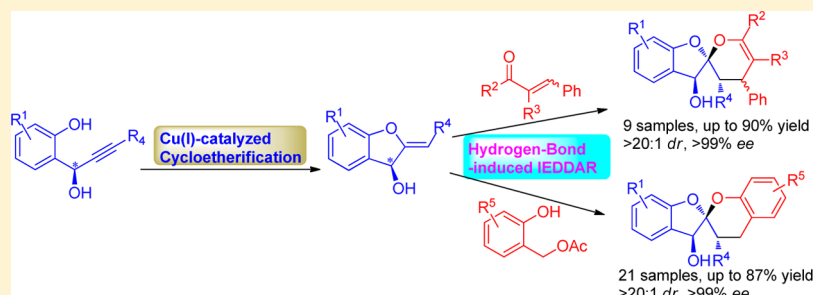


Enantioselective Syntheses of Spiroketal via a Tandem Reaction of Cu(I)-Catalyzed Cycloetherification and Hydrogen-Bond-Induced [4 + 2] Cyclization

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S Supporting Information



ABSTRACT: A tandem reaction consisting of a copper(I)-catalyzed cycloetherification and a hydrogen-bond-induced inverse-electron-demand oxa-Diels–Alder cycloaddition was performed from chiral propargyl alcohol, generating several kinds of optically pure [5, 6] spiroketals in excellent stereoselectivities and yields. The investigation on mechanism found that the cyclization prompted by a hydrogen bond not only improved the efficiency but also determined the diastereoselectivity.

Spiroketal moieties are found in a variety of natural products, such as rubromycins, berkelic acids, virgatolides, and papulacandins, and have demonstrated compelling bioactivity (Figure 1).¹

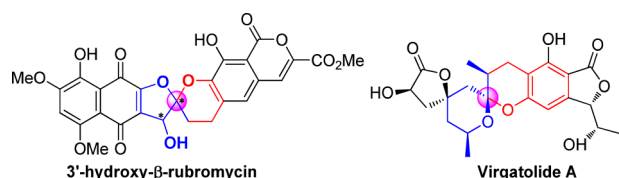


Figure 1. Selected natural products containing spiroketal cores (*configuration unknown).

As spiroketal cores are essential for bioactivity in natural products and pharmacophores in drug discovery,^{1,2} constructing spiroketals, especially those with optically pure cores, would be very useful for the syntheses of natural compounds and characterization of their chiral centers. Thus, construction of chiral spiroketals has been widely investigated. Tan and co-workers reported a systematic stereocontrolled synthesis of spiroketals using a kinetic spirocyclization reaction of glycol epoxides.³ Groundbreaking investigations have identified Brønsted acid-catalyzed asymmetric spiroacetalizations.⁴ Ding and co-workers synthesized chiral benzannulated spiroketals using precious metal Ir as a catalyst.⁵ Pettus and co-workers reported the diastereoselective formal synthesis of Berkelic acid using a hetero Diels–Alder reaction of an *o*-quinone methide

(*o*-QM) with a chiral enol ether.⁶ Our group has focused on this field and found a series of efficient methods for the syntheses of racemic spiroketals.⁷ Although significant progress has been made in recent years, great demand remains for the development of efficient methods for the synthesis of chiral spiroketal centers, especially chiral bisbenzannulated [5, 6] and [6, 6] spiroketals in natural products.⁸ In accordance with our interest in developing synthetic tools for the synthesis of natural products, we wanted to determine a new and efficient method for the stereocontrolled synthesis of spiroketals.

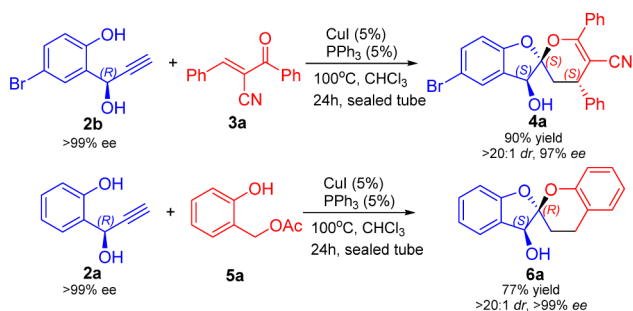
Copper, which is a cheap and green catalyst that has been used to catalyze intramolecular alkyne hydroalkoxylation, was regarded as one of the most attractive approaches due to its high atom economy and mild reaction conditions,⁹ and the inverse-electron-demand Diels–Alder reaction (IEDAR), one of the most useful organic synthesis tools, has attracted continuous interests from chemists and has been studied extensively.¹⁰ On the basis of these two advantages, we have previously developed a tandem approach to spiroketals using copper(I)-catalyzed cycloetherification and IEDAR cycloaddition.¹¹ However, this procedure could only provide racemic bisbenzannulated spiroketals. To address this problem, we envisioned an improved entry to chiral spiroketal from chiral propargyl alcohol. Two to three stereocenters were built in a

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one pot reaction, which will be beneficial for natural product synthesis and derivatization.

Our work was initiated with the syntheses of chiral substrate **2a** and analogues. Using asymmetric (*S*)-Me-CBS-catalyzed reduction, **2a** and its analogues could be prepared in excellent ee values and good yields; configurations were also confirmed according to the literature.¹² Fortunately, when **2b** and **3a** were heated in the presence of 5 mol % CuI and 5 mol % PPh₃, desired product **4a** formed in more than 97% ee, >20:1 dr ratio, and 90% yield after a 24 h reaction (Scheme 1). A similar result

Scheme 1. Initial Examination of Enantioselective Spiroketalization in Optimal Conditions^a



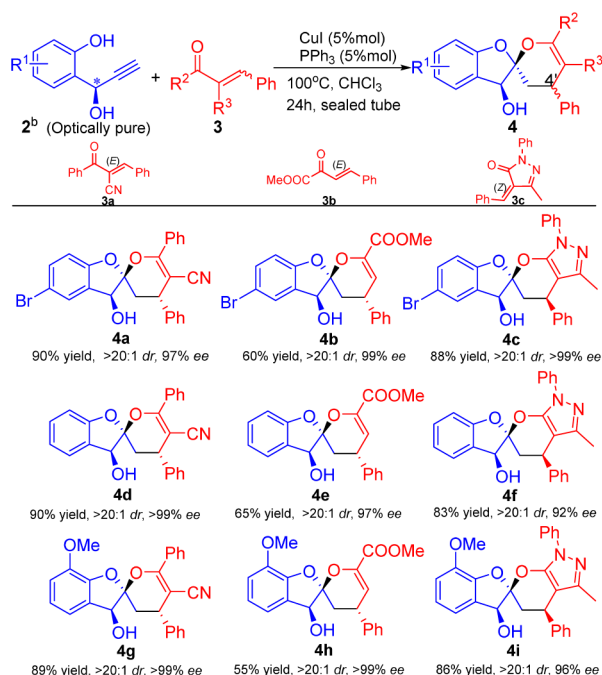
^aReaction conditions: substrate (0.1 mmol), CuI catalyst (5 mol %), PPh₃ (5 mol %), CHCl₃ (2 mL), 100 °C in a sealed tube for 24 h. Isolated yields are shown. dr = syn/anti determined via ¹H NMR spectroscopy and HPLC. The ee value was determined via HPLC.

was found in the reaction of **2a** with **5a**, which gave **6a** in more than 99% ee, >20:1 dr ratio, and 77% yield (Scheme 1). X-ray crystallography showed that the relative structures of **4a** and **6a** both have syn configurations between the hydroxyl groups and C–O bond of the pyran ring.¹³ Because the substrates **2a** and **2b** have the *R*-configuration, the spiroketal center was confirmed accordingly (Scheme 1).

With the optimal reaction condition in hand, we consequently investigated the substrate scope. At first, three propargyl alcohols **2** were explored in reactions with β,γ -unsaturated- α -keto-ester **3b**. In comparison with the results of **4b**, the **4e** and **4h** electron-donating groups with **2** slightly decreased the yield. When α,β -unsaturated ketone (**3a**, **3c**) reacted with phenol **2** in optimal conditions, the corresponding spiroketals were produced in high yields with excellent dr and ee values; meanwhile, different substituents on alcohol **2** had little influence on the yield.¹⁴ However, the electronic influence of substrates **3** should be responsible for the difference in yields. When R² is COOMe (**4b**, **4e**, **4h**, Scheme 2), the reactions are obviously less efficient and gave lower yields than others. The configuration of the 4'-position was determined by substrate **3**. When phenyl group and R³ in substrate **3** are in the *cis*-configuration, the phenyl group at the 4'-position of product **4** stretched to the back of ground (**4a**, **4b**, **4d**, **4e**, **4g**, **4h**, Scheme 2). Otherwise, it stretched to the front of ground (**4c**, **4f**, **4i**, Scheme 2).

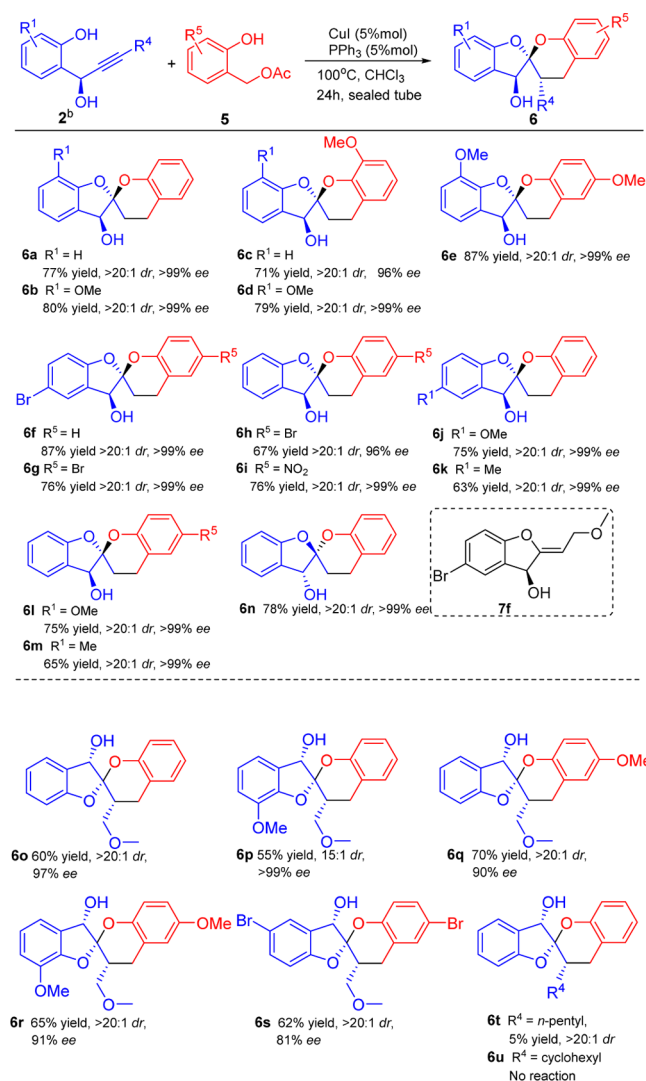
Inspired by the excellent result for spiroketal **6a**, we examined the generality of this method. A number of chiral propargyl alcohols **2** and *o*-methylenedioxyphenols **5** were utilized in the spiroketalization to afford the corresponding optical active benzannulated spiroketals in excellent diastereo- and enantioselectivities (>20:1 dr and >81% ee, Scheme 3), which indicated high adaptability to variations in the substituents of the substrates. Compared with **2a**, the methoxyl

Scheme 2. Substrate Scope of Syntheses Compound 4^a



^aReaction conditions: substrate (0.1 mmol), CuI catalyst (5 mol %), PPh₃ (5 mol %), CHCl₃ (2 mL), 100 °C in a sealed tube for 24 h. Isolated yields are shown. dr = syn/anti determined via ¹H NMR spectroscopy and HPLC. The ee value was determined via HPLC. **2a**: R¹ = H, >99% ee; **2b**: R¹ = 4-Br, >99% ee; **2c**: R¹ = 6-OMe, >99% ee.

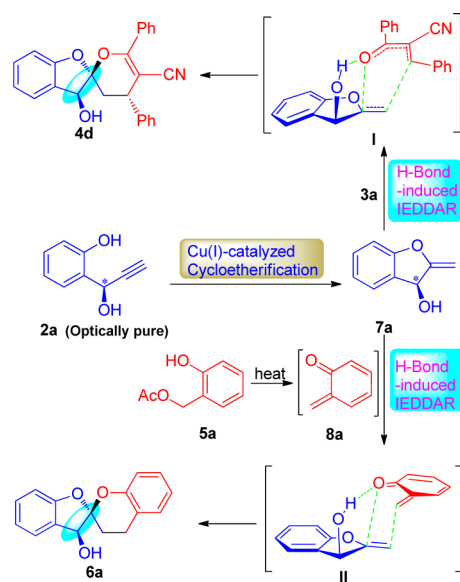
group on the phenyl ring of **2** did not have obvious effect on the yields, enantio-, or diastereoselectivities (**6a** and **6b**, **6j**; **6c** and **6d**, Scheme 3). However, when R⁵ in **5** was 2-OMe, the ee value was slightly decreased (**6c**, Scheme 3). More interestingly, the yield increased when R¹ in compound **2** was 4-Br (**6f**, Scheme 3); however, compared with **6a**, the yield decreased when R⁵ was 4-Br (**6g**, **6h**, Scheme 3). Comparing **6d** and **6e** in Scheme 3, the position of the methoxyl group shows an effect on the yield, which may be due to steric hindrance from the methoxyl group. Similar to **6k**, the methyl group on the phenyl ring of compound **5** also caused the yield to decrease (**6m**, Scheme 3). In addition, **6n**, the enantiomer of **6a**, was generated from (*S*)-**2a** in >20:1 dr with >99% ee, demonstrating that the reaction could proceed with high efficiency regardless of whether (*R*)- or (*S*)-alcohol **2** was utilized. Notably, compounds **2** with methoxymethyl group at R⁴ could participate in the cycloaddition to afford the desired three stereo center products in 81 to over 99% ee and 15:1 to 20:1 dr (**6o–s**, Scheme 3). The yields of **6o–s** were controlled by the steric environment and electronic effects. Compared with **6t** (5% yield), compounds **6o–s** have an electron-donating methoxymethyl group that induces the reaction more efficiently in the same steric environment. When changing the substituent from *n*-pentyl to cyclohexyl, cyclo-etherification occurred without cycloaddition (**6u**, Scheme 3). Unfortunately, when R¹ and R⁵ were 4-Br, the ee value of **6s** decreased to provide only 81% ee. Meanwhile, the crystal structure of **7f** was characterized via X-ray crystallography analysis, and the structure showed that the methoxymethyl group was in the *cis* position to the C–O bond of the furan ring (Scheme 3).¹⁵ Thus, on the basis of our hydrogen-bond-induced strategy and the Alder–Stein principle, the configurations of **6o–u** were

Scheme 3. Substrate Scope of Syntheses Compound 6 and Structure of Compound 7f^a

determined as shown in Scheme 3. It can also be observed that electronic effects have little influence on the stereoselectivities; thus, all cases gave excellent ee and dr values.

On the basis of these results, a mechanism was proposed. Similar to the previous report, the Cu(I)-catalyzed hydroalkoxylation formed exocyclic enol ether 7a, which was subsequently captured by 3a or 8a to form the spiroketal 4d or 6a.¹⁶ Because of the high syn configuration diastereoselectivity obtained, we propose that the reaction should proceed through transition state I or II (Scheme 4).¹⁷ Because the hydrogen-bond interaction between the hydroxy group of 7a and the carbonyl of 3a or 8a may be responsible for the stereoselectivity of the IEDDAR stage, the optically pure

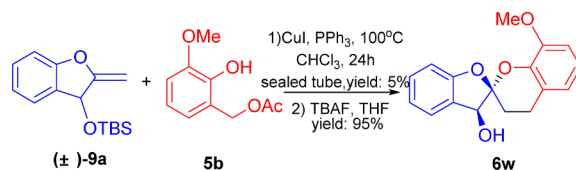
Scheme 4. Overall Approach for the Stereocontrolled Syntheses of Benzannulated Spiroketal



alcohol 2a determined the configuration of the spiroketal chiral center.

To demonstrate the proposed mechanism, a controlled experiment was designed and performed under the same conditions. Using compound (±)-9a with a protected hydroxyl group as the substrate, a reaction with compound 5b generated spiroketal 6v in very low yield (5%). After removing the TBS group of 6v, compound 6w was formed and compared with compound 6c by ¹H NMR and ¹³C NMR spectra. We found that 6w is the anti diastereoisomer of 6c, which reflects a reaction proceeding through an endo orientation on the face opposite of the TBS group that met the result of another group.^{8g} The yield is also affected if the hydrogen-bond-induced process is prevented. Meanwhile, the relative configuration of 6a showed that the hydroxyl group was in the syn position to the oxygen atom of the pyran ring. These results indicate that a hydrogen-bond is a key factor to the cyclization, which not only induced the syn stereoselectivity, but also improved the yield (Scheme 5).¹⁸

Scheme 5. Carrying the Reaction with Protected Secondary Propargyl Alcohol



CONCLUSION

In conclusion, an enantio- and diastereoselective approach toward various spiroketals was developed that combined Cu(I)-catalyzed cycloetherification of chiral propargyl alcohols and hydrogen-bond-induced inverse-electron-demand hetero-Diels–Alder cycloaddition reaction in one pot. The method could construct two or three chiral centers in one sequence, and gave a series of [5, 6] spiroketal cores in excellent enantioselectivities, diastereoselectivities, and good yields. This

is the first method to provide optically pure bisbenzannulated spiroketal cores of natural products and will be helpful for the syntheses of rubromycin natural products and other spiroketal compounds.

Experimental Section. General Experimental Methods. All manipulations were conducted with a round-bottom flask in dry air. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on GF254 plates. Silica gel (200–300 meshes) was used for column chromatography. Unless otherwise noted, commercially available reagents and solvents were used without any purification. The distillation range of petro ether was 60–90 °C. DCM was freshly distilled from CaH₂, and THF was dried by distillation over Na/K. ¹H and ¹³C NMR spectra were recorded at 400/600 (100/150) MHz instruments, respectively, and spectral data were reported in ppm relative to tetramethylsilane (TMS) as the internal standard. High-resolution mass spectra (HRMS) were obtained on a mass spectrometer using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QToF). IR spectra were recorded on an FT-IR spectrometer, and major peaks were reported in cm⁻¹. Enantiomeric excesses (ee) were determined by HPLC analysis using the corresponding commercial chiral column as stated. Melting points were determined on a microscopic apparatus and were uncorrected. The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; brs, broad singlet for proton spectra. Coupling constants (*J*) are reported in hertz (Hz).

General Procedure for the Syntheses of Propargyl Alcohols 2. To a solution of corresponding alkyne (11 mmol) in dry THF (25 mL) was slowly added *n*-BuLi (12.1 mmol, 2.5 M in THF) at –78 °C under argon. The reaction mixture was heated to –40 °C and then cooled to –78 °C. A solution of the corresponding salicylaldehyde (10 mmol in 15 mL of THF) was added dropwise. The reaction mixture was stirred at –78 °C for 4 h and was then quenched with saturated NH₄Cl solution. The aqueous phase was extracted with EtOAc. Combined organic layers were washed with brine, dried over Na₂SO₄, and evaporated. The residue was purified by flash chromatography on silica gel to give intermediate product **s1** for the next step.

Alcohol **s1** (3 mmol) was dissolved in CH₂Cl₂ (50 mL) at room temperature (rt); MnO₂ (30 mmol) was added, and the mixture was stirred at rt overnight. Then, the reaction mixture was filtered through a neutral SiO₂ column and washed with CH₂Cl₂ (100 mL). The combined organic solution was concentrated in vacuo to obtain ketone **s2** for the next step.

Me-(S)-CBS (1 M in toluene, 0.4 mL, 0.4 mmol) was added to the solution of ketone **s2** (0.8 mmol) in THF (15 mL) at –30 °C under an argon atmosphere. After the mixture was stirred for 10 min, BH₃·Me₂S (2.0 M in THF, 0.96 mmol) was added dropwise and stirred at –30 °C under an argon atmosphere for 40 min. CH₃OH (0.6 mL) was added followed by aq NaHCO₃. The mixture was extracted by EtOAc, and the combined extracts were dried (Na₂SO₄) and concentrated. The crude product obtained was purified by flash column chromatography to afford alcohol **s3**.

To a solution of the alcohol **s3** (0.5 mmol) in 20 mL dry THF was added a solution of tetrabutylammonium fluoride (1.05 mmol, 2.1 equiv) in 5 mL of dry THF at 0 °C. After 1 h, water (5 mL) was added to the reaction mixture; the aqueous phase was extracted with ethyl acetate, and the extract was

concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford **2**.

1-(2-((tert-Butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (s1-a). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 2.74 g, 82%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.20 (s, 9H), 0.29 (s, 3H), 0.31 (s, 3H), 1.05 (s, 9H), 2.76 (d, *J* = 5.6, 1H), 5.72 (d, *J* = 5.6, 1H), 6.84 (d, *J* = 6, 1H), 7.00 (t, *J* = 7.6, 1H), 7.22 (td, *J* = 7.6, 1.6, 1H), 7.59 (dd, *J* = 7.6, 1.6, 1H). ¹³C NMR (100 MHz, CDCl₃): δ –4.2, –0.2, 18.2, 25.8, 61.2, 90.7, 104.9, 118.3, 121.3, 128.0, 129.3, 130.8, 153.0. IR [*ν*_{max}, cm⁻¹]: 3434, 2957, 2930, 2858, 1638, 1488, 1252, 917, 841, 757, 663. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₈H₃₀O₂Si₂Na, 357.1677; found, 357.1683.

1-(5-Bromo-2-((tert-butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (s1-b). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 3.43 g, 83%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.20 (s, 9H), 0.28 (d, *J* = 6.4, 6H), 1.03 (s, 9H), 2.67 (d, *J* = 5.6, 1H), 5.64 (d, *J* = 5.6, 1H), 6.71 (d, *J* = 8.8, 1H), 7.29–7.32 (dd, *J* = 8.8, 2.8, 1H), 7.70 (d, *J* = 2.8, 1H). ¹³C NMR (100 MHz, CDCl₃): δ –4.2, –0.2, 18.2, 25.8, 60.6, 91.4, 104.1, 113.6, 120.0, 130.9, 132.0, 133.0, 152.1. IR [*ν*_{max}, cm⁻¹]: 3431, 2956, 2929, 2858, 2360, 1479, 1273, 1254, 915, 842, 818, 782, 760, 670, 568. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₈H₂₉BrO₂Si₂Na, 435.0782; found, 435.0784.

1-(2-((tert-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (s1-c). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 3.06 g, 84%, as a brown oil. ¹H NMR (400 MHz, CDCl₃): δ 0.20 (s, 9H), 0.26 (s, 6H), 1.03 (s, 9H), 3.80 (s, 3H), 5.84 (d, *J* = 4, 1H), 6.85 (dd, *J* = 8, 1.6, 1H), 6.96 (t, *J* = 8, 1H), 7.26 (dd, *J* = 7.6, 1.6, 1H). ¹³C NMR (100 MHz, CDCl₃): δ –4.0, –0.2, 18.9, 26.2, 54.9, 60.5, 91.0, 104.8, 111.6, 119.6, 121.2, 131.6, 142.4, 149.6. IR [*ν*_{max}, cm⁻¹]: 3423, 2956, 2929, 2857, 1637, 1482, 1252, 912, 841, 782. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₉H₃₂O₃Si₂Na, 387.1782; found, 387.1786.

1-(2-((tert-Butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-ol (s1-d). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 2.45 g, 80%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.30 (d, *J* = 6.0, 6H), 1.05 (s, 9H), 3.40 (s, 3H), 4.19 (d, *J* = 1.6, 2H), 5.79 (s, 1H), 6.84 (dd, *J* = 8.4, 0.8, 1H), 6.97–7.01 (td, *J* = 7.2, 0.8, 1H), 7.19–7.24 (td, *J* = 8, 1.6, 1H), 7.70 (dd, *J* = 7.6, 2, 1H). ¹³C NMR (100 MHz, CDCl₃): δ –4.2, 18.2, 25.8, 57.6, 60.0, 60.8, 81.9, 86.1, 118.5, 121.4, 128.0, 129.4, 130.8, 152.9. IR [*ν*_{max}, cm⁻¹]: 3409, 2955, 2930, 2895, 2858, 1600, 1489, 1454, 1279, 1258, 1097, 921, 840, 807, 783. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₇H₂₆O₃SiNa, 329.1543; found, 329.1542.

1-(2-((tert-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-4-methoxybut-2-yn-1-ol (s1-e). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 2.69 g, 80%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.21 (s, 3H), 0.25 (s, 3H), 1.03 (s, 9H), 2.64 (d, *J* = 4.4, 1H), 3.39 (s, 3H), 3.80 (s, 3H), 4.19 (s, 2H), 5.91 (t, *J* = 4.4, 1H), 6.84 (dd, *J* = 8.0, 1.6, 1H), 6.95 (t, *J* = 8.0, 1H), 7.25 (dd, *J* = 8, 0.8, 1H). ¹³C NMR (100 MHz, CDCl₃): δ –3.9, 18.9, 26.1, 54.9, 57.6, 60.0, 81.9, 86.1, 111.6, 119.5, 121.3, 131.7, 142.2, 149.7. IR [*ν*_{max}, cm⁻¹]: 3417, 2954, 2930, 2900, 2857, 1484, 1301, 1256, 1227, 1086, 918, 840, 783. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₈H₂₈O₄SiNa, 359.1649; found, 359.1647.

1-(5-Bromo-2-((tert-butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-ol (s1-f). Purified by flash chromatography

(petroleum ether/EtOAc = 8:1). Yield: 2.92 g, 76%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.27 (s, 3H), 0.28 (s, 3H), 1.03 (s, 9H), 2.66 (d, J = 4.2, 1H), 3.40 (s, 3H), 4.18 (s, 2H), 5.72 (d, J = 4.2, 1H), 6.71 (d, J = 8.4, 1H), 7.29–7.32 (dd, J = 8.8, 2.4, 1H), 7.70 (d, J = 2.4, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.2, -4.2, 18.2, 25.7, 57.7, 59.9, 60.0, 82.3, 85.4, 113.6, 120.1, 130.8, 132.1, 133.0, 152.0. IR [ν_{max} , cm^{-1}]: 3406, 2954, 2930, 2893, 2858, 1481, 1272, 1259, 1104, 919, 842, 783. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{25}\text{BrO}_3\text{SiNa}$, 409.0628; found, 409.0624.

1-(2-((tert-Butyldimethylsilyl)oxy)-5-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (s1-g). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 3.1 g, 85%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.20 (s, 9H), 0.27 (d, J = 10, 6H), 1.04 (s, 9H), 2.85 (t, J = 5.2, 1H), 3.79 (s, 3H), 5.68 (d, J = 5.2, 1H), 6.75 (d, J = 1.6, 2H), 7.18 (t, J = 1.6, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.2, -0.2, 18.1, 25.8, 55.5, 61.2, 90.9, 104.7, 113.0, 114.7, 119.1, 131.4, 146.7, 153.8. IR [ν_{max} , cm^{-1}]: 3432, 2360, 1636, 1491, 1275, 1152, 1025. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{33}\text{O}_3\text{Si}_2$, 365.1963; found, 365.1951.

1-(2-((tert-Butyldimethylsilyl)oxy)-5-methylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (s1-h). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 2.96 g, 85%, as a brown oil. ^1H NMR (400 MHz, CDCl_3): δ 0.20 (s, 9H), 0.29 (d, J = 8.4, 6H), 1.04 (s, 9H), 2.31 (s, 3H), 2.80 (d, J = 5.6, 1H), 5.67 (d, J = 5.6, 1H), 6.73 (d, J = 8.4, 1H), 6.99–7.02 (dd, J = 8, 1.2, 1H), 7.32 (d, J = 1.2, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.2, -0.2, 18.2, 20.6, 25.8, 61.4, 90.6, 105.0, 118.2, 128.6, 129.7, 130.4, 130.6, 150.7. IR [ν_{max} , cm^{-1}]: 3451, 2957, 2924, 2854, 2360, 1648, 1488, 1252, 1020, 918, 842, 669. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{33}\text{O}_2\text{Si}_2$, 349.2014; found, 349.2021.

1-(2-((tert-Butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-one (s2-a). Purified by flash chromatography (petroleum ether/EtOAc = 32:1). Yield: 897 mg, 90%, as a brown oil. ^1H NMR (400 MHz, CDCl_3): δ 0.24 (s, 6H), 0.28 (s, 9H), 1.03 (s, 9H), 6.89 (d, J = 7.6, 1H), 7.05 (d, J = 7.2, 1H), 7.44 (d, J = 7.6, 1H), 7.97 (d, J = 7.2, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.2, -0.7, 18.4, 25.8, 98.3, 102.6, 120.9, 121.5, 129.0, 133.1, 134.2, 155.8, 177.1. IR [ν_{max} , cm^{-1}]: 2957, 2930, 2900, 2858, 1651, 1597, 1568, 1478, 1287, 1254, 1223, 1157, 1011, 914, 844, 759, 697, 625, 548. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{29}\text{O}_2\text{Si}_2$, 333.1701; found, 333.1713.

1-(5-Bromo-2-((tert-butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-one (s2-b). Purified by flash chromatography (petroleum ether/EtOAc = 32:1). Yield: 1.14 g, 92%, as a brown oil. ^1H NMR (400 MHz, CDCl_3): δ 0.23 (s, 6H), 0.29 (s, 9H), 1.01 (s, 9H), 6.78 (d, J = 8.8, 1H), 7.48–7.51 (dd, J = 8.8, 2.4, 1H), 8.03 (d, J = 2.4, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.3, -0.8, 18.4, 25.7, 99.7, 102.0, 112.9, 123.2, 130.5, 135.3, 136.8, 154.8, 175.7. IR [ν_{max} , cm^{-1}]: 2955, 2925, 2854, 1656, 1621, 1587, 1466, 1379, 1283, 1253, 1195, 1017, 911, 845, 821, 759, 675. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{28}\text{BrO}_2\text{Si}_2$, 411.0806; found, 411.0812.

1-(2-((tert-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-one (s2-c). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 989 mg, 91%, as a brown oil. ^1H NMR (400 MHz, CDCl_3): δ 0.18 (s, 6H), 0.27 (s, 9H), 1.00 (s, 9H), 3.82 (s, 3H), 6.97 (t, J = 8, 1H), 7.02 (dd, J = 8, 1.6, 1H), 7.50 (dd, J = 8, 1.6, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.0, -0.7, 18.9, 25.8, 55.3, 98.4,

102.7, 115.8, 120.6, 123.8, 129.8, 145.5, 151.3, 177.5. IR [ν_{max} , cm^{-1}]: 2957, 2851, 2359, 1645, 1457, 1384, 1317, 1254, 1222, 1068, 1027, 905. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{31}\text{O}_3\text{Si}_2$, 363.1806; found, 363.1810.

1-(2-((tert-Butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-one (s2-d). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 802 mg, 88%, as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.24 (s, 6H), 1.02 (s, 9H), 3.44 (s, 3H), 4.32 (s, 2H), 6.89 (d, J = 8, 1H), 7.02 (t, J = 7.6, 1H), 7.39–7.43 (m, 1H), 7.92–7.95 (dd, J = 8, 2, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.3, 18.4, 25.7, 58.0, 59.8, 86.1, 88.2, 120.9, 121.4, 128.8, 132.7, 134.4, 155.8, 176.7. IR [ν_{max} , cm^{-1}]: 2957, 2930, 2900, 2858, 1651, 1597, 1568, 1478, 1287, 1254, 1223, 1157, 1011, 914, 844, 759. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3\text{SiNa}$, 327.1387; found, 327.1388.

1-(2-((tert-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-4-methoxybut-2-yn-1-one (s2-e). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 912 mg, 91%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.17 (s, 6H), 0.99 (s, 9H), 3.43 (s, 3H), 3.80 (s, 3H), 4.31 (s, 2H), 6.95 (t, J = 8, 1H), 7.00–7.03 (dd, J = 8, 1.6, 1H), 7.44–7.46 (dd, J = 7.6, 1.6, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.1, 18.8, 25.7, 55.2, 58.0, 59.8, 86.2, 88.2, 115.9, 120.7, 123.3, 129.8, 145.4, 151.3, 177.1. IR [ν_{max} , cm^{-1}]: 3417, 2954, 2930, 2900, 2857, 1651, 1597, 1568, 1478, 1287, 1254, 1223, 1157, 1011, 918, 840, 783. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{26}\text{O}_4\text{SiNa}$, 357.1493; found, 357.1492.

1-(5-Bromo-2-((tert-butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-one (s2-f). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 974 mg, 85%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.23 (s, 6H), 1.00 (s, 9H), 3.45 (s, 3H), 4.33 (s, 2H), 6.78 (d, J = 8.8, 1H), 7.48–7.50 (dd, J = 8.8, 2.4, 1H), 8.00 (d, J = 2.4, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.3, 18.4, 25.7, 58.1, 59.8, 85.6, 89.2, 113.0, 123.2, 130.2, 134.8, 137.0, 154.8, 175.3. IR [ν_{max} , cm^{-1}]: 2954, 2930, 2894, 2858, 1657, 1597, 1589, 1471, 1283, 1255, 1217, 1106, 842, 824, 809, 784. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{24}\text{BrO}_3\text{Si}$, 383.0673; found, 383.0669.

1-(2-((tert-Butyldimethylsilyl)oxy)-5-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-one (s2-g). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 989 mg, 91%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.19 (s, 6H), 0.27 (s, 9H), 1.01 (s, 9H), 3.80 (s, 3H), 6.82 (d, J = 8.8, 1H), 6.97–7.00 (dd, J = 8.8, 3.2, 1H), 7.46 (d, J = 3.2, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.3, -0.7, 18.4, 25.9, 55.6, 98.6, 102.5, 116.0, 121.1, 122.6, 128.9, 149.7, 153.3, 176.9. IR [ν_{max} , cm^{-1}]: 2956, 2931, 2900, 2858, 2360, 2149, 1653, 1567, 1489, 1413, 1278, 1253, 1197, 1176, 1042, 1013, 921, 846, 782, 763, 739, 626. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{31}\text{O}_3\text{Si}_2$, 363.1806; found, 363.1809.

1-(2-((tert-Butyldimethylsilyl)oxy)-5-methylphenyl)-3-(trimethylsilyl)prop-2-yn-1-one (s2-h). Purified by flash chromatography (petroleum ether/EtOAc = 32:1). Yield: 935 mg, 90%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.21 (s, 6H), 0.28 (s, 9H), 1.02 (s, 9H), 2.33 (s, 3H), 6.78 (d, J = 8.4, 1H), 7.19–7.22 (td, J = 8.4, 2.0, 1H), 7.73 (d, J = 2.0, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.3, -0.7, 18.4, 20.4, 25.8, 98.3, 102.7, 121.3, 128.6, 130.2, 133.0, 135.0, 153.6, 177.3. IR [ν_{max} , cm^{-1}]: 2957, 2930, 2898, 2858, 2360, 2148, 1651, 1607, 1565, 1490, 1405, 1287, 1254, 1181, 1020, 920, 845, 782, 689, 627, 534. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{31}\text{O}_2\text{Si}_2$, 347.1857; found, 347.1862.

(*S*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-a**). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 265 mg, 99%, as a colorless oil. $[\alpha]_{\text{D}}^{27} +3$ (c 1, CHCl₃, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 100:1, 1 mL/min, λ = 254 nm, *t* (major) = 16.57 min. All spectroscopic data were consistent with the racemic compound.

(*S*)-1-(5-Bromo-2-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-b**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 307 mg, 93%, as a colorless oil. $[\alpha]_{\text{D}}^{27} -18$ (c 1, CHCl₃). All spectroscopic data were consistent with the racemic compound.

(*S*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-c**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 288 mg, 99%, as a brown oil. $[\alpha]_{\text{D}}^{26} +12$ (c 0.5, CHCl₃, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 98:2, 1 mL/min, λ = 254 nm, *t* (major) = 8.65 min. All spectroscopic data were consistent with the racemic compound.

(*R*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-ol (**s3-d**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 235 mg, 96%, as a colorless oil. $[\alpha]_{\text{D}}^{26} -15$ (c 1, CHCl₃, 98% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 98:2, 1 mL/min, λ = 273 nm, *t* (major) = 11.56 min, *t* (minor) = 8.49 min. All spectroscopic data were consistent with the racemic compound.

(*R*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)-3-methoxyphenyl)-4-methoxybut-2-yn-1-ol (**s3-e**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 263 mg, 98%, as a colorless oil. $[\alpha]_{\text{D}}^{26} +8$ (c 1, CHCl₃, >99% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 98:2, 1 mL/min, λ = 273 nm, *t* (major) = 12.97 min. All spectroscopic data were consistent with the racemic compound.

(*R*)-1-(5-Bromo-2-((*tert*-butyldimethylsilyl)oxy)phenyl)-4-methoxybut-2-yn-1-ol (**s3-f**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 295 mg, 96%, as a colorless oil. $[\alpha]_{\text{D}}^{18} -6$ (c 1, CHCl₃, 93% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 99:1, 0.8 mL/min, λ = 230 nm, *t* (major) = 21.03 min, *t* (minor) = 15.19. All spectroscopic data were consistent with the racemic compound.

(*R*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-g**). Me-(*R*)-CBS (1 M in toluene, 0.4 mL, 0.4 mmol) was added to the solution of ketone **s2-a** (0.8 mmol) in THF (15 mL) at -30 °C under an argon atmosphere. After the mixture was stirred for 10 min, BH₃·Me₂S (2.0 M in THF, 0.96 mmol) was added dropwise and stirred at -30 °C under an argon atmosphere for 40 min. CH₃OH (0.6 mL) was added followed by aq NaHCO₃. The mixture was extracted by EtOAc, and the combined extracts were dried (Na₂SO₄) and concentrated. The crude product obtained was purified by flash column chromatography to afford alcohol **s3-g**. Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 265 mg, 99%, as a colorless oil. $[\alpha]_{\text{D}}^{25} -0.77$ (c 1.3, CHCl₃, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 100:1, 1 mL/min, λ = 254 nm, *t* (major) = 18.83 min. All spectroscopic data were consistent with the racemic compound.

(*S*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-h**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 277 mg, 95%, as a yellow oil. $[\alpha]_{\text{D}}^{26} -5.9$ (c 0.17, CHCl₃). All spectroscopic data were consistent with the racemic compound.

(*S*)-1-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**s3-i**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 276 mg, 99%, as a brown oil. $[\alpha]_{\text{D}}^{27} -14$ (c 1, CHCl₃). All spectroscopic data were consistent with the racemic compound.

(*R*)-2-(1-Hydroxyprop-2-yn-1-yl)phenol (**2a**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 73 mg, 99%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 2.77 (d, *J* = 2, 1H), 5.69 (d, *J* = 2, 1H), 6.90–6.94 (m, 2H), 7.23–7.25 (dd, *J* = 7.6, 1.2, 1H), 7.38–7.40 (dd, *J* = 7.6, 1.2, 1H). $[\alpha]_{\text{D}}^{27} -44$ (c 1, CHCl₃). All spectroscopic data were consistent with our previously reported data.¹¹

(*R*)-4-Bromo-2-(1-hydroxyprop-2-yn-1-yl)phenol (**2b**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 109 mg, 96%, as a brown oil. ¹H NMR (400 MHz, CDCl₃): δ 2.81–2.83 (m, 2H), 5.67 (d, *J* = 4, 1H), 6.81 (d, *J* = 8, 1H), 7.12 (s, 1H), 7.34–7.37 (dd, *J* = 8, 4, 1H), 7.52 (d, *J* = 4, 1H). $[\alpha]_{\text{D}}^{26} +9.2$ (c 0.65, CHCl₃, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak IC (25 cm), hexanes/IPA = 100:0, 31 min, 99:1, 11 min, 98:2, 10 min. 1 mL/min, λ = 254 nm, *t* (major) = 34.57 min. All spectroscopic data were consistent with our previously reported data.¹¹

(*R*)-2-(1-Hydroxyprop-2-yn-1-yl)-6-methoxyphenol (**2c**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 86 mg, 97%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 2.65 (d, *J* = 2.4, 1H), 3.90 (s, 3H), 5.74 (d, *J* = 2.4, 1H), 6.86–6.91 (m, 2H), 7.13–7.15 (dd, *J* = 6.8, 2.4, 1H). $[\alpha]_{\text{D}}^{25} +10$ (c 0.2, CHCl₃). All spectroscopic data were consistent with our previously reported data.¹¹

(*R*)-2-(1-Hydroxy-4-methoxybut-2-yn-1-yl)phenol (**2d**). To a solution of the intermediate product (0.5 mmol) in 20 mL dry THF was added a solution of tetrabutylammonium fluoride (1.1 equiv) in 5 mL dry THF. After 1 h, water (5 mL) was added to the reaction mixture; the aqueous phase was extracted with ethyl acetate, and the extract was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford **2d**. Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 95 mg, 99%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 3.40 (s, 3H), 4.19 (d, *J* = 1.6, 2H), 5.72 (s, 1H), 6.87–6.91 (m, 2H), 7.20–7.24 (td, *J* = 7.6, 1.6, 1H), 7.33–7.35 (m, 1H), 7.56 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 57.7, 59.9, 63.5, 83.3, 84.8, 116.9, 120.2, 124.6, 127.6, 130.0, 155.0. IR [ν_{max} , cm⁻¹]: 3322, 2954, 2928, 2852, 1459, 1279, 1238, 1092, 756, 737. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₁H₁₂O₃Na, 215.0679; found, 215.0680. $[\alpha]_{\text{D}}^{26} -77$ (c 1, CHCl₃).

(*R*)-2-(1-Hydroxy-4-methoxybut-2-yn-1-yl)-6-methoxyphenol (**2e**). To a solution of the intermediate product (0.5 mmol) in 20 mL dry THF was added a solution of tetrabutylammonium fluoride (1.1 equiv) in 5 mL dry THF. After 1 h, water (5 mL) was added to the reaction mixture; the aqueous phase was extracted with ethyl acetate, and the extract was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 4:1) on silica gel to afford **2e**. Yield: 110 mg, 99%, as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 3.00 (d, *J* = 5.6, 1H), 3.41 (s, 3H), 3.90 (s, 3H), 4.20 (d, *J* = 1.6, 2H), 5.79 (d, *J* = 3.6, 1H), 6.13 (s, 1H), 6.85–6.90 (m, 2H), 7.12–7.14 (dd, *J* = 9.6, 3.6, 1H). ¹³C

NMR (100 MHz, CDCl_3): δ 56.0, 57.5, 59.8, 60.8, 81.7, 85.6, 110.9, 119.6, 119.7, 126.1, 143.2, 146.7. IR [ν_{max} , cm^{-1}]: 3382, 2926, 1483, 1275, 1225, 1093, 735. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{14}\text{O}_4\text{Na}$, 245.0784; found, 245.0782. $[\alpha]_{\text{D}}^{26}$ -23 (c 1, CHCl_3).

(*R*)-4-Bromo-2-(1-hydroxy-4-methoxybut-2-yn-1-yl)phenol (**2f**). To a solution of the intermediate product (0.5 mmol) in 20 mL dry THF was added a solution of tetrabutylammonium fluoride (1.1 equiv) in 5 mL dry THF. After 1 h, water (5 mL) was added to the reaction mixture; the aqueous phase was extracted with ethyl acetate, and the extract was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 8:1) on silica gel to afford **2f**. Yield: 132 mg, 98%, as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 3.40 (s, 3H), 4.20 (d, J = 1.6, 2H), 5.67 (s, 1H), 6.75 (d, J = 8.8, 1H), 7.28–7.31 (dd, J = 8.8, 2.4, 1H), 7.44 (d, J = 2.4, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 57.8, 59.9, 62.8, 83.7, 84.1, 111.9, 118.7, 126.5, 130.2, 132.6, 154.3. IR [ν_{max} , cm^{-1}]: 3304, 2955, 2927, 2853, 1713, 1510, 1420, 1360, 1276, 1223, 1104, 1023, 1002. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{11}\text{BrO}_3\text{Na}$, 292.9784; found, 292.9780. $[\alpha]_{\text{D}}^{18}$ $+20$ (c 1, CHCl_3).

(*S*)-2-(1-Hydroxyprop-2-yn-1-yl)phenol (**2g**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 73 mg, 99%, as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 2.78 (d, J = 2.4, 1H), 2.82 (d, J = 6, 1H), 5.69–5.70 (m, 1H), 6.90–6.94 (m, 2H), 7.01 (s, 1H), 7.24–7.28 (m, 1H), 7.37–7.40 (dd, J = 8, 1.2, 1H). $[\alpha]_{\text{D}}^{25}$ $+47$ (c 1, CHCl_3). All spectroscopic data were consistent with our previously reported data.¹¹

(*R*)-2-(1-Hydroxyprop-2-yn-1-yl)-4-methoxyphenol (**2h**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 87 mg, 98%, as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 2.75 (d, J = 2, 1H), 3.76 (s, 3H), 5.63 (d, J = 1.6, 1H), 6.75–6.79 (m, 2H), 6.81 (s, 1H), 6.91–6.96 (m, 1H). $[\alpha]_{\text{D}}^{27}$ -15 (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 90:10, 1 mL/min, λ = 254 nm, t (major) = 18.02 min. All spectroscopic data were consistent with our previously reported data.¹¹

(*R*)-2-(1-Hydroxyprop-2-yn-1-yl)-4-methylphenol (**2i**). Purified by flash chromatography (petroleum ether/EtOAc = 2:1). Yield: 79 mg, 98%, as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 2.28 (s, 3H), 2.75 (d, J = 2, 1H), 5.63 (d, J = 2, 1H), 6.78 (d, J = 8, 1H), 7.01–7.04 (dd, J = 8, 2, 1H), 7.17 (d, J = 1.2, 1H). $[\alpha]_{\text{D}}^{27}$ -16 (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak IC (25 cm), hexanes/IPA = 100:0, 31 min, 99:1, 11 min, 98:2, 10 min, 1 mL/min, λ = 254 nm, t (major) = 54.79 min. All spectroscopic data were consistent with our previously reported data.¹¹

(*E*)-2-Benzoyl-3-phenylacrylonitrile (**3a**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 83%, as a yellow solid, mp 67–69 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.52–7.56 (m, 4H), 7.59 (d, J = 7.2, 1H), 7.65 (t, J = 7.2, 1H), 7.90–7.92 (m, 2H), 8.04 (d, J = 7.6, 2H), 8.07 (s, 1H). All spectroscopic data were consistent with previously reported data.^{14a}

Methyl (*E*)-2-Oxo-4-phenylbut-3-enoate (**3b**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 45%, as a yellow solid, mp 67–69 °C. ^1H NMR (400 MHz, CDCl_3): δ 3.93 (s, 3H), 7.34–7.47 (m, 4H), 7.61–7.63 (m, 2H), 7.87 (d, J = 16, 1H). All spectroscopic data were consistent with previously reported data.^{14b}

(*Z*)-4-Benzylidene-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**3c**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 55%, as a red solid, mp 105–107 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.36 (s, 3H), 7.20 (t, J = 8, 1H), 7.40–7.45 (m, 3H), 7.50–7.56 (m, 3H), 7.97 (d, J = 8, 2H), 8.50 (d, J = 8, 2H). All spectroscopic data were consistent with previously reported data.^{14c}

General Procedure for the Syntheses of 5,6-Spiroketals (4**).** A reaction tube was charged with 2-(1-hydroxyprop-2-ynyl)phenol **2** (0.1 mmol), α,β -unsaturated keto **3** (0.12 mmol), CuI (0.005 mmol), PPh_3 (0.005 mmol), and CHCl_3 (2 mL). The tube was filled with argon was then sealed and heated at 100 °C for 24 h in a drying oven. The resulting reaction mixture was cooled to ambient temperature; then the solvent evaporated, and the residue was purified by flash silica gel chromatography giving the desired spiroketal **4**.

(2*S*,3*S*,4'*S*)-5-Bromo-3-hydroxy-4',6'-diphenyl-3',4'-dihydro-3H-spiro[benzofuran-2,2'-pyran]-5'-carbonitrile (**4a**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 35 mg, 76%, as a white solid, mp 198–200 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.50 (d, J = 10.6, 1H), 2.55–2.60 (dd, J = 14, 6.8, 1H), 2.65–2.71 (dd, J = 14, 6.8, 1H), 4.10 (t, J = 6.8, 1H), 5.23 (d, J = 10.6, 1H), 6.70 (d, J = 8.8, 1H), 7.31–7.35 (m, 1H), 7.40–7.70 (m, 9H), 7.71–7.72 (m, 2H). ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$): δ 36.8, 37.9, 76.1, 88.5, 110.5, 112.3, 113.4, 119.1, 127.5, 128.0, 128.2, 128.3, 128.4, 128.9, 130.9, 131.2, 132.5, 132.7, 140.8, 155.3, 164.5. IR [ν_{max} , cm^{-1}]: 3397, 3062, 2956, 2925, 2852, 2210, 1615, 1599, 1469, 1340, 1251, 1184, 1162, 1145, 1049, 1024, 1001, 968, 816, 766, 737, 698. $[\alpha]_{\text{D}}^{19}$ -85 (c 1, CHCl_3 , 97% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 86:14, 1 mL/min, λ = 273 nm, t (major) = 37.11 min, t (minor) = 33.46 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{19}\text{BrNO}_3$, 460.0543; found, 460.0536.

(2*S*,3*S*,4'*R*)-Methyl 5-Bromo-3-hydroxy-4'-phenyl-3',4'-dihydro-3H-spiro[benzofuran-2,2'-pyran]-6'-carboxylate (**4b**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 25 mg, 60%, as a white solid, mp 198–200 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.38–2.44 (dd, J = 14, 7.2, 1H), 2.49–2.54 (dd, J = 14, 7.2, 1H), 3.25 (d, J = 9.6, 1H), 3.79 (s, 3H), 3.88–3.93 (td, J = 7.2, 3.6, 1H), 5.09 (d, J = 8, 1H), 6.38 (d, J = 3.6, 1H), 6.64 (d, J = 8.4, 1H), 7.28–7.38 (m, 6H), 7.48 (d, J = 0.8, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 35.7, 36.7, 52.4, 78.1, 108.2, 112.3, 114.0, 114.9, 127.1, 127.7, 128.3, 128.6, 129.5, 133.1, 141.8, 142.1, 155.8, 162.5. IR [ν_{max} , cm^{-1}]: 3361, 2970, 2928, 1722, 1654, 1467, 1379, 1299, 1256, 1161, 1128, 1106, 952, 816, 701. $[\alpha]_{\text{D}}^{19}$ -20 (c 1, CHCl_3 , 99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 94:6, 1 mL/min, λ = 254 nm, t (major) = 32.26 min, t (minor) = 29.51 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{17}\text{BrO}_5\text{Na}$, 439.0152; found, 439.0149.

(2*S*,3*S*,4'*R*)-5-Bromo-3'-methyl-1',4'-diphenyl-4',5'-dihydro-1'H,3H-spiro[benzofuran-2,6'-pyrano[2,3-c]pyrazol]-3-ol (**4c**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 43 mg, 88%, as a yellow solid, mp 196–198 °C. ^1H NMR (400 MHz, CDCl_3): δ 1.89 (s, 3H), 2.08 (s, 1H), 2.49–2.54 (dd, J = 14, 5.6, 1H), 2.62–2.68 (dd, J = 14.4, 6.8, 1H), 4.22 (t, J = 6, 1H), 5.20 (s, 1H), 6.59 (d, J = 8.4, 1H), 7.20 (t, J = 7.2, 1H), 7.31–7.37 (m, 8H), 7.47 (d, J = 0.6, 1H), 7.60 (d, J = 0.4, 1H), 7.62 (d, J = 0.6, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.1, 33.7, 38.6, 77.4, 98.3, 111.4, 112.5, 114.3, 120.8, 126.0, 126.8, 127.9, 128.3, 128.5, 129.0, 129.1,

133.4, 138.1, 142.2, 147.2, 148.2, 155.6. IR [ν_{max} cm^{-1}]: 3375, 2922, 2854, 1598, 1460, 1384, 1257, 1152, 1095, 1026, 936, 808, 756, 698, 663. [α]_D²⁰ –80 (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80:20, 1 mL/min, λ = 273 nm, t (major) = 50.73 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{H}$]⁺ calcd for $\text{C}_{26}\text{H}_{22}\text{BrN}_2\text{O}_3$, 489.0808; found, 489.0804.

(2*S*,3*S*,4'*S*)-3-Hydroxy-4',6'-diphenyl-3',4'-dihydro-3*H*-spiro[benzofuran-2,2'-pyran]-5'-carbonitrile (**4d**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 34 mg, 90%, as a white solid, mp 218–220 °C. ¹H NMR (400 MHz, CDCl_3): δ 2.46 (d, J = 9.6, 1H), 2.55–2.61 (dd, J = 14, 7.2, 1H), 2.63–2.68 (dd, J = 14, 7.2, 1H), 4.11 (t, J = 7.2, 1H), 5.25 (d, J = 9.6, 1H), 6.83 (d, J = 8, 1H), 7.05 (t, J = 8, 1H), 7.29–7.53 (m, 10H), 7.73–7.75 (m, 2H). ¹³C NMR (150 MHz, DMSO- d_6): δ 37.6, 38.5, 76.9, 88.8, 110.4, 110.4, 119.6, 122.6, 125.9, 127.9, 128.5, 128.7, 128.9, 129.0, 129.3, 130.2, 131.2, 133.3, 141.4, 156.5, 165.2. IR [ν_{max} cm^{-1}]: 3405, 3270, 3049, 2957, 2926, 2853, 2252, 2206, 1716, 1617, 1601, 1478, 1464, 1264, 1164, 1147, 1056, 1028, 1008, 821, 760, 732, 700. [α]_D²⁰ +9 (c 1, MeOH, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 88:12, 1 mL/min, λ = 273 nm, t (major) = 36.37 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{Na}$]⁺ calcd for $\text{C}_{25}\text{H}_{19}\text{NO}_3\text{Na}$, 404.1257; found, 404.1267.

Methyl (2*S*,3*S*,4'*R*)-3-Hydroxy-4'-phenyl-3',4'-dihydro-3*H*-spiro[benzofuran-2,2'-pyran]-6'-carboxylate (**4e**). Purified by flash chromatography (petroleum ether/EtOAc = 3:1). Yield: 22 mg, 65%, as a yellow solid, mp 141–143 °C. ¹H NMR (400 MHz, CDCl_3): δ 2.36–2.42 (dd, J = 13.6, 8, 1H), 2.44–2.49 (dd, J = 13.6, 7.2, 1H), 3.14 (d, J = 10.4, 1H), 3.75 (s, 3H), 3.88–3.92 (td, J = 7.2, 3.2, 1H), 5.10 (d, J = 8.4, 1H), 6.32 (d, J = 3.2, 1H), 6.75 (d, J = 8, 1H), 6.96 (t, J = 7.6, 1H), 7.21 (t, J = 7.6, 1H), 7.25–7.36 (m, 6H). ¹³C NMR (100 MHz, CDCl_3): δ 36.0, 37.1, 52.3, 78.5, 107.9, 110.6, 114.8, 122.0, 125.3, 127.0, 127.0, 127.7, 128.7, 130.4, 142.0, 142.4, 156.8, 162.5. IR [ν_{max} cm^{-1}]: 3430, 2928, 2857, 2361, 1717, 1652, 1602, 1477, 1464, 1439, 1335, 1292, 1240, 1115, 1068, 1028, 914, 876, 754, 701. [α]_D²⁶ +2 (c 1, CHCl_3 , 97% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 94:6, 1 mL/min, λ = 254 nm, t (major) = 18.08 min, t (minor) = 16.19 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{Na}$]⁺ calcd for $\text{C}_{20}\text{H}_{18}\text{O}_5\text{Na}$, 361.1046; found, 361.1050.

(2*S*,3*S*,4'*R*)-3'-Methyl-1',4'-diphenyl-4',5'-dihydro-1'*H*,3*H*-spiro[benzofuran-2,6'-pyrano[2,3-*c*]pyrazol]-3-ol (**4f**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 34 mg, 83%, as a white solid, mp 118–120 °C. ¹H NMR (400 MHz, CDCl_3): δ 1.89 (s, 3H), 2.47 (d, J = 11.2, 1H), 2.52–2.57 (dd, J = 14.4, 6, 1H), 2.63–2.69 (dd, J = 14.4, 6.8, 1H), 4.25 (t, J = 6, 1H), 5.24 (d, J = 11.2, 1H), 6.73 (d, J = 8, 1H), 7.01 (t, J = 7.2, 1H), 7.17–7.63 (m, 11H), 7.65 (d, J = 0.8, 2H). ¹³C NMR (100 MHz, CDCl_3): δ 13.3, 33.9, 38.9, 77.3, 77.7, 98.5, 110.7, 111.0, 120.7, 122.3, 125.3, 125.7, 126.6, 126.8, 128.0, 128.4, 129.0, 130.6, 138.3, 142.3, 147.1, 148.4, 156.6. IR [ν_{max} cm^{-1}]: 3376, 2956, 2923, 2852, 2373, 1737, 1599, 1460, 1383, 1263, 1121, 1075, 1037, 857, 802, 751, 698, 667, 405. [α]_D²⁰ –35 (c 1, MeOH, 92% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80:20, 1 mL/min, λ = 254 nm, t (major) = 31.06 min, t (minor) = 11.36 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{H}$]⁺ calcd for $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_3$, 411.1703; found, 411.1712.

(2*R*,3*S*,4'*S*)-3-Hydroxy-7-methoxy-4',6'-diphenyl-3',4'-dihydro-3*H*-spiro[benzofuran-2,2'-pyran]-5'-carbonitrile (**4g**).

Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 36 mg, 89%, as a yellow solid, mp 198–200 °C. ¹H NMR (400 MHz, CDCl_3): δ 2.56–2.69 (m, 3H), 3.85 (s, 3H), 4.08–4.11 (dd, J = 9.2, 2.4, 1H), 5.27 (d, J = 10.8, 1H), 6.88–6.90 (m, 1H), 6.99–7.01 (m, 2H), 7.31–7.35 (m, 1H), 7.37–7.44 (m, 7H), 7.75–7.77 (m, 2H). ¹³C NMR (100 MHz, CDCl_3): δ 37.1, 38.5, 56.4, 78.8, 89.1, 109.1, 114.3, 116.9, 118.7, 123.4, 127.8, 127.8, 128.0, 128.3, 128.4, 128.9, 130.9, 132.4, 139.9, 144.6, 145.0, 164.1. IR [ν_{max} cm^{-1}]: 3358, 2957, 2923, 2854, 2215, 1615, 1494, 1458, 1264, 1162, 1064, 1045, 1023, 799, 740, 698. [α]_D¹⁸ –14 (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 86:14, 1 mL/min, λ = 273 nm, t (major) = 37.90 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{Na}$]⁺ calcd for $\text{C}_{26}\text{H}_{21}\text{NO}_4\text{Na}$, 434.1363; found, 434.1358.

(2*S*,3*S*,4'*R*)-Methyl 3-hydroxy-7-methoxy-4'-phenyl-3',4'-dihydro-3*H*-spiro[benzofuran-2,2'-pyran]-6'-carboxylate (**4h**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield, 20 mg, 55%, as a white solid, mp 192–194 °C. ¹H NMR (400 MHz, CDCl_3): δ 2.48 (s, 1H), 2.50 (s, 1H), 2.94 (s, 1H), 3.78 (s, 3H), 3.81 (s, 3H), 3.91–3.95 (td, J = 7.6, 3.2, 1H), 5.14 (s, 1H), 6.31 (d, J = 2.8, 1H), 6.84 (d, J = 7.6, 1H), 6.95 (t, J = 8, 1H), 7.01 (d, J = 7.6, 1H), 7.28–7.38 (m, 5H). ¹³C NMR (100 MHz, CDCl_3): δ 36.0, 37.2, 52.2, 56.3, 79.0, 108.4, 114.2, 114.8, 117.1, 122.8, 127.1, 127.6, 128.3, 128.7, 141.9, 142.4, 144.5, 145.3, 162.5. IR [ν_{max} cm^{-1}]: 3368, 2923, 2856, 2367, 1594, 1459, 1260, 1157, 1118, 1046, 748. [α]_D¹⁸ +24 (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 93:7, 1 mL/min, λ = 254 nm, t (major) = 34.67 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{Na}$]⁺ calcd for $\text{C}_{21}\text{H}_{20}\text{O}_6\text{Na}$, 391.1152; found, 391.1147.

(2*S*,3*S*,4'*R*)-7-Methoxy-3'-methyl-1',4'-diphenyl-4',5'-dihydro-1'*H*,3*H*-spiro[benzofuran-2,6'-pyrano[2,3-*c*]pyrazol]-3-ol (**4i**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 37 mg, 86%, as a yellow solid, mp 94–96 °C. ¹H NMR (400 MHz, CDCl_3): δ 1.83 (s, 3H), 2.04 (s, 1H), 2.59 (dd, J = 3.2, 1H), 2.61 (d, J = 3.2, 1H), 3.76 (s, 3H), 4.22 (t, J = 6.4, 1H), 5.23 (s, 1H), 6.84 (d, J = 7.2, 1H), 6.93–7.00 (m, 2H), 7.17 (t, J = 7.6, 1H), 7.25–7.36 (m, 7H), 7.66–7.68 (m, 2H). ¹³C NMR (100 MHz, CDCl_3): δ 13.2, 26.9, 34.1, 39.3, 56.4, 77.8, 98.7, 111.5, 114.5, 117.2, 120.8, 123.1, 125.7, 126.8, 127.9, 127.9, 128.5, 129.0, 138.2, 142.0, 144.5, 145.0, 146.9, 148.6. IR [ν_{max} cm^{-1}]: 3325, 3061, 2958, 2925, 2853, 1718, 1599, 1518, 1496, 1456, 1282, 1260, 1058, 1035, 1019, 757, 739, 700. [α]_D¹⁹ –22 (c 1, CHCl_3 , 96% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80:20, 1 mL/min, λ = 254 nm, t (major) = 36.97 min, t (minor) = 12.40 min. HRMS (ESI-TOF) m/z : [$\text{M} + \text{H}$]⁺ calcd for $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_4$, 441.1809; found, 441.1808.

General Procedure for the Syntheses of Bisbenzannulated 5,6-Spiroketal (6). A reaction tube was charged with phenol **2** (0.1 mmol), *o*-methylenecetoxy-phenol **5** (0.12 mmol), CuI (0.005 mmol), PPh_3 (0.005 mmol), and CHCl_3 (2 mL). The tube was filled with argon and was then sealed and heated at 100 °C for 24 h in a drying oven. The resulting reaction mixture was cooled to ambient temperature; then, the solvent evaporated, and the residue was purified by flash silica gel chromatography giving desired spiroketal **6**.

(2*R*,3*S*)-3*H*-Spiro[benzofuran-2,2'-chroman]-3-ol (**6a**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 20 mg, 77%, as a white solid, mp 142–144 °C. ¹H NMR (400 MHz, CDCl_3): δ 2.30–2.34 (m, 2H), 2.84–2.92 (m, 2H),

3.20–3.29 (m, 1H), 5.19 (d, $J = 10.8$, 1H), 6.81 (d, $J = 8$, 1H), 6.84 (d, $J = 8$, 1H), 6.95–6.98 (m, 1H), 7.03 (t, $J = 7.6$, 1H), 7.13–7.17 (m, 2H), 7.24 (d, $J = 8$, 1H), 7.46 (d, $J = 7.2$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 28.5, 77.6, 106.7, 110.7, 117.0, 121.7, 121.8, 121.9, 125.2, 127.6, 128.2, 129.2, 130.1, 151.6, 156.8. $[\alpha]_{\text{D}}^{25} -201$ (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, $\lambda = 254$ nm, t (major) = 24.37 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{16}\text{H}_{18}\text{O}_3\text{N}$, 272.1281; found, 272.1276.

(2*R*,3*S*)-7-Methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6b**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 22 mg, 80%, as a white solid, mp 135–137 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.26–2.34 (td, $J = 12.4$, 5.6, 1H), 2.35–2.41 (ddd, $J = 13.6$, 6, 3.2, 1H), 2.85–2.90 (m, 2H), 3.24–3.33 (m, 1H), 3.83 (s, 3H), 5.19 (d, $J = 10.4$, 1H), 6.85 (t, $J = 8.8$, 2H), 6.94 (d, $J = 7.6$, 1H), 6.99 (t, $J = 7.6$, 1H), 7.08 (d, $J = 7.2$, 1H), 7.13 (t, $J = 7.6$, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 28.7, 56.1, 77.9, 107.2, 113.5, 116.9, 117.1, 121.6, 121.9, 122.6, 127.6, 129.1, 129.4, 144.7, 145.2, 151.7. $[\alpha]_{\text{D}}^{26} -133$ (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 94:6, 1 mL/min, $\lambda = 254$ nm, t (major) = 38.56 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{17}\text{O}_4$, 285.1121; found, 285.1123.

(2*S*,3*S*)-8'-Methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6c**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 20 mg, 71%, as a white solid, mp 136–137 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.20–2.28 (td, $J = 13$, 5.6, 1H), 2.31–2.36 (ddd, $J = 13.6$, 6, 2.8, 1H), 2.83–2.89 (ddd, $J = 16.2$, 5.2, 2.8, 1H), 3.19–3.27 (m, 2H), 3.75 (s, 3H), 5.18 (d, $J = 10.4$, 1H), 6.74–6.77 (m, 2H), 6.80 (d, $J = 8$, 1H), 6.90 (t, $J = 8$, 1H), 6.99–7.03 (td, $J = 7.4$, 0.8, 1H), 7.23 (d, $J = 7.2$, 1H), 7.46 (d, $J = 7.2$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 28.8, 55.7, 77.5, 106.7, 110.1, 110.6, 120.9, 121.1, 121.8, 122.9, 125.3, 128.2, 130.0, 141.2, 148.4, 156.8. $[\alpha]_{\text{D}}^{25} -112.5$ (c 0.4, CHCl_3 , 96% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 92:8, 1 mL/min, $\lambda = 254$ nm, t (major) = 14.53 min, t (minor) = 15.80 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4\text{N}$, 302.1387; found, 302.1390.

(2*R*,3*S*)-7,8'-Dimethoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6d**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 25 mg, 79%, as a yellow solid, mp 152–153 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.19–2.27 (m, 1H), 2.35–2.41 (ddd, $J = 13.6$, 5.6, 2.8, 1H), 2.81–2.87 (ddd, $J = 16$, 5.2, 2.8, 1H), 3.23–3.38 (m, 2H), 3.74 (s, 3H), 3.83 (s, 3H), 5.17 (d, $J = 10$, 1H), 6.72–6.75 (m, 2H), 6.83–6.90 (m, 2H), 6.97 (t, $J = 7.6$, 1H), 7.08 (d, $J = 7.2$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 29.0, 55.7, 56.1, 77.8, 107.2, 110.0, 113.3, 117.2, 120.8, 121.0, 122.5, 123.1, 129.3, 141.2, 144.6, 145.2, 148.4. $[\alpha]_{\text{D}}^{26} -106$ (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 95:5, 1 mL/min, $\lambda = 254$ nm, t (major) = 22.70 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{18}\text{H}_{22}\text{O}_5\text{N}$, 332.1492; found, 332.1495.

(2*R*,3*S*)-6',7-Dimethoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6e**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 27 mg, 87%, as a white solid, mp 194–195 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.23–2.31 (td, $J = 13.2$, 5.6, 1H), 2.32–2.38 (m, 1H), 2.81–2.89 (m, 2H), 3.22–3.31 (m, 1H), 3.77 (s, 3H), 3.83 (s, 3H), 5.17 (d, $J = 10.8$, 1H), 6.68–6.71 (m, 2H), 6.77 (d, $J = 8.8$, 1H), 6.86 (d, $J = 8$, 1H), 6.98 (t, $J = 7.8$, 1H), 7.07 (d, $J = 7.2$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.8, 28.7, 55.7, 56.1, 77.8, 107.2, 113.5, 113.7, 117.1, 117.5, 122.5, 122.6, 129.4, 144.7, 145.2, 145.7, 154.2. $[\alpha]_{\text{D}}^{26} -95$ (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 90:10, 1 mL/min, $\lambda = 254$ nm, t (major) = 28.12 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{19}\text{O}_5$, 315.1227; found, 315.1224.

(2*R*,3*S*)-5-Bromo-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6f**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 29 mg, 87%, as a white solid, mp 145–146 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.27–2.33 (m, 2H), 2.86–2.92 (m, 2H), 3.18–3.27 (m, 1H), 5.17 (d, $J = 11.2$, 1H), 6.68 (d, $J = 8.8$, 1H), 6.83 (d, $J = 8$, 1H), 6.96–7.00 (m, 1H), 7.13–7.17 (m, 2H), 7.33–7.35 (dd, $J = 8.4$, 2, 1H), 7.56 (d, $J = 0.8$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.4, 28.3, 77.3, 107.3, 112.4, 113.9, 116.9, 121.7, 121.9, 127.7, 128.3, 129.2, 130.6, 132.9, 151.4, 155.8. $[\alpha]_{\text{D}}^{25} -202.2$ (c 0.92, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, $\lambda = 254$ nm, t (major) = 31.76 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{BrO}_3\text{Na}$, 354.9940; found, 354.9939.

(2*R*,3*S*)-5,6'-Dibromo-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6g**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 31 mg, 76%, as a yellow solid, mp 145–146 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.27–2.32 (m, 2H), 2.80 (d, $J = 11.2$, 1H), 2.83–2.89 (m, 1H), 3.15–3.24 (m, 1H), 5.17 (d, $J = 11.2$, 1H), 6.68 (d, $J = 8.4$, 1H), 6.71 (d, $J = 8.4$, 1H), 7.22–7.25 (dd, $J = 8.8$, 2.4, 1H), 7.29 (s, 1H), 7.33–7.36 (dd, $J = 8.4$, 2, 1H), 7.55 (d, $J = 0.4$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 27.9, 77.3, 107.2, 112.4, 114.1, 114.1, 118.7, 123.9, 128.3, 130.4, 130.6, 131.8, 133.0, 150.5, 155.6. $[\alpha]_{\text{D}}^{26} -112$ (c 1, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, $\lambda = 254$ nm, t (major) = 41.34 min, t (minor) = 44.12 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{12}\text{Br}_2\text{O}_3\text{Na}$, 432.9045; found, 432.9044.

(2*R*,3*S*)-6'-Bromo-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6h**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 22 mg, 67%, as a white solid, mp 142–144 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.28–2.33 (m, 2H), 2.74 (d, $J = 10.8$, 1H), 2.84–2.90 (m, 1H), 3.18–3.27 (m, 1H), 5.20 (d, $J = 10.8$, 1H), 6.72 (d, $J = 8.8$, 1H), 6.80 (d, $J = 8$, 1H), 7.04 (t, $J = 7.6$, 1H), 7.22–7.32 (m, 3H), 7.45 (d, $J = 7.2$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.4, 28.2, 77.6, 106.6, 110.7, 113.9, 118.8, 122.1, 124.0, 125.2, 128.0, 130.2, 130.5, 131.8, 150.9, 156.6. $[\alpha]_{\text{D}}^{25} -128.9$ (c 0.52, CHCl_3 , 96% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, $\lambda = 254$ nm, t (major) = 29.70 min, t (minor) = 34.12 min. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{BrO}_3\text{Na}$, 354.9940; found, 354.9936.

(2*R*,3*S*)-6'-Nitro-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6i**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 23 mg, 76%, as a yellow solid, mp 160–161 °C. ^1H NMR (400 MHz, CDCl_3): δ 2.34–2.41 (m, 2H), 2.98–3.04 (m, 1H), 3.27–3.35 (m, 1H), 5.26 (s, 1H), 6.82 (d, $J = 7.6$, 1H), 6.92 (d, $J = 8.8$, 1H), 7.07 (t, $J = 7.2$, 1H), 7.29 (d, $J = 7.6$, 1H), 7.46 (d, $J = 7.2$, 1H), 8.03–8.06 (dd, $J = 8.8$, 2.4, 1H), 8.12 (d, $J = 7.4$, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 27.9, 77.7, 107.2, 110.7, 117.6, 122.5, 122.7, 123.7, 125.2, 125.3, 127.5, 130.4, 142.1, 156.4, 157.1. $[\alpha]_{\text{D}}^{26} -151.7$ (c 0.87, CHCl_3 , >99% ee). The enantiomeric ratio was determined by Daicel

Chiralpak AD-H (25 cm), hexanes/IPA = 88:12, 1 mL/min, λ = 254 nm, t (major) = 29.22 min, t (minor) = 27.43. HRMS (ESI-TOF) m/z : $[M + NH_4]^+$ calcd for $C_{16}H_{17}N_2O_5$, 317.1132; found, 317.1129.

(2*R*,3*S*)-5-Methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6j**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 21 mg, 75%, as a white solid, mp 176–177 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.29–2.33 (m, 2H), 2.85–2.94 (m, 2H), 3.19–3.27 (m, 1H), 3.81 (s, 3H), 5.17 (d, J = 10.8, 1H), 6.71 (d, J = 8.8, 1H), 6.78–6.80 (dd, J = 8.8, 2.4, 1H), 6.84 (d, J = 8, 1H), 6.96 (t, J = 7.2, 1H), 7.03 (d, J = 2, 1H), 7.12–7.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 28.5, 56.0, 78.0, 107.0, 110.4, 111.0, 115.8, 117.0, 121.7, 121.8, 127.6, 128.9, 129.2, 150.6, 151.7, 155.2. $[\alpha]_D^{25}$ –175 (c 1, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 92:8, 1 mL/min, λ = 254 nm, t (major) = 25.14 min. HRMS (ESI-TOF) m/z : $[M + NH_4]^+$ calcd for $C_{17}H_{20}O_4N$, 302.1387; found, 302.1386.

(2*R*,3*S*)-5-Methyl-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6k**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 17 mg, 63%, as a white solid, mp 135–137 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.26–2.30 (m, 2H), 2.33 (s, 3H), 2.83–2.89 (m, 2H), 3.17–3.26 (m, 1H), 5.14 (d, J = 10.8, 1H), 6.67 (d, J = 8.4, 1H), 6.82 (d, J = 8, 1H), 6.92–6.96 (m, 1H), 7.03 (d, J = 8.4, 1H), 7.09–7.14 (m, 2H), 7.24 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 21.5, 28.5, 77.7, 106.8, 110.3, 117.0, 121.7, 121.8, 125.6, 127.6, 128.1, 129.2, 130.5, 131.4, 151.7, 154.7. $[\alpha]_D^{26}$ –174.5 (c 0.98, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 95:5, 1 mL/min, λ = 254 nm, t (major) = 27.99 min. HRMS (ESI-TOF) m/z : $[M + NH_4]^+$ calcd for $C_{17}H_{20}O_3N$, 286.1438; found, 286.1433.

(2*R*,3*S*)-6'-Methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6l**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 21 mg, 75%, as a white solid, mp 148–150 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.28–2.32 (m, 2H), 2.82–2.89 (m, 2H), 3.19–3.28 (m, 1H), 3.78 (s, 3H), 5.17 (d, J = 10.8, 1H), 6.70–6.72 (m, 2H), 6.76–6.81 (m, 2H), 7.02 (t, J = 7.2, 1H), 7.24 (d, J = 8, 1H), 7.45 (d, J = 7.2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 28.6, 55.7, 77.5, 106.6, 110.7, 113.6, 113.8, 117.6, 121.9, 122.4, 125.2, 128.2, 130.1, 145.6, 154.3, 156.8. $[\alpha]_D^{25}$ –220 (c 0.6, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 92:8, 1 mL/min, λ = 254 nm, t (major) = 25.89 min. HRMS (ESI-TOF) m/z : $[M + NH_4]^+$ calcd for $C_{17}H_{20}O_4N$, 302.1387; found, 302.1389.

(2*R*,3*S*)-6'-Methyl-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6m**). Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 17 mg, 65%, as a white solid, mp 126–128 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.28–2.32 (m, 5H), 2.81–2.87 (m, 2H), 3.17–3.26 (m, 1H), 5.18 (d, J = 10.8, 1H), 6.74 (d, J = 8, 1H), 6.80 (d, J = 8, 1H), 6.94–6.97 (m, 2H), 7.00–7.04 (td, J = 7.6, 0.8, 1H), 7.24 (d, J = 7.6, 1H), 7.45 (d, J = 7.6, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5, 21.5, 28.7, 77.6, 106.7, 110.7, 116.7, 121.4, 121.8, 125.2, 128.2, 128.2, 129.5, 130.1, 131.0, 149.5, 156.8. $[\alpha]_D^{26}$ –103 (c 1, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, λ = 254 nm, t (major) = 20.79 min. HRMS (ESI-TOF) m/z : $[M + NH_4]^+$ calcd for $C_{17}H_{20}O_3N$, 286.1438; found, 286.1443.

(2*S*,3*R*)-3*H*-Spiro[benzofuran-2,2'-chroman]-3-ol (**6n**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1).

Yield: 20 mg, 78%, as a white solid, mp 142–144 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.30–2.34 (m, 2H), 2.83–2.92 (m, 2H), 3.20–3.29 (m, 1H), 5.19 (d, J = 10.8, 1H), 6.80 (d, J = 8, 1H), 6.84 (d, J = 8, 1H), 6.94–6.98 (td, J = 7.6, 0.8, 1H), 7.01–7.05 (td, J = 7.6, 0.8, 1H), 7.12–7.17 (m, 2H), 7.24 (d, J = 7.6, 1H), 7.46 (d, J = 7.2, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.5, 28.5, 77.6, 106.6, 110.7, 117.0, 121.7, 121.8, 121.9, 125.2, 127.6, 128.1, 129.2, 130.1, 151.6, 156.7. $[\alpha]_D^{25}$ +233.3 (c 0.3, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 96:4, 1 mL/min, λ = 254 nm, t (major) = 30.77 min. HRMS (ESI-TOF) m/z : $[M + H]^+$ calcd for $C_{16}H_{15}O_3$, 255.1016; found, 255.1019.

(2*R*,3*S*,3'*R*)-3'-(Methoxymethyl)-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6o**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 18 mg, 60%, as a white solid, mp 102–104 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.61–2.69 (m, 1H), 2.88–2.96 (m, 3H), 3.32 (s, 3H), 3.39–3.43 (m, 1H), 3.66–3.70 (m, 1H), 5.73 (d, J = 10.8, 1H), 6.79 (d, J = 8, 1H), 6.82 (d, J = 8, 1H), 6.94–6.98 (td, J = 7.2, 1.2, 1H), 7.02–7.06 (td, J = 7.6, 0.8, 1H), 7.12–7.16 (m, 2H), 7.22–7.26 (m, 1H), 7.46 (d, J = 7.6, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 36.7, 58.9, 72.6, 74.9, 107.7, 110.6, 116.6, 121.3, 121.7, 122.0, 125.2, 127.6, 128.6, 129.0, 129.9, 151.0, 156.7. IR [ν_{max} , cm^{-1}]: 3393, 2955, 2925, 1477, 1460, 1226, 1172, 1110, 1076, 907, 754. $[\alpha]_D^{27}$ –146 (c 1, $CHCl_3$, 97% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 80:20, 1 mL/min, λ = 273 nm, t (major) = 23.74 min, t (minor) = 41.30 min. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{18}H_{18}O_4Na$, 321.1097; found, 321.1093.

(2*R*,3*S*,3'*R*)-7-Methoxy-3'-(methoxymethyl)-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6p**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 18 mg, 55%, as a white solid, mp 114–116 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.60–2.68 (td, J = 12.4, 6, 1H), 2.91–3.06 (m, 3H), 3.31 (s, 3H), 3.41–3.45 (dd, J = 10, 6, 1H), 3.70–3.74 (dd, J = 9.6, 6.4, 1H), 3.81 (s, 3H), 5.72 (d, J = 10.4, 1H), 6.82 (d, J = 8, 1H), 6.85 (d, J = 8, 1H), 6.94 (t, J = 7.2, 1H), 6.99 (t, J = 8, 1H), 7.08–7.14 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 36.9, 56.2, 58.8, 72.6, 75.2, 108.2, 113.5, 116.5, 117.1, 121.4, 121.7, 122.7, 127.6, 129.0, 129.9, 144.6, 145.1, 151.1. IR [ν_{max} , cm^{-1}]: 3396, 2955, 2925, 1492, 1458, 1283, 1224, 1171, 1054, 904, 754. $[\alpha]_D^{25}$ –158 (c 1, $CHCl_3$, >99% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 98:2, 1 mL/min, λ = 273 nm, t (major) = 34.10 min. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{19}H_{20}O_5Na$, 351.1203; found, 351.1198.

(2*R*,3*S*,3'*R*)-6'-Methoxy-3'-(methoxymethyl)-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6q**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 23 mg, 70%, as a white solid, mp 94–96 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.59–2.67 (m, 1H), 2.91–2.94 (m, 3H), 3.31 (s, 3H), 3.37–3.41 (dd, J = 10, 6, 1H), 3.65–3.69 (dd, J = 10, 6.4, 1H), 3.77 (s, 3H), 5.70 (d, J = 11.2, 1H), 6.69–6.71 (m, 2H), 6.74–6.80 (m, 2H), 7.03 (t, J = 7.6, 1H), 7.23 (t, J = 8, 1H), 7.45 (d, J = 7.6, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1, 36.8, 55.6, 58.8, 72.6, 74.8, 107.6, 110.6, 113.5, 113.6, 117.2, 121.9, 122.0, 125.2, 128.6, 129.8, 145.0, 154.3, 156.7. IR [ν_{max} , cm^{-1}]: 3399, 2924, 2852, 1498, 1477, 1463, 1213, 1152, 1117, 1076, 1024, 906. $[\alpha]_D^{27}$ –152 (c 1, $CHCl_3$, 90% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 85:15, 1 mL/min, λ = 273 nm, t (major) = 11.87 min, t (minor) = 9.07 min. HRMS (ESI-TOF)

m/z : $[M + Na]^+$ calcd for $C_{19}H_{20}O_5Na$, 351.1203; found, 351.1199.

(2*R*,3*S*,3'*R*)-6'-7-Dimethoxy-3'-(methoxymethyl)-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6r**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 23 mg, 65%, as a yellow solid, mp 128–130 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.58–2.66 (td, J = 12, 6, 1H), 2.88–3.03 (m, 3H), 3.31 (s, 3H), 3.410–3.43 (dd, J = 10, 6, 1H), 3.70–3.72 (dd, J = 10, 6.4, 1H), 3.76 (s, 1H), 3.81 (s, 3H), 5.69 (d, J = 10.8, 1H), 6.67–6.70 (m, 2H), 6.74–6.76 (m, 1H), 6.85 (d, J = 8, 1H), 6.98 (t, J = 8, 1H), 7.07 (d, J = 8, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 37.0, 55.6, 56.2, 58.8, 72.6, 75.1, 108.1, 113.4, 113.5, 113.6, 117.1, 122.0, 122.6, 129.9, 144.6, 145.0, 145.1, 154.2. IR [ν_{max} , cm^{-1}]: 3414, 2955, 2922, 2852, 1494, 1460, 1435, 1291, 1275, 1220, 1117, 1053, 1008, 903, 801, 748. $[\alpha]_D^{27}$ –163 (c 1, $CHCl_3$, 91% ee). The enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 90:10, 1 mL/min, λ = 273 nm, t (major) = 12.79 min, t (minor) = 8.17 min. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{20}H_{22}O_6Na$, 381.1309; found, 381.1304.

(2*R*,3*S*,3'*R*)-5,6'-Dibromo-3'-(methoxymethyl)-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6s**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 28 mg, 62%, as a white solid, mp 86–88 °C. 1H NMR (400 MHz, $CDCl_3$): δ 2.57–2.65 (m, 1H), 2.83–2.89 (m, 3H), 3.32 (s, 3H), 3.37–3.41 (dd, J = 10, 5.2, 1H), 3.61–3.66 (dd, J = 10, 7.2, 1H), 5.75 (d, J = 11.2, 1H), 6.66–6.70 (m, 2H), 7.22–7.24 (m, 1H), 7.32–7.35 (m, 1H), 7.55 (t, J = 0.8, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.3, 36.2, 58.9, 72.3, 74.6, 108.4, 112.4, 114.2, 114.2, 118.4, 123.4, 128.3, 130.6, 130.9, 131.6, 132.8, 150.0, 155.5. IR [ν_{max} , cm^{-1}]: 3395, 2925, 2850, 1480, 1467, 1250, 1256, 1172, 1120, 1080, 1022, 909, 814, 738, 660. $[\alpha]_D^{18}$ –166 (c 1, $CHCl_3$, 81% ee). The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80:20, 1 mL/min, λ = 280 nm, t (major) = 15.07 min, t (minor) = 27.43 min. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{18}H_{16}Br_2O_4Na$, 476.9308; found, 476.9309.

3'-Pentyl-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6t**). Purified by flash chromatography (petroleum ether/EtOAc = 4:1). Yield: 2 mg, 5%, as a white solid, mp 98–100 °C. 1H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, J = 6.8, 3H), 1.27–1.38 (m, 7H), 1.65–1.68 (m, 1H), 2.20–2.28 (m, 1H), 2.85–3.04 (m, 3H), 5.51 (d, J = 11.2, 1H), 6.78–6.83 (m, 2H), 6.93–6.97 (td, J = 7.6, 0.8, 1H), 7.02 (t, J = 7.2, 1H), 7.11–7.15 (m, 2H), 7.24 (t, J = 8, 1H), 7.46 (d, J = 7.6, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 22.6, 26.6, 27.3, 29.6, 31.8, 36.3, 74.2, 108.9, 110.6, 116.5, 121.6, 121.9, 121.9, 125.3, 127.5, 128.3, 129.0, 130.1, 151.1, 157.0. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{21}H_{24}O_3Na$, 347.1618; found, 347.1619.

tert-Butyl((8'-methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-yl)oxy)dimethylsilane (**6v**). Purified by flash chromatography (petroleum ether/EtOAc = 16:1). Yield: 2 mg, 5%, as a white solid, mp 110–112 °C. 1H NMR (400 MHz, $CDCl_3$): δ 0.20 (s, 3H), 0.21 (s, 3H), 0.92 (s, 9H), 1.98–2.06 (td, J = 13.6, 6, 1H), 2.37–2.43 (m, 1H), 2.84–2.89 (m, 1H), 3.16–3.24 (m, 1H), 3.75 (s, 3H), 5.37 (s, 1H), 6.73–6.81 (m, 3H), 6.88 (t, J = 7.6, 1H), 6.96 (t, J = 7.6, 1H), 7.21–7.25 (m, 1H), 7.33–7.35 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ –4.4, –4.1, 21.4, 24.9, 25.8, 29.7, 56.2, 78.7, 110.4, 110.7, 111.2, 120.8, 121.2, 121.3, 123.3, 125.8, 128.3, 130.0, 142.1, 148.6, 158.3. IR [ν_{max} , cm^{-1}]: 2926, 1600, 1479, 1464, 1381, 1301, 1257, 1213, 1198, 1175, 1123, 1086, 1063, 1048, 921, 838, 798, 776, 750. HRMS

(ESI-TOF) m/z : $[M + H]^+$ calcd for $C_{22}H_{29}O_3Si$, 369.1880; found, 369.1876.

8'-Methoxy-3*H*-spiro[benzofuran-2,2'-chroman]-3-ol (**6w**). To a solution of the **6v** (0.005 mmol) in 2 mL of THF was added a solution of tetrabutylammonium fluoride (1.1 equiv) in 2 mL THF. After 0.5 h, water (2 mL) was added to the reaction mixture; the aqueous phase was extracted with ethyl acetate, and the extract was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford **6w**. Purified by flash chromatography (petroleum ether/EtOAc = 8:1). Yield: 1.5 mg, 95%, as a yellow oil. 1H NMR (400 MHz, $CDCl_3$): δ 1.87 (d, J = 8, 1H), 2.16–2.24 (td, J = 13.2, 6, 1H), 2.36–2.41 (m, 1H), 2.90–2.96 (m, 1H), 3.15–3.24 (m, 1H), 3.75 (s, 3H), 5.31 (d, J = 8, 1H), 6.74 (d, J = 8, 1H), 6.78 (d, J = 8, 1H), 6.84–6.91 (m, 2H), 7.01 (t, J = 7.2, 1H), 7.30 (d, J = 7.6, 1H), 7.47 (d, J = 7.6, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.4, 29.7, 56.1, 78.1, 110.2, 110.9, 110.9, 120.9, 121.2, 121.7, 123.0, 125.9, 127.6, 130.9, 141.8, 148.5, 158.5. IR [ν_{max} , cm^{-1}]: 3400, 2926, 1615, 1480, 1465, 1377, 1266, 1200, 1175, 1122, 1046, 916, 880, 752, 732. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{16}H_{14}O_3Na$, 277.0835; found, 277.0833.

(*Z*)-5-Bromo-2-(2-methoxyethylidene)-2,3-dihydrobenzofuran-3-ol (**7f**). CuI (0.05 mmol, 10 mg) and PPh₃ (0.05 mol, 13 mg) were added to a solution of compound **2f** (1 mmol, 270 mg) in $CHCl_3$ (3 mL). The tube was filled with argon and was then sealed and heated at 100 °C for 24 h in a drying oven. The resulting reaction mixture was cooled to ambient temperature; then, the solvent evaporated, and the residue was purified by flash silica gel chromatography (petroleum ether/EtOAc = 4:1) giving **7f**. Yield: 189 mg, 70%, as a white solid; mp 70–72 °C. 1H NMR (400 MHz, $CDCl_3$): δ 3.39 (s, 3H), 4.21 (d, J = 8, 2H), 5.29–5.33 (td, J = 8, 1.6, 1H), 5.63 (s, 1H), 6.86 (d, J = 8, 1H), 7.40–7.43 (dd, J = 8, 2, 1H), 7.57 (d, J = 2, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 58.1, 66.1, 70.7, 103.0, 112.0, 114.7, 128.7, 129.5, 133.5, 156.3, 159.2. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{11}H_{11}BrO_3Na$, 292.9784; found, 292.9788.

tert-Butyldimethyl((2-methylene-2,3-dihydrobenzofuran-3-yl)oxy)silane (**9a**). To a solution of intermediate 2-methylene-2,3-dihydrobenzofuran-3-ol (1 mmol, 148 mg) in dry THF (8 mL) was slowly added NaH (70%, 1.1 mmol, 38 mg) at rt. A solution of TBSCl (1.1 mmol in 2 mL of THF) was then added dropwise. The reaction mixture was stirred at rt overnight and was then quenched with saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc. Combined organic layers were washed with brine, dried over Na_2SO_4 , and evaporated. The residue was purified by flash chromatography (petroleum ether/EtOAc = 16:1) on silica gel to give the product **9a**. Yield: 130 mg, 50%, as a brown oil. 1H NMR (400 MHz, $CDCl_3$): δ 0.13 (s, 3H), 0.19 (s, 3H), 0.94 (s, 9H), 4.60–4.61 (m, 1H), 4.91–4.92 (t, J = 2, 1H), 5.78 (s, 1H), 6.92 (d, J = 8, 1H), 7.00–7.04 (td, J = 8, 0.8, 1H), 7.25–7.29 (m, 1H), 7.34 (d, J = 8, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ –4.1, –3.9, 18.0, 25.7, 71.4, 89.0, 110.1, 122.1, 125.5, 128.0, 130.1, 157.4, 164.1. HRMS (ESI-TOF) m/z : $[M + Na]^+$ calcd for $C_{15}H_{22}O_2SiNa$, 285.1281; found, 285.1286.

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystallographic data and copies of 1H , ^{13}C , and HPLC spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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