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Supporting Information

Ruthenium-Catalyzed Asymmetric Dehydrative Allylic Cyclization of Five-Membered Chalcogen Heteroaromatics

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Figures S1–S26 and **Table S1** are attached at the end of the supporting information.

1. General.

Manipulation. A Teflon-coated magnetic bar was used for stirring of a reaction mixture. Room temperature (rt) was in the range of 25 °C to 28 °C. Catalytic asymmetric allylative cyclizations at 50–100 °C were carried out by use of an EYELA *ChemiStation*^{TM}. Reactions for substrate syntheses at –78 °C, –40 °C, 0 °C, and 50–100 °C were carried out by use of a dry ice/CH_3OH bath, dry ice/acetonitrile, an ice bath, and an oil bath equipped with a temperature control, respectively. A Dimroth condenser was used for a reflux process. Solvents after general workup processes were removed by means of a rotary evaporator. Concentration of a reaction mixture in a Schlenk tube was performed by connecting to a vacuum-Ar line via a cold trap cooled by liquid nitrogen. Organic extracts obtained by a general partition-based workup were dried over anhydrous Na_2SO_4 for ca. 30 min. The Na_2SO_4 was removed by cotton filtration. "Aqueous" and "saturated" were abbreviated "aq." and "sat.," respectively. Brine means sat. aq. NaCl. All metal-catalyzed reactions were carried out under an argon (Ar) atmosphere by use of a general Schlenk technique unless otherwise specified. A Schlenk with a Teflon J. Young valve was specified by "Young-type Schlenk." Schlenks were dried, before use, at ca. 250 °C by use of a heat gun under a reduced pressure, and a silicon grease was used for connecting to a cold finger-type condenser and a glass stopper. Solvents and liquid reagents were introduced by use of a syringe via a septum rubber. After introduction, the septum was replaced with a glass stopper or with a Young valve. Heating in a closed system was carried out after reducing an inner pressure of the whole system or after raising the temperature under an Ar stream followed by closing the system. Degassed solvents and degassed solutions of reagents, catalysts, and substrates were transferred to another Schenk by use of a gas-tight syringe or a cannulation method. Cannulation was performed by use of a Teflon or stainless tube through a septum rubber under a slightly positive pressure of Ar. One freeze-thaw cycle consists of i) freezing a liquid mixture, ii) evacuation of the system at the freezing stage, iii) closing the system, iv) thawing the frozen liquid, and v) releasing the negative pressure to an atmospheric pressure by filling Ar gas. For the general syntheses of substrates under an Ar atmosphere, non-degassed solvents were used. In gas/liquid biphasic reaction, 1 atm gas was introduced by connecting Tedlar gas sampling bag which was filled by the appropriate gas.

Gases. Ar gas was purified by being passed through a column of BASF R3-11 catalyst at 80 °C and then through a column of granular-type $CaSO_4$ solids. Hydrogen

(H_2) gas of 99.99999% grade was purchased from Taiyo Nippon Sanso Corporation and used for hydrogenation without purification.

Solvents. Solvents for preparation of Ru complexes and catalytic reactions were dried and degassed at the reflux temperature in the presence of appropriate drying agents (2.5 g/L) under an Ar stream for 6 h and distilled into Schlenk flasks: *tert*-butyl alcohol (*t*-BuOH), dichloromethane (CH_2Cl_2), *N*,*N*-dimethylacetamide (DMA), and *N*,*N*-dimethylformamide (DMF), *N*-methylpyrrolidone (NMP) from CaH_2; tetrahydrofuran (THF) and toluene from sodium benzophenone ketyl. These were degassed by three freeze-thaw cycles immediately before use. First grade solvents were used without purification for processes such as an extraction, a partition, and a silica-gel column chromatography and for general organic syntheses. Spectrochemical analysis-grade chloroform ($CHCl_3$) was used for measurement of an optical rotation. Solvents purified by GlassContour solvent purification system were used for water-sensitive reactions in a synthetic procedure. Hexane for an HPLC analysis was used after filtration (0.5 μM pored PTFE filter). HPLC grade 2-propanol (*i*-PrOH) was purchased from FUJIFILM Wako Pure Chemical Corporation.

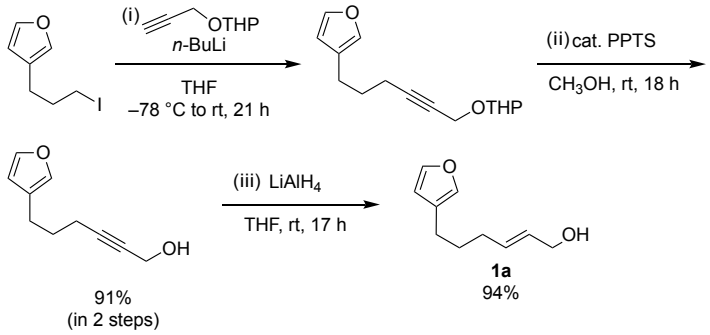
Reagents. All of reagents were purchased and used without further purification unless otherwise specified. **Kanto Chemical**: 2.6–2.8 M *n*-butyllithium (*n*-BuLi) hexane solution, sodium periodate ($NaIO_4$). **FUJIFILM Wako Pure Chemical**: iodomethane (CH_3I), 2,2-dimethoxypropane. **Nacalai Tesque**: acetic acid (AcOH), ammonium chloride (NH_4Cl), Hyflo Super-Cel, iodine (I_2), sodium bicarbonate ($NaHCO_3$), sodium carbonate (Na_2CO_3), sodium hydride (NaH) 60% oil suspension, sodium hydroxide (NaOH), anhydrous sodium sulfate (Na_2SO_4), sodium thiosulfate ($Na_2S_2O_3$). **Sigma-Aldrich**: 1.0 M tetrabutylammonium fluoride (TBAF) in THF, 1.0 M lithium aluminum tetrahydride ($LiAlH_4$) in hexane, 4-methylmorpholine *N*-oxide (NMO), palladium on carbon (Pd-C). **Strem**: trisacetonitrilecyclopentadienylruthenium hexafluorophosphate ($[CpRu(CH_3CN)_3]PF_6$). **Tokyo Chemical Industry**: ethyl (triphenylphosphoranylidene)acetate, 1.0 M diisobutylaluminum hydride (DIBAL) in toluene, 3-furylboronic acid, imidazole, dimethyl malonate, *N*-(4-nitrophenyl)maleimide, 4% aq. osmium tetraoxide (OsO_4), paraformaldehyde, triphenylphosphine (PPh_3), tetrakistriphenylphosphinepalladium ($Pd(PPh_3)_4$),

potassium sodium (+)-tartrate tetrahydrate, propargyl bromide, pyridinium *p*-toluenesulfonate (PPTS), sodium tetrahydroborate ($NaBH_4$).

2. Substrate Preparation.

(*E*)-6-(Furan-3-yl)hex-2-en-1-ol (1a) (Scheme S1).

Scheme S1



Process (i). 2-(Prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran[1] (360 μL, 2.55 mmol) and THF (110 mL) were placed in a 100-mL two-necked round-bottom flask, and the solution was cooled to –78 °C. *n*-BuLi (2.8 M in hexane; 1.00 mL, 2.80 mmol) was slowly added and stirred at –78 °C for 30 min. To this was added 3-(3-iodopropyl)furan[2] (580 mg, 2.32 mmol) in THF (3 mL). After 24-h stirring at rt, the reaction mixture was quenched by addition of sat. aq. NH_4Cl (20 mL). The organic layer was separated, and aq. layer was extracted by Et_2O (30 mL x 2). The combined organic layers were washed with brine (50 mL) and dried over Na_2SO_4 (ca. 15 g). Filtration/evaporation process afforded a crude product (668 mg), which was used in the next reaction without further purification.

Process (ii). The above crude product was placed in a 30-mL three-necked round-bottom flask. After addition of CH_3OH (12 mL), the solution was cooled to 0 °C, and PPTS (58.3 mg, 232 μmol) was added. After 24-h stirring at rt, the reaction was quenched by addition of sat. aq. $NaHCO_3$ (10 mL) at 0 °C. The organic layer was separated, and the aq. layer was extracted by EtOAc (20 mL x 2). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4 (ca.10 g). Filtration/evaporation process afforded a crude product (424 mg). This was purified by silica-gel-column chromatography (SiO_2-chlormatography) (30 g, 1:4 ethyl acetate (EtOAc)–hexane eluent) afforded 6-(furan-3-yl)hex-2-yn-1-ol (264 mg, 64%, 2 steps) as an colorless oil. ^1H NMR

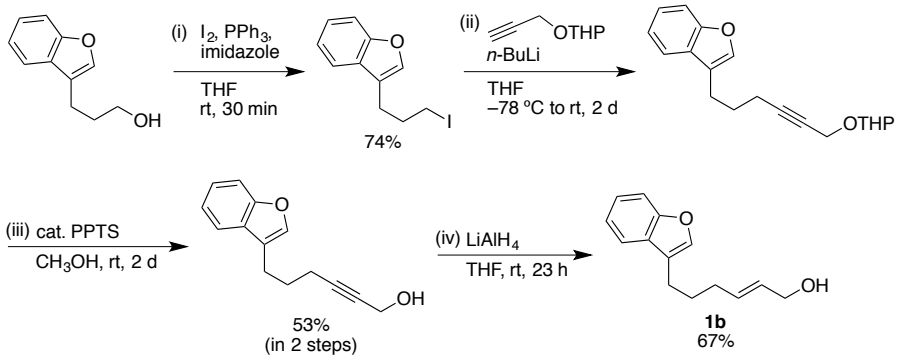
($CDCl_3$) δ 7.34 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.26 (s, 1H, ArH), 5.66 (m, 2H, C*H*$_2$OH), 2.53 (t, *J* = 6.18 Hz, 2H, ArC*H*$_2$), 2.25 (m, 2H, CH$_2$C*H*$_2$C≡C), 1.77 (quin, *J* = 7.40 Hz, 2H, CH$_2$C*H*$_2$CH$_2$), 1.45 (t, *J* = 6.18 Hz, 1H, OH).

Process (iii). 6-(Furan-3-yl)hex-2-yn-1-ol (264 mg, 1.48 mmol) and THF (14.8 mL) were placed in a 50-mL two-necked round-bottom flask. To the solution was added $LiAlH_4$ (1.0 M in THF; 3.00 mL, 3.00 mmol) at 0 °C. After 8-h stirring at rt, the reaction was quenched at 0 °C by addition of H_2O (4.0 mL), 10% aq NaOH (1.0 mL), and sat. aq. potassium sodium (+)-tartrate tetrahydrate (10 mL). Organic layer was separated, and the aqueous layer was extracted by Et_2O (30 mL x 2). The combined organic layers were washed by brine (30 mL) and dried over Na_2SO_4 (ca.15 g). Filtration/evaporation process afforded a crude product (258 mg). This was purified SiO_2-chlormatography (30 g, 1:2 Et_2O–hexane eluent) afforded (E)-6-(furan-3-yl)hex-2-en-1-ol (**1a**) (242 mg, 91%, 2 steps). ^{1}H NMR ($CDCl_3$) δ 7.34 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.25 (s, 1H, ArH), 5.68 (dt, *J* = 15.14, 6.90 Hz, 1H, CH$_2$C*H*=CH), 5.63 (dt, *J* = 15.14, 4.80 Hz, 1H, CH=C*H*CH$_2$OH), 4.08 (d, *J* = 4.80 Hz, 2H, C*H*$_2$OH), 2.42 (t, *J* = 7.56 Hz, 2H, ArC*H*$_2$CH$_2$), 2.08 (m, 2H, C*H*$_2$CH=CH), 1.72 (br s, 1H, OH), 1.62 (quin, *J* = 7.56 Hz, 2H, CH$_2$C*H*$_2$CH$_2$); ^{13}C NMR ($CDCl_3$) δ 142.6, 138.8, 132.5, 129.3, 124.7, 110.9, 63.6, 31.6, 29.3, 24.1; HRMS (ESI) *m*/*z* [M+Na]$^+$ calcd. for $C_{10}H_{14}NaO_2$ 189.0892, found 189.0889.

Figure S1 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-6-(Benzofuran-3-yl)hex-2-en-1-ol (1b) (Scheme S2).

Scheme S2



Process (i). 3-(Benzofuran-3-yl)propan-1-ol[3] (352 mg, 2.00 mmol) was placed in a 50-mL two-necked round-bottom flask and to this was added THF (14 mL), PPh_3 (632 mg, 2.40 mmol), and imidazole (410 mg, 6.00 mmol). The solution was

cooled to 0 °C and I_2 (662 mg, 2.6 mmol) was added. After 30-min stirring at rt, the reaction was quenched by addition of sat. aq. $Na_2S_2O_3$ (10 mL) at 0 °C. The organic layer was separated, and aq. layer was extracted by EtOAc (30 mL x 2). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4 (ca. 10 g). Filtration/evaporation process afforded a crude product (614 mg). This was purified by SiO_2-chromatography (20 g, 1:10 EtOAc–hexane eluent) to give 3-(3-iodopropyl)benzofuran (424 mg, 74%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.56 (d, *J* = 7.62 Hz, 1H, ArH), 7.47 (d, *J* = 8.26 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 7.30 (t, *J* = 7.92 Hz, 1H, ArH), 7.25 (t, *J* = 7.56 Hz, 1H, ArH), 3.23 (t, *J* = 6.87 Hz, 2H, CH_2I), 2.83 (t, *J* = 7.23 Hz, 2H, $ArCH_2$), 2.21 (quin, *J* = 7.05 Hz, 2H, $CH_2CH_2CH_2$).

Process (ii). The procedure is same as that of **1a**, process (i). Conditions: 2-(Prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran[1] (240 μL, 1.60 mmol), THF (5 mL), –78 °C, *n*-BuLi (2.8 M in hexane; 640 mL, 1.80 mmol), 30 min, 3-(3-iodopropyl)benzofuran (424 mg, 1.50 mmol), THF (2.4 mL), rt, 48 h. Work up: sat. aq. NH_4Cl (10 mL), EtOAc (30 mL x 2), brine (30 mL), Na_2SO_4 (ca.10 g) afforded a crude product (576 mg), which was used in the next reaction without further purification.

Process (iii). The procedure is same as that of **1a**, process (ii). Conditions: Crude product (576 mg), CH_3OH (7.4 mL), PPTS (37.2 mg, 148 μmol), rt, 96 h. Work up: sat. aq. $NaHCO_3$ (10 mL), EtOAc (30 mL x 2), brine (50 mL), Na_2SO_4 (ca. 10 g) afforded a crude product (358 mg). Purification: SiO_2-chromatography (10 g, 1:4 EtOAc–hexane eluent) afforded 6-(benzofuran-3-yl)hex-3-yn-1-ol (168 mg, 53%, 2 steps) as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.56 (d, *J* = 7.56 Hz, 1H, ArH), 7.47 (d, *J* = 8.28 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.29 (t, *J* = 7.92 Hz, 1H, ArH), 7.24 (t, *J* = 6.87 Hz, 1H, ArH), 4.27 (dt, *J* = 2.07, 5.46 Hz, 2H, CH_2OH), 2.80 (t, *J* = 7.92 Hz, 2H, $ArCH_2$), 2.31 (tt, *J* = 2.07, 6.87 Hz, 2H, $CH_2C{\equiv}C$), 1.93 (quin, *J* = 7.40 Hz, 2H, $CH_2CH_2CH_2$), 1.43 (t, *J* = 6.18 Hz, 1H, OH).

Process (iv). The procedure is same as that of **1a**, process (iii). Conditions: 6-(Benzofuran-3-yl)hex-3-yn-1-ol (388 mg, 2.20 mmol), THF (7.8 mL), 0 °C, $LiAlH_4$ (1.0 M in THF; 1.60 mL, 1.60 mmol), rt, 23 h. Work up: H_2O (0.2 mL), 10% aq. NaOH (0.2 mL), H_2O (0.6 mL), sat. aq. potassium sodium (+)-tartrate tetrahydrate (10 mL), EtOAc (150 mL x 2), brine (150 mL), Na_2SO_4 (ca. 8 g)

afforded a crude product (170 mg). Purification: SiO_2-chromatography (20 g, 1:2 EtOAc–hexane eluent) afforded (*E*)-6-(benzofuran-3-yl)hex-2-en-1-ol (**1b**) (114 mg, 67%) as colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.55 (d, *J* = 7.56 Hz, 1H, ArH), 7.46 (d, *J* = 8.28 Hz, 1H, ArH), 7.40 (s, 1H, ArH), 7.29 (t, *J* = 6.87 Hz, 1H, ArH), 7.23 (t, *J* = 7.56 Hz, 1H, ArH), 5.70 (m, 2H, CH=CH), 4.11 (t, *J* = 5.49 Hz, 2H,C*H*$_2$OH), 2.69 (t, *J* = 7.59 Hz, 2H, ArCH_2), 2.16 (q, *J* = 6.90 Hz, 2H, C*H*$_2$CH=CH), 1.82 (q, *J* = 7.40 Hz, 2H, CH_2C*H*$_2$$CH_2$), 1.24 (t, *J* = 5.85 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 155.4, 141.1, 132.5, 129.6, 128.3, 124.1, 122.2, 120.2, 120.0, 111.4, 63.7, 31.8, 28.4, 23.0; HRMS (ESI) *m/z* [M+Na]$^+$ calcd. for $C_{14}H_{16}NaO_2$ 239.1043, found 239.1042.

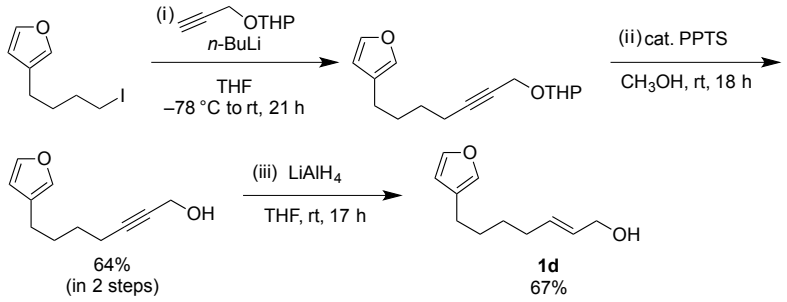
Figure S2 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-5-(Furan-3-yl)pent-2-en-1-ol (1c)

This compound was synthesized according to procedure reported.[4]

(*E*)-7-(Furan-3-yl)hept-2-en-1-ol (1d) (Scheme S3).

Scheme S3



This compound was synthesized in similar procedure for synthesis of **1a**.

Process (i). Conditions: 2-(Prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran[1] (360 μL, 2.55 mmol), THF (9 mL), –78 °C, *n*-BuLi (2.8 M in hexane; 1.00 mL, 2.78 mmol), 30 min, 3-(4-iodobutyl)furan[2] (580 mg, 2.32 mmol), THF (3 mL), rt, 24 h. Work up: sat. aq. NH_4Cl (20 mL), Et_2O (30 mL x 2), brine (50 mL), Na_2SO_4 (ca. 20 g) afford a crude product (668 mg), which was used in the next reaction without further purification.

Process (ii). Conditions: Crude product (668 mg), CH_3OH (12 mL), PPTS (58.3 mg, 232 μmol), rt, 72 h. Work up: sat. aq. $NaHCO_3$ (10 mL), EtOAc (20 mL x 2), brine (20 mL), Na_2SO_4 (ca. 10 g) afford a crude product (424 mg). Purification: SiO_2-chromatography (10 g, 1:4 EtOAc–hexane eluent) afforded

7-(furan-3-yl)hept-2-yn-1-ol (264 mg, 64%, 2 steps) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.35 (s, 1H, ArH), 7.22 (s, 1H, ArH), 6.27 (s, 1H, ArH), 4.25 (dd, *J* = 2.07, 5.51 Hz, 2H, C*H*$_2$OH), 2.44 (t, *J* = 7.57 Hz, 2H, ArC*H*$_2$), 2.25 (t, *J* = 7.23 Hz, 2H, CH$_2$C*H*$_2$C≡C), 1.66 (dt, *J* = 7.57, 15.8 Hz, 2H, C*H*$_2$CH$_2$C≡C), 1.55 (dt, *J* = 6.89, 15.2 Hz, 2HH, ArCH$_2$C*H*$_2$), 1.45 (t, *J* = 6.20 Hz, 1H, OH).

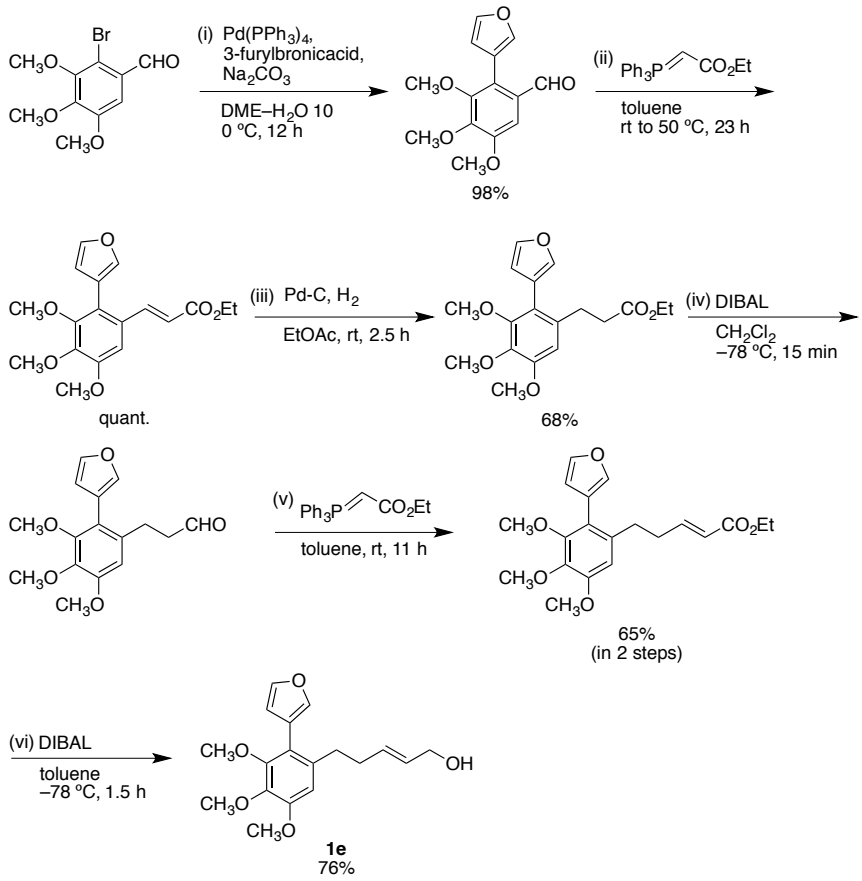
Process (iii). Conditions: 7-(Furan-3-yl)hept-2-yn-1-ol (264 mg, 1.48 mmol), THF (15 mL), 0 °C, $LiAlH_4$ (1.0 M in THF; 3.0 mL, 3.0 mmol), 0 °C to rt, 8 h. Work up: H_2O (1 mL), 10% aq. NaOH (1 mL), H_2O (3.0 mL), sat. aq. potassium sodium (+)-tartrate tetrahydrate (10 mL), EtOAc (30 mL x 2), brine (30 mL), Na_2SO_4 (ca. 10 g) afforded a crude product (258 mg). Purification: SiO_2-chromatography (10 g, 1:2 EtOAc–hexane eluent) afforded (*E*)-7-(furan-3-yl)hept-2-en-1-ol (**1d**) (242 mg, 67%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.34 (t, *J* = 3.44 Hz, 1H, ArH), 7.20 (s, 1H, ArH), 6.26 (s, 1H, ArH), 5.69 (dt, *J* = 6.89, 15.15 Hz, 1H, CH=C*H*), 5.65 (dt, *J* = 6.20, 11.02 Hz, 1H, C*H*=CH), 4.08 (m, 2H, C*H*$_2$OH), 2.41 (t, *J* = 7.57 Hz, 2H, ArC*H*$_2$), 2.07 (dd, *J* = 7.23, 14.12 Hz, 2H, C*H*$_2$CH=CH), 1.57 (dt, *J* = 7.57, 15.2 Hz, 2H, ArCH$_2$C*H*$_2$CH$_2$), 1.43 (dt, *J* = 7.57, 15.2 Hz, 2H, ArCH$_2$CH$_2$C*H*$_2$); ^{13}C NMR ($CDCl_3$) δ 142.7, 138.8, 133.2, 129.2, 125.1, 111.1, 63.9, 32.1, 29.6, 28.8, 24.7; HRMS (ESI) *m*/*z* [M+Na]$^+$ calcd. for $C_{11}H_{16}NaO_2$ 203.1043, found 203.1041.

Figure S3 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-5-(2-(Furan-3-yl)-3,4,5-trimethoxyphenyl)pent-2-en-1-ol (1e) (Scheme S4).

Process (i). 2-Bromo-3,4,5-trimethoxybenzaldehyde[5] (5.86 g, 21.3 mmol), 3-furylboronic acid (4.77 g, 42.6 mmol), Na_2CO_3 (6.77 g, 63.9 mmol), DME (160 mL), and H_2O (54 mL) were placed in a 1000-mL Schlenk flask and the mixture was degassed. To this was added $Pd(PPh_3)_4$ (1.24 g, 1.07 mmol). The reaction mixture was stirred at 100 °C for 12 h. After cooled to rt, H_2O (100 mL) was added. The organic layer was separated, and the aq. layer was extracted by EtOAc (50 mL x 2). The combined organic layers were washed with brine (300 mL) and dried over Na_2SO_4 (ca. 50 g). Filtration/concentration process afforded a crude product (7.60 g). This was purified by SiO_2-chromatography (35 g, 1:5–1:3 EtOAc–hexane eluent) afforded 2-(furan-3-yl)-3,4,5-trimethoxybenzaldehyde (5.49 g, 98%) as a

Scheme S4



colorless oil. ^{1}H NMR ($CDCl_3$) δ 9.94 (s, 1H, CHO), 7.56 (s, 1H, ArH), 7.49 (s, 1H, ArH), 7.34 (s, 1H, ArH), 6.57 (s, 1H, ArH), 4.00 (s, 3H, CH_3), 3.94 (s, 3H, CH_3), 3.70 (s, 3H, CH_3).

Process (ii). 2-(Furan-3-yl)-3,4,5-trimethoxybenzaldehyde (3.58 g, 13.7 mmol), toluene (137 mL), and ethyl (triphenylphosphoranylidene)acetate (9.55 g, 27.4 mmol) were placed in a 100-mL round-bottom flask. After 7.5-h stirring at rt, ethyl (triphenylphosphoranylidene)acetate (4.01 g, 5.78 mmol) was added. The reaction mixture was heated to 50 °C and stirred for 15 h. Concentration of reaction mixture afforded a crude product (15.4 g). This was purified by SiO_2-chromatography (100 g, 1:10 EtOAc–hexane eluent) afforded ethyl (*E*)-3-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)acrylate (5.06 g, quant) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.72 (d, *J* = 15.8 Hz, 1H, C*H*=CHCOO), 7.49 (s, 1H, ArH), 7.40 (s, 1H, ArH), 6.93 (s, 1H, ArH), 6.48 (s, 1H, ArH), 6.26 (d, *J* = 15.8 Hz, 1H, CH=C*H*COO), 4.20 (q, *J* = 7.56 Hz, 2H, OC*H*$_2$CH$_3$), 3.92 (s, 3H, CH_3), 3.90 (s, 3H, CH_3), 3.66 (s, 3H, CH_3), 1.28 (t, *J* = 7.56 Hz, 3H, C*H*$_2$CH$_3$).

Process (iii). Ethyl (*E*)-3-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)acrylate (1.94 g, 5.84 mmol), EtOAc (58.4 mL), and Pd-C (295 mg, 15 wt%) were placed in a 200-mL round-bottom flask. H_2 (1 atm) was introduced into the vessel. After 2.5-h stirring at rt, the resulting suspension was filtered through Hyflo Super-Cel, and evaporation of the filtrate afforded a crude product (1.82 g). This was purified by SiO_2-chromatography (175 g, 1:5 EtOAc–hexane eluent) to give ethyl 3-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)propionate (1.32 g, 68%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.51 (s, 1H, ArH), 7.41 (s, 1H, ArH), 6.61 (s, 1H, ArH), 6.42 (s, 1H, ArH), 4.10 (q, *J* = 6.90 Hz, 2H, CH_3CH_2), 3.87 (s, 6H, CH_3 x 2), 3.66 (s, 3H, CH_3), 2.85 (t, *J* = 8.22 Hz, 2H, CH_2COO), 2.43 (t, *J* = 8.22 Hz, 2H, $ArCH_2$), 1.22 (t, *J* = 6.90 Hz, 3H, CH_3CH_2).

Process (iv). 3-(2-(Furan-3-yl)-3,4,5-trimethoxyphenyl)propionate (1.32 g, 3.95 mmol) and CH_2Cl_2 (15.3 mL) were placed in a 200-mL round-bottom flask. After cooled to –78 °C, DIBAL (1.0 M in THF; 3.20 mL, 3.20 mmol) was added. After 15-min stirring at same temperature, the reaction was quenched by addition of sat. aq. potassium sodium (+)-tartrate tetrahydrate (15 mL) and EtOAc (50 mL), then vigorously stirring. The organic layer was separated, and the aq. layer was extracted by EtOAc (40 mL x 4). The combined organic layers were washed with brine (100 mL) and dried over Na_2SO_4 (ca. 20 g). Filtration/evaporation process afforded a crude product (868 mg), which was used in the next reaction without further purification.

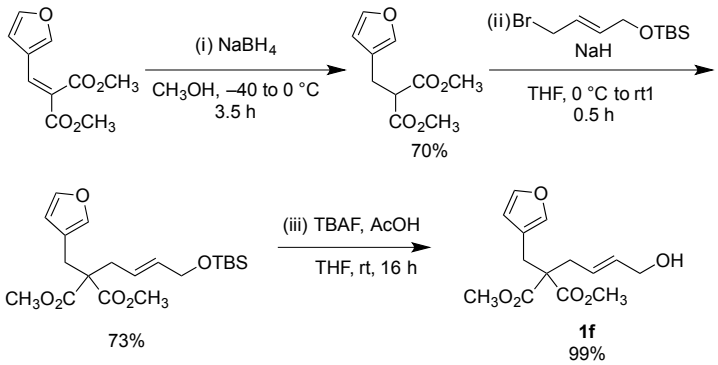
Process (v). The crude product (868 mg), toluene (30.5 mL), and ethyl (triphenylphosphoranylidene)acetate (2.08 g, 5.97 mmol) were placed in a 300-mL round-bottom flask. After 11-h stirring at rt, the reaction mixture was concentrated to give a crude product (2.54 g). This was purified by SiO_2-chromatography (250 g, 1:2 EtOAc–hexane eluent) to give ethyl (*E*)-5-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)pent-2-enoate (718 mg, 65%, 2 steps) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.51 (s, 1H, ArH), 7.38 (s, 1H, ArH), 6.88 (dt, *J* = 15.8, 7.56 Hz, 1H, CH=CHCOOEt), 6.56 (s, 1H, ArH), 6.40 (s, 1H, ArH), 5.74 (d, *J* = 15.8 Hz, 1H, CH=CHCOOEt), 4.17 (q, *J* = 6.90 Hz, 2H, OCH_2CH_3), 3.88 (s, 6 H, CH_3 x 2), 3.67 (s, 3H, CH_3), 2.66 (t, *J* = 7.56 Hz, 2H, $ArCH_2$), 2.34 (q, *J* = 7.56 Hz, 2H, CH_2CH=CH), 1.28 (t, *J* = 6.90 Hz, 3H, CH_2CH_3).

Process (vi). Ethyl (*E*)-5-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)pent-2-enoate (718 mg, 1.99 mmol) and toluene (19.9 mL) were placed in a 300-mL three-necked round-bottom flask. After cooled to –78 °C, DIBAL (1.0 M in THF; 4.98 mL, 4.98 mmol) and toluene (19.9 mL) were added. After 1.5-h stirring at same temperature, the reaction was quenched by addition of sat. aq. potassium sodium (+)-tartrate tetrahydrate (20 mL) and vigorous stirring for 15 h. The organic layer was separated, and the aq. layer was extracted by EtOAc (20 mL x 4). The combined organic layers were washed with brine (200 mL) and dried over Na_2SO_4 (ca. 20 g). Filtration/evaporation process afforded a crude product (868 mg). This was purified by SiO_2-chromatography (65 g, 1:2 EtOAc–hexane eluent) to give (*E*)-5-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)pent-2-en-1-ol (**1e**) (481 mg, 76%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.51 (s, 1H, ArH), 7.39 (s, 1H, ArH), 6.58 (s, 1H, ArH), 6.41 (s, 1H, ArH), 5.64 (dt, *J* = 15.1, 6.90 Hz, 1H, CH_2CH=CH), 5.58 (dt, *J* = 15.1, 5.52 Hz, 1H, CH=C*H*CH_2OH), 4.06 (t, *J* = 5.52 Hz, 2H, CH_2OH), 3.88 (s, 6H, CH_3 x 2), 3.67 (s, 3H, CH_3), 2.60 (t, *J* = 6.90 Hz, 2H, $ArCH_2$), 2.22 (d, *J* = 6.90 Hz, 2H, CH_2CH=CH), 1.25 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 152.6, 152.1, 142.4, 140.6, 140.5, 136.6, 132.0, 129.4, 119.5, 119.1, 112.8, 108.2, 63.6, 61.1, 61.0, 55.9, 33.9, 33.3; HRMS (ESI) *m*/*z* $[M+Na]^+$ calcd. for $C_{18}H_{22}NaO_5$ 341.1365, found 341.1341.

Figure S4 shows the ^{1}H- and ^{13}C-NMR spectra.

Dimethyl (*E*)-2-(furan-3-ylmethyl)-2-(4-hydroxybut-2-en-1-yl)malonate (1f) (Scheme S5).

Scheme S5



Process (i). Dimethyl 2-(furan-3-ylmethylene)malonate[6] (2.58 g, 12.3 mmol) and CH_3OH (30.7 mL) were placed in a 200-mL round-bottom flask. After cooled

to –40 °C, $NaBH_4$ (464 mg, 12.3 mmol) was added. After 3-h stirring at the same temperature, the reaction mixture was warmed to 0 °C and stirred for 3.5 h. The reaction was quenched by addition of sat. aq. NH_4Cl (20 mL). The organic layer was separated, and the aq. layer was extracted by CH_2Cl_2 (20 mL x 3). The combined organic layers were dried over Na_2SO_4 (ca. 20 g). Filtration/evaporation process afforded a crude product (2.43 g). This was purified by SiO_2-chromatography (125 g, 1:5 EtOAc–hexane eluent) to give dimethyl 2-(furan-3-ylmethyl)malonate (1.82 g, 70%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.33 (s, 1H, ArH), 7.26 (s, 1H, ArH), 6.25 (s, 1H, ArH), 3.73 (s, 6H, CH_3 x 2), 3.59 (t, J = 7.56 Hz, 1H, C*H*($COOCH_3$)$_2$), 3.04 (d, J = 7.56 Hz, 2H, $ArCH_2$).

Process (ii). 2-(Furan-3-ylmethyl)malonate (638 mg, 3.01 mmol) and THF (15 mL) were placed in a 100-mL two-necked round-bottom flask. To this was added NaH (60%; 144 mg, 3.01 mmol) and stirred for 20 min. The resulting mixture was cooled to 0 °C, (*E*)-((4-bromobut-2-en-1yl)oxy)(*tert*-butyl)dimethylsilane[7] (1.0 M in THF; 3.61 mL, 3.61 mmol) was added. After 10.5-h stirring at rt, the reaction mixture was quenched by addition of sat. aq. NH_4Cl (10 mL) at 0 °C. The organic layer was separated, and the aq. layer was extracted by EtOAc (10 mL x 3). The combined organic layers were washed with brine (50 mL) and dried over Na_2SO_4 (ca. 20 g). Filtration/evaporation process afforded a crude product (1.41 g). This was purified by SiO_2-chromatography (150 g, 1:7 EtOAc–hexane eluent) to give dimethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(furan-3-ylmethyl)malonate (870 mg, 73%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.32 (s, 1H, ArH), 7.19 (s, 1H, ArH), 6.14 (s, 1H, ArH), 5.64 (dt, J = 15.1, 4.80 Hz, 1H, C*H*=CHCH_2O), 5.52 (dt, J = 15.1, 7.56 Hz, 1H, CH=C*H*CH_2O), 4.12 (d, J = 4.80 Hz, 2H, CH_2OTBS), 3.72 (s, 6H, (CH_3 of $COOCH_3$) x 2), 3.03 (s, 2H, $ArCH_2$), 2.59 (d, J = 7.56 Hz, 2H, C*H*$_2$C=CH), 0.91 (s, 9H, C(CH_3)$_3$), 0.06 (s, 6H, $SiCH_3$ x 2).

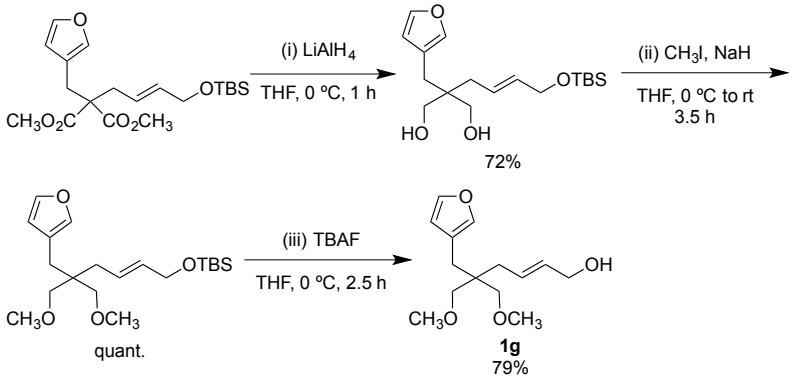
Process (iii). Dimethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(furan-3-ylmethyl)malonate (869 mg, 2.19 mmol) and THF (11 mL) were placed in a 100-mL round-bottom flask. After cooled to 0 °C, AcOH (188 μL, 3.28 mmol) and TBAF (1.0 M in THF; 3.28 mL, 3.28 mmol) were added. After 16-h stirring at rt, the reaction was quenched by addition of sat. aq. NH_4Cl (10 mL). The organic layer was separated, and the aq. layer was extracted by EtOAc (10 mL x 2). The combined organic layers were washed with brine (50 mL) and dried over

Na_2SO_4 (ca. 10 g). Filtration/evaporation process afforded a crude product (991 mg). This was purified by SiO_2-chromatography (20 g, 1:2–1:1 EtOAc–hexane eluent) to give dimethyl (*E*)-2-(furan-3-ylmethyl)-2-(4-hydroxybut-2-en-1-yl)malonate (**1f**) (610 mg, 99%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 1H, ArH), 7.19 (s, 1H, ArH), 6.12 (s, 1H, ArH), 5.71 (dt, *J* = 15.2, 5.52 Hz, 1H, CH=C*H*CH$_2$OH), 5.55 (dt, *J* = 15.2, 6.90 Hz, 1H, CH$_2$C*H*=CH), 4.09 (d, *J* = 5.52 Hz, 2H, C*H*$_2$OH), 3.71 (s, 6H, CH$_3$ x 2), 3.03 (s, 2H, ArCH$_2$), 2.58 (d, *J* = 6.90 Hz, 2H, C*H*$_2$CH=CH), 1.26 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 171.1, 142.9, 140.9, 134.0, 125.7, 118.6, 111.5, 63.1, 58.3, 52.4, 35.1, 27.9; HRMS (ESI) *m*/*z* [M+Na]$^+$ calcd for $C_{14}H_{18}NaO_6$ 305.1001, found 305.0996.

Figure S5 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-6-(Furan-3-yl)-5,5-di(methoxymethyl)hex-2-en-1-ol (1g) (Scheme S6).

Scheme S6



Process (i). The procedure is same as that of **1a**, process (iii). Conditions: Dimethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(furan-3-ylmethyl)malonate (1.24 g, 3.13 mmol), THF (15.7 mL), $LiAlH_4$ (1.0 M in THF; 7.82 mL, 7.82 mmol), 0 °C, 1 h. Work up : sat. aq. potassium sodium (+)-tartrate tetrahydrate (10 mL), EtOAc (10 mL), 10-h stirring, EtOAc (20 mL x 4), brine (100 mL), Na_2SO_4 (ca. 15 g) afforded a crude product (1.1 g). Purification : SiO_2-chromatography (100 g, 1:2–1:1 EtOAc–hexane eluent) afforded (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(furan-3-ylmethyl)propan-1,3-diol (756 mg, 72%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.34 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.24 (s, 1H, ArH), 5.66 (dt, *J* = 15.1, 7.56 Hz, 1H, CH$_2$C*H*=CH), 5.58 (td, *J* = 15.1, 4.8 Hz, 1H, CH=C*H*CH$_2$OTBS), 4.15 (d, *J* = 4.86 Hz, 2H,

CH_2OTBS), 3.09 (s, 4H, C*H*$_2$OH x 2), 2.41 (s, 2H, ArCH_2), 2.01 (d, *J* = 6.84 Hz, 2H, C*H*$_2$CH=CH), 0.92 (s, 9H, C$(CH_3)_3$), 0.08 (s, 6H, SiCH_3 x 2).

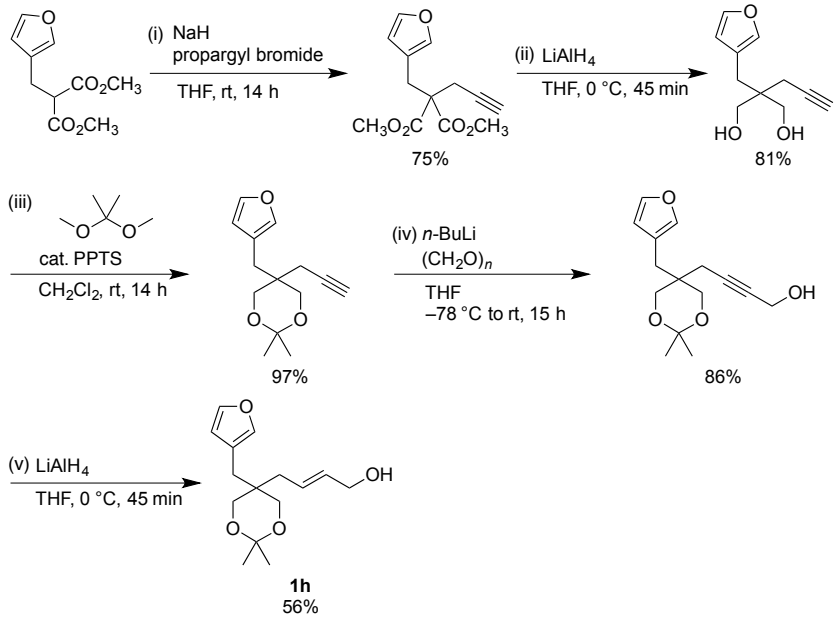
Process (ii). (*E*)-2-(4-((*tert*-Butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(furan-3-ylmethyl)propan-1,3-diol (620 mg, 1.82 mmol) and THF (18.2 mL) were placed in a 200-mL three-necked round-bottom flask. After cooled to 0 °C, to this was added NaH (60%; 219 mg, 5.46 mmol). After 30-min stirring at rt, CH_3I (456 μL, 7.28 mmol) was added at 0 °C. The reaction mixture was warmed to rt and stirred for 30 °C. After cooled to 0 °C, the reaction was quenched by addition of sat. aq. NH_4Cl (10 mL) and H_2O (10 mL). The organic layer was separated, and the aq. layer was extracted by Et_2O (20 mL x 3). The combined organic layers were washed with H_2O (300 mL x 2) and brine (200 mL), and dried over Na_2SO_4 (ca. 15 g). Filtration/evaporation process afforded a crude product (750 mg). This was purified by SiO_2-chromatography (15 g, 1:4 EtOAc–hexane eluent) to give (*E*)-*tert*-butyl((6-(furan-3-yl)-5,5-bis(methoxymethyl)hex-2-en-1-yl)oxy)dimethylsilane (690 mg, quant) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.34 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.24 (s, 1H, ArH), 5.66 (dt, *J* = 15.1, 7.56 Hz, 1H, CH_2CH=CH), 5.58 (td, *J* = 15.1, 4.8 Hz, 1H, CH=C*H*CH_2OTBS), 4.15 (d, *J* = 4.86 Hz, 2H, CH_2OTBS), 3.31 (s, 6 H, OCH_3 x 2), 3.09 (s, 4H, C*H*$_2$$OCH_3$ x 2), 2.41 (s, 2H, ArCH_2), 2.01 (d, *J* = 6.84 Hz, 2H, C*H*$_2$CH=CH), 0.92 (s, 9H, C$(CH_3)_3$), 0.08 (s, 6H, SiCH_3 x 2).

Process (iii). The procedure is same as that of **1f**, process (iii). Conditions: (*E*)-*tert*-Butyl((6-(furan-3-yl)-5,5-bis(methoxymethyl)hex-2-en-1-yl)oxy)dimethylsilane (620 mg, 1.82 mmol), THF (18.7 mL), 0 °C, TBAF (1.0 M in THF; 2.81 mL, 2.81 mmol), 0 °C, 2.5 h. Work up: sat. aq. NH_4Cl (15 mL), EtOAc (20 mL x 4), brine (200 mL), Na_2SO_4 (ca. 15 g) afforded a crude product (3.06 g). Purification: SiO_2-chromatography (75 g, 1:2 EtOAc–hexane eluent) afforded (*E*)-6-(furan-3-yl)-5,5-bis(methoxymethyl)hex-2-en-1-ol (**1g**) (1.18 g, 79%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.39 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.24 (s, 1H, ArH), 5.66–5.76 (m, 2H, CH=CH), 4.14 (d, *J* = 3.42 Hz, 2H, C*H*$_2$OH), 3.32 (s, 6H, CH_3 x2), 3.09 (s, 4H, C*H*$_2$$OCH_3$ x 2), 2.41 (s, 2H, ArCH_2), 2.05 (d, *J* = 5.52 Hz, 2H, C*H*$_2$CH=CH), 1.30 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 142.2, 141.0. 132.2, 128.3, 120.0, 112.9, 74.4, 63.7, 58.9, 42.0, 34.9, 27.0; HRMS (ESI) *m*/*z* [M+Na]$^+$ calcd for $C_{14}H_{22}NaO_4$ 277.1410, found 277.1410.

Figure S6 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-4-(5-(Furan-3-ylmethyl)-2,2-dimethyl-1,3-dioxan-5-yl)but-2-en-1-ol (1h) (Scheme S7).

Scheme S7



Process (i). Dimethyl 2-(furan-3-ylmethyl)malonate (5.02 g, 23.6 mmol) and THF (47.2 mL) were placed in a 500-mL three-necked round-bottom flask. After cooled to 0 °C, to this was added NaH (60%; 1.41 g, 35.3 mmol) and the resulting mixture was stirred for 30 min. To the solution, propargyl bromide (2.64 mL, 35.3 mmol) was added. After 14-h stirring at rt, the reaction was quenched by addition of sat. aq. NH_4Cl (50 mL) at 0 °C. The organic layer was separated, and the aq. layer was extracted by EtOAc (100 mL x 3). The combined organic layers were washed by brine (200 mL) and dried over Na_2SO_4 (ca. 15 g). Filtration/evaporation process afforded a crude product (5.60 g). This was purified by SiO_2-chromatography (150 g, 1:5 EtOAc–hexane) to give dimethyl 2-(furan-3-ylmethyl)-2-(prop-2-yn-1-yl)malonate (4.44 g, 75%) as a yellow oil. ^1H NMR ($CDCl_3$) δ 7.37 (s, 1H, ArH), 7.26 (s, 1H, ArH), 6.18 (s, 1H, ArH), 3.75 (s, 6H, CH_3 x 2), 3.24 (s, 2H, $ArCH_2$), 2.74 (s, 2H, $CH_2C{\equiv}C$), 2.09 (s, 1H, $C{\equiv}CH$).

Process (ii). The procedure is same as that of **1a**, process (iii). Conditions: Dimethyl 2-(furan-3-ylmethyl)-2-(prop-2-yn-1-yl)malonate (4.44 g, 17.7 mmol), THF (59.0 mL), $LiAlH_4$ (1.0 M in THF; 53.1 mL, 53.1 mmol), 0 °C, 45 min. Work up: sat. aq. potassium sodium (+)-tartrate tetrahydrate (100 mL), EtOAc (20 mL),

12-h stirring, EtOAc (100 mL x 4), brine (400 mL), Na_2SO_4 (ca. 30 g) afforded a crude product (3.41 g). Purification: SiO_2-chromatography (300 g, 1:2–1:1 EtOAc–hexane eluent) afforded 2-(furan-3-ylmethyl)-2-(prop-2-yn-1-yl)propan-1,3-diol (2.78 g, 81%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.37 (s, 1H, ArH), 7.26 (s, 1H, ArH), 6.36 (s, 1H, ArH), 3.68 (dd, *J* = 10.3, 4.8 Hz, 2H, C*H*HOH x 2), 3.63 (dd, *J* = 10.3, 4.8 Hz, 2H, CH*H*OH x 2), 2.56 (s, 2H, $ArCH_2$), 2.18 (d, *J* = 2.76 Hz, 2H, $CH_2C{\equiv}C$), 2.09 (s, 1H, C≡CH).

Process (iii). 2-(Furan-3-ylmethyl)-2-(prop-2-yn-1-yl)propan-1,3-diol (708 mg, 3.66 mmol), CH_2Cl_2 (12.2 mL), and 2,2-dimethoxypropane (2.24 mL, 18.2 mmol) were placed in a 30-mL three-necked round-bottom flask. After cooled to 0 °C, PPTS (95.0 mg, 0.378 mmol) was added. After 14-h stirring at rt, the reaction was quenched by addition of sat. aq. $NaHCO_3$ (15 mL) at 0 °C. The organic layer was separated, and the aq. layer was extracted by CH_2Cl_2 (15 mL x 3). The combined organic layers were dried over Na_2SO_4 (ca. 10 g). Filtration/evaporation process afforded a crude product (861 mg). This was purified by SiO_2-chromatography (90 g, 1:5 EtOAc–hexane eluent) to give 5-(furan-3-ylmethyl)-2,2-dimethyl-5-(prop-2-yn-1-yl)-1,3-dioxane (830 mg, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.37 (s, 1H, ArH), 7.29 (s, 1H, ArH), 6.32 (s, 1H, ArH), 3.66 (s, 4H, CH_2OC x 2), 2.58 (s, 2H, $ArCH_2$), 2.25 (s, 2H, $CH_2C{\equiv}C$), 2.08 (s, 1H, C≡CH), 1.42 (s, 3H, CH_3), 1.41 (s, 3H, CH_3).

Process (iv). 5-(Furan-3-ylmethyl)-2,2-dimethyl-5-(prop-2-yn-1-yl)-1,3-dioxane (830 mg, 3.54 mmol) and THF (11.8 mL) were placed in a 200-mL three-necked round-bottom flask. After cooled to –78 °C, *n*-BuLi (2.8 M in hexane; 1.53 mL, 4.25 mmol) was added slowly. After 30-min stirring at –78 °C, paraformaldehyde (88%; 213 mg, 7.08 mmol) was added. After 15-h stirring at rt, the reaction was quenched by addition of sat. aq. NH_4Cl (10 mL) at 0 °C. The organic layer was separated, and the aq. layer was extracted by EtOAc (15 mL x 3). The combined organic layers were washed by brine (50 mL x 2) and dried over Na_2SO_4 (ca. 15 g). Filtration/evaporation process afforded a crude product (875 mg). This was purified by SiO_2-chromatography (100 g, 5:1–1:1 EtOAc–hexane elulent) to give 4-(5-(furan-3-ylmethyl)-2,2-dimethyl-1,3-dioxan-5-yl)but-2-yn-1-ol (618 mg, 86%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.37 (s, 1H, ArH), 7.28 (s, 1H, ArH), 6.30 (s, 1H, ArH), 4.30 (m, 2H, CH_2OH), 3.67 (d, *J* = 11.7 Hz, 2H, C*H*HOC

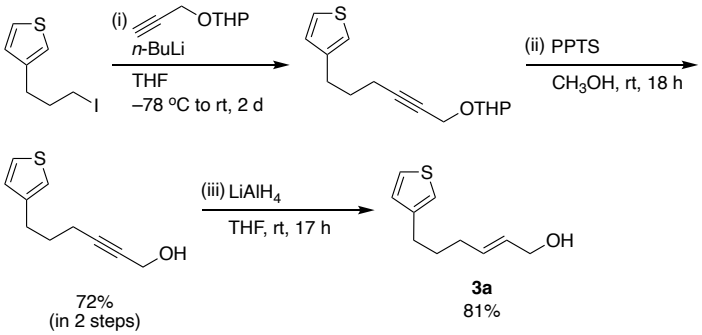
x 2), 3.63 (d, J = 11.7 Hz, 2H, CH*H*OC x 2), 2.55 (s, 2H, $ArCH_2$), 2.32 (s, 2H, $CH_2C{\equiv}C$), 1.55 (br s, 1H, OH), 1.43 (s, 3H, CCH_3), 1.41 (s, 3H, CCH_3).

Process (v). The procedure is same as that of **1a**, process (iii). Conditions: 4-(5-(Furan-3-ylmethyl)-2,2-dimethyl-1,3-dioxan-5-yl)but-2-yn-1-ol (490 mg, 1.85 mmol), THF (18.5 mL), $LiAlH_4$ (1.0 M in THF; 3.70 mL, 3.70 mmol), 0 °C to rt, 11 h. Work up: sat. aq. potassium sodium (+)-tartrate tetrahydrate (20 mL), 12-h stirring, EtOAc (20 mL x 3), brine (100 mL), Na_2SO_4 (ca. 10 g) afforded a crude product (472 mg). Purification: SiO_2-chromatography (100 g, 1:2–1:1 EtOAc–hexane eluent), (*E*)-4-(5-(furan-3-ylmethyl)-2,2-dimethyl-1,3-dioxan-5-yl)but-2-en-1-ol (**1h**) (277 mg, 56%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.37 (s, 1H, ArH), 7.25 (s, 1H, ArH), 6.27 (s, 1H, ArH), 5.66–5.78 (m, 2H, CH=CH), 4.15 (m, 2H, C*H*$_2$OH), 3.60 (d, J = 11.7 Hz, 2H, C*H*HOC x 2), 3.57 (d, J = 11.7 Hz, 2H, CH*H*OC x 2), 2.53 (s, 2H, $ArCH_2$), 2.06 (d, J = 6.90 Hz, 2H, C*H*$_2$CH=CH), 1.42 (s, 3H, CCH_3), 1.41 (s, 3H, CCH_3), 1.35 (br, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 142.7, 140.8, 133.1, 126.7, 119.5, 112.6, 98.0, 67.1, 63.5, 35.8, 34.9, 27.3, 24.6, 23.1; HRMS (ESI) m/z [M+Na]$^+$ calcd for $C_{15}H_{22}NaO_4$ 289.1410, found 289.1411.

Figure S7 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-6-(Thiophen-3-yl)hex-2-en-1-ol (3a) (Scheme S8).

Scheme S8



This compound was synthesized in similar procedure for synthesis of **1a**.

Process (i). Conditions: 2-(Prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran[1] (5.54 g, 39.5 mmol), THF (114 mL), *n*-BuLi (2.77 M in hexane; 14.2 mL, 39.5 mmol), –78 °C, 30 min, 3-(3-iodopropyl)thiophene[8] (8.30 g, 32.9 mmol) in THF (50 mL), rt, 48 h. Work up: sat. aq. NH_4Cl (100 mL), 0 °C, Et_2O (100 mL x 2), brine (200 mL),

Na_2SO_4 (ca. 30 g) afforded a crude product (9.41 g), which was used in the next reaction without further purification.

Process (ii). Conditions: Crude product (9.41 g), CH_3OH (165 mL), PPTS (827 mg, 3.29 mol), rt, 24 h. Work up: sat. aq. $NaHCO_3$ (100 mL), EtOAc (200 mL x 2), brine (200 mL), Na_2SO_4 (ca. 30 g) afforded a crude product (6.57 g). Purification: SiO_2-chromatography (60 g, 1:4 EtOAc–hexane eluent) afforded 6-(thiophen-3-yl)hex-1-yn-1-ol (4.29 g, 72%, 2 steps) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7 25 (m, 1H, ArH), 6.96 (m, 1H, ArH), 6.94 (m, 1H, ArH), 4.27 (dt, *J* = 6.26, 2.04 Hz, 2H, C*H*$_2$OH), 2.75 (t, *J* = 7.56 Hz, 2H, ArC*H*$_2$), 2.25 (tt, *J* = 6.90, 2.04 Hz, 2H, CH$_2$C*H*$_2$C), 1.84 (quin, *J* = 6.90 Hz, 2H, CH$_2$C*H*$_2$CH$_2$), 1.44 (td, *J* = 6.18, 2.04 Hz, 1H, OH).

Process (iii). 6-(Thiophen-3-yl)hex-1-yn-1-ol (4.29 g, 23.8 mmol), THF (240 mL), $LiAlH_4$ (1.0 M in THF; 47.6 mL, 47.6 mmol), rt, 24 h. Work up: sat. aq. potassium sodium (+)-tartrate tetrahydrate (100 mL), 10-h stirring, EtOAc (150 mL x 2), brine (150 mL), Na_2SO_4 (ca. 30 g) afforded a crude product (4.71 g). Purification: SiO_2-chromaography (60 g, 1:6 EtOAc–hexane eluent) afforded (*E*)-6-(thiophen-3-yl)hex-2-en-1-ol (**3a**) (3.51 g, 81%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.24 (dd, *J* = 4.86, 4.80 Hz, 1H, ArH), 6.94 (m, 1H, ArH), 6.93 (s, 1H, ArH), 5.70 (dt, *J* = 15.2, 6.18 Hz, 1H, CH$_2$C*H*=CH), 5.65 (dt, *J* = 15.2, 5.49 Hz, 1H, CH=C*H*CH$_2$OH), 4.10 (br s, 2H, C*H*$_2$OH), 2.65 (t, *J* = 7.56 Hz, 2H, ArC*H*$_2$), 2.10 (q, *J* = 7.56 Hz, 2H, C*H*$_2$CH=CH), 1.73 (quin, *J* = 7.56 Hz, 2H, CH$_2$C*H*$_2$CH$_2$), 1.31 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 142.6, 132.7, 129.4, 128.2, 125.2, 120.0, 63.7, 31.7, 29.8, 29.7; HRMS (ESI) *m*/*z* [M+Na]$^+$ calcd for $C_{10}H_{14}NaOS$ 205.0658, found 205.0659.

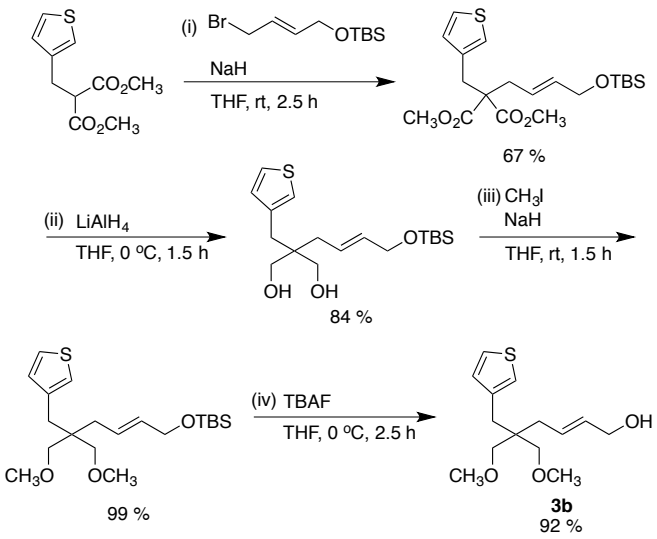
Figure S8 shows the ^{1}H- and ^{13}C-NMR spectra.

(*E*)-6-Methoxy-5-(methoxymethyl)-5-(thiophen-3-ylmethyl)hex-2-en-1-ol (3b) (Scheme S9).

This compound was synthesized in similar procedure for synthesis of **1a**.

Process (i). The procedure is same as that of **1f**, process (ii). Conditions: Dimethyl 2-(thiophen-3-ylmethyl)malonate[9] (2.53 g, 11.1 mmol), THF (65 mL), NaH (60%; 517 mg, 12.9 mmol), 0 °C, 35 min, (*E*)-((4-bromobut-2-en-1yl)oxy)(*tert*-butyl)dimethylsilane[7] (2.45 g, 9.24 mmol), THF (15 mL), rt, 2.5 h.

Scheme S9



Work up: sat. aq. NH_4Cl (30 mL), EtOAc (200 mL x 4), brine (300 mL), Na_2SO_4 (ca. 50 g) afforded a crude product (4.83 g). Purification: SiO_2-chromatography (500 g, 1:8 EtOAc–hexane eluent) afforded dimethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(thiophen-3-ylmethyl)malonate (3.09 g, 67%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.32 (dd, *J* = 1.38, 7.56 Hz, 1H, ArH), 6.96 (s, 1H, ArH), 6.82 (d, *J* = 4.80 Hz, 1H, ArH), 5.65 (dt, *J* = 4.83, 15.2 Hz, 1H, C*H*=CHCH$_2$OTBS), 5.55 (dt, *J* = 7.59, 15.2 Hz, 1H, CH=C*H*CH$_2$OTBS), 4.13 (d, *J* = 4.08 Hz, 2H, C*H*$_2$OTBS), 3.71 (s, 6H, COOCH$_3$ x 2), 3.25 (s, 2H, ArCH$_2$), 2.57 (d, *J* = 7.62 Hz, 2H, C*H*$_2$CH=CH), 0.91 (s, 9H, C(CH$_3$)$_3$), 0.07 (s, 6H, SiCH$_3$ x 2).

Process (ii). Conditions: Dimethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but -2-en-1-yl)-2-(thiphen-3-ylmethyl)malonate (7.52 g, 18.2 mmol), THF (45.5 mL), $LiAlH_4$ (1.0 M in THF; 45.5 mL, 45.5 mmol), 0 °C, 1.5 h. Work up: sat. aq. potassium sodium (+)-tartrate tetrahydrate (100 mL), 10-h stirring, EtOAc (100 mL x 3), brine (500 mL), Na_2SO_4 (ca. 75 g) afforded a crude product (6.71 g). Purification: SiO_2-chromatography (300 g, 1:1 EtOAc–hexane eluent) afforded (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but- 2-en-1-yl)-2-(thiophen-3-ylmethyl)propan-1,3-diol (5.43 g, 84%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.25 (d, *J* = 4.82 Hz, 1H, ArH), 7.03 (m, 1H, ArH), 6.99 (d, *J* = 4.82 Hz, 1H, ArH), 5.75 (dt, *J* = 7.57, 15.15 Hz, 1H, CH=C*H*), 5.65 (dt, *J* = 4.82, 15.15 Hz, 1H, C*H*=CH), 4.16 (d, *J* = 4.82 Hz, 2H, CH=CHC*H*$_2$O), 3.60 (dd, *J* = 5.17, 10.7 Hz, 2H, C*H*HOH

x 2), 3.56 (dd, *J* = 5.51, 11.0 Hz, 2H, CH*H*OH x 2), 2.72 (br s, 2H, CH_2OH x 2), 2.05 (m, 2H, $ArCH_2$), 2.02 (d, *J* = 7.57 Hz, 2H, CH_2CH=CH), 0.92 (s, 9H, $C(CH_3)_3$), 0.08 (s, 6H, $SiCH_3$ x 2).

Process (iii). Conditