*PrOH, 60:40; flow rate = 0.8 mL/min; λ = 220 nm): t_R = 9.59 min; 99.8% *ee*.

(*R*)-1-(5,8-Dimethoxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)-4-methylpent-3-enyl Acetate (13) and (*R*)-1-(1,4-Dimethoxy-5,8-dioxo-5,8-dihydronaphthalen-2-yl)-4-methylpent-3-enyl Acetate (14): To a solution of **12** (346 mg, 1 mmol), pyridine (0.16 mL, 2 mmol), and DMAP (24.4 mg, 0. 2 mmol) in dry CH_2Cl_2 (10 mL) was added Ac_2O (0.19 mL, 2 mmol) at 0 °C, and the mixture was stirred for 20 min at room temperature. Then, a solution of CAN (1.37 g, 2.5 mmol) in water (10 mL) was added dropwise to the reaction mixture which was stirred for 15 min at room temperature. After completion of the reaction, the mixture was diluted with water, and the resulting solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuum to furnish the residue which was purified by silica gel column chromatography (PE/EtOAc, 2:1) to afford **13** (89 mg, 25%) as a red oil and **14** (240 mg, 67%) as a yellow oil. Data for **13**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (s, 2 H, Ar), 6.57 (s, 1 H, H_{quin}), 5.85–5.82 (m, 1 H, C*H*OCOCH$_3$), 5.05–5.01 (m, 1 H, C*H*=C), 3.86 (s, 6 H, 2 OCH_3), 2.53–2.48 (m, 1 H, CH_2), 2.39–2.34 (m, 1 H, CH_2), 2.03 (s, 3 H, OCOCH_3), 1.58 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.4 (C_{quin}=O), 183.3 (C_{quin}=O), 169.5 (*C*=O), 153.7 (C_{Ar}OCH$_3$), 153.3 (C_{Ar}OCH$_3$), 148.0 (C_{quin}CH), 135.5 (C_{quin}H), 133.1 (*C*=CH), 120.8 (C_{Ar}), 120.6 (C_{Ar}H), 120.3 (C_{Ar}H), 120.2 (C=*C*H), 117.9 (C_{Ar}), 69.6 (*C*HOCOCH$_3$), 56.6 (OCH$_3$), 32.6 (*C*H$_2$), 25.5 (*C*H$_3$), 20.8 (*C*H$_3$), 17.8 (*C*H$_3$) ppm. Data for **14**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (s, 1 H, Ar), 6.66 (s, 2 H, H_{quin}), 6.05–6.02 (m, 1 H, C*H*OCOCH$_3$), 5.02 (t, *J* = 7.2 Hz, 1 H, C*H*=C), 3.87 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 2.45–2.37 (m, 2 H, CH_2), 2.02 (s, 3 H, OCOCH_3), 1.56 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.1 (C_{quin}=O), 183.6 (C_{quin}=O), 169.4 (*C*=O), 155.6 (C_{Ar}OCH$_3$), 150.1 (C_{Ar}OCH$_3$), 143.9 (C_{quin}H), 138.3 (C_{quin}H), 137.3 (C_{Ar}CH), 135.0 (*C*=CH), 124.7 (C=*C*H), 119.7 (C_{Ar}H), 117.8 (C_{Ar}), 116.5 (C_{Ar}), 70.0 (*C*HOCOCH$_3$), 61.5 (OCH$_3$), 56.2 (OCH$_3$), 33.5 (*C*H$_2$), 25.2 (*C*H$_3$), 20.5 (*C*H$_3$), 17.3 (*C*H$_3$) ppm. MS (ESI): *m*/*z* = 381 [M + Na]$^+$.

(*R*)-2-(1-Acetoxy-4-methylpent-3-enyl)-5,8-dimethoxynaphthalene-1,4-diyl Diacetate (15): To a stirred solution of **13** (79 mg, 0.22 mmol), Ac_2O (5 mL), Et_3N (1 mL), and DMAP (2.4 mg, 0.02 mmol) was added Zn powder (143 mg, 2.2 mmol) at 5 °C, and the reaction mixture was stirred for 4 h at 20 °C. Then, the mixture was poured into water (10 mL), and the resulting solution was extracted with EtOAc (3 × 20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 20 mL) and brine (20 mL) and then concentrated under vacuum to furnish the crude residue which was purified by silica gel column chromatography (PE/EtOAc, 4:1) to afford **15** (74 mg, 76%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.11 (m, 1 H, Ar), 6.78 (s, 2 H, Ar), 6.19–6.00 (m, 1 H, C*H*OCOCH$_3$), 5.08–5.03 (m, 1 H, C*H*=C), 3.85 (s, 6 H, OCH_3), 2.63–2.46 (m, 2 H, CH_2), 2.38 (s, 3 H, ArOCOCH_3), 2.36 (s, 3 H, ArOCOCH_3), 2.04 (s, 3 H, CHOCOCH_3), 1.66 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1 (*C*=O), 169.9 (*C*=O), 169.8 (*C*=O), 149.7 (C_{Ar}OCH$_3$), 149.4 (C_{Ar}OCH$_3$), 141.3 (C_{Ar}OCOCH$_3$), 135.3 (C_{Ar}CH), 130.1 (*C*=CH), 121.6 (C_{Ar}OCOCH$_3$), 121.1 (C=*C*H), 118.8 (C_{Ar}H), 118.5 (C_{Ar}), 118.3 (C_{Ar}), 107.8 (C_{Ar}H), 107.5 (C_{Ar}H), 70.6 (*C*HOCOCH$_3$), 56.8 (OCH$_3$), 56.7 (OCH$_3$), 33.6 (*C*H$_2$), 25.7 (*C*H$_3$), 21.1 (*C*H$_3$), 20.9 (*C*H$_3$), 20.8 (*C*H$_3$), 17.8 (*C*H$_3$) ppm. MS (ESI): *m*/*z* = 467 [M + Na]$^+$.

(*R*)-6-(1-Acetoxy-4-methylpent-3-enyl)-5,8-dimethoxynaphthalene-1,4-diyl Diacetate (16): To a stirred solution of **14** (174 mg, 0.5 mmol), Ac_2O (8 mL), Et_3N (2 mL), and DMAP (6.1 mg, 0.05 mmol) was added Zn powder (325 mg, 5 mmol) at 5 °C, and the reaction mixture was stirred for 2 h at 20 °C. Then, the mixture was poured into water (15 mL), and the resulting solution was extracted with EtOAc (3 × 30 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 30 mL) and brine (30 mL) and then concentrated under vacuum to obtain a residue which was purified by silica gel column chromatography (PE/EtOAc, 5:1) to afford **16** (191 mg, 86%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09 (dd, *J* = 25.6, 8.4 Hz, 2 H, Ar), 6.83 (s, 1 H, Ar), 6.30–6.24 (m, 1 H, C*H*OCOCH$_3$), 5.10 (t, *J* = 7.2 Hz, 1 H, C*H*=C), 3.90 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 2.60–2.44 (m, 2 H, CH_2), 2.35 (s, 3 H, ArOCOCH_3), 2.34 (s, 3 H, ArOCOCH_3), 2.09 (s, 3 H, CHOCOCH_3), 1.67 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1 (*C*=O), 170.0 (*C*=O), 169.2 (*C*=O), 151.9 (C_{Ar}OCH$_3$), 145.2 (C_{Ar}OCOCH$_3$), 144.7 (C_{Ar}OCOCH$_3$), 143.7 (C_{Ar}OCH$_3$), 134.9 (*C*=CH), 131.5 (C_{Ar}CH), 123.6 (C=*C*H), 121.1 (C_{Ar}), 120.3 (C_{Ar}), 119.4 (C_{Ar}H), 118.6 (C_{Ar}H), 105.0 (C_{Ar}H), 70.4 (*C*HOCOCH$_3$), 62.6 (OCH$_3$), 56.5 (OCH$_3$), 34.6 (*C*H$_2$), 25.6 (*C*H$_3$), 21.2 (*C*H$_3$), 20.8 (*C*H$_3$), 20.6 (*C*H$_3$), 17.7 (*C*H$_3$) ppm. MS (ESI): *m*/*z* = 467 [M + Na]$^+$.

(*R*)-5,8-Dihydroxy-2-(1-hydroxy-4-methylpent-3-enyl)naphthalene-1,4-dione (Shikonin, 2): To a stirred solution of **15** (67 mg, 0.15 mmol) and **16** (177 mg, 0.4 mmol) in CH_3CN (10 mL) was added a solution of CAN (1.37 g, 2.5 mmol) in water (5 mL) dropwise until the solution turned dark red. The solution was stirred for 15 min at room temperature. Then, NaOH (1 M solution, 5 mL) was added, and the reaction mixture was stirred for 2 h and then carefully acidified with HCl (10% solution) to neutralize the mixture. The deep blue color disappeared and turned deep red. The mixture was extracted with EtOAc (3 × 20 mL) and brine (20 mL) and then concentrated under vacuum to obtain the residue which was purified by silica gel column chromatography (PE/EtOAc, 10:1) to afford **2** (135 mg, 85%) as a red powder; m.p. 145–147 °C; ref.[12k] m.p. 143–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.58 (s, 1 H, ArOH), 12.48 (s, 1 H, ArOH), 7.19–7.16 (m, 3 H, Ar and H_{quin}), 5.20 (dd, *J* = 8.0, 6.8 Hz, 1 H, C*H*=C), 4.93–4.90 (m, 1 H, ArC*H*OH), 2.39–2.32 (m, 2 H, CH_2), 1.76 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 180.6 (*C*=O), 179.7 (*C*=O), 164.0 (C_{Ar}OH), 163.4 (C_{Ar}OH), 153.6 (C_{Ar}CH), 132.9 (C_{Ar}H), 131.8 (CH=*C*), 131.7 (C_{Ar}H), 131.6 (C_{Ar}H), 120.4 (*C*H=C), 111.7 (C_{Ar}), 111.2 (C_{Ar}), 66.4 (*C*OH), 35.3 (*C*H$_2$), 25.5 (CH_3), 17.7 (CH_3) ppm. HPLC (Sino-chiral OD Chiralpak AD-H; hexane/*i*PrOH, 9:1; flow rate = 0.6 mL/min; λ = 516 nm): t_R = 10.58 min; 99.8% *ee* (shikonin, **2**).

Supporting Information (see footnote on the first page of this article): Characterisation data for all the products and copies of ^{1}H NMR, ^{13}C NMR and HPLC data.

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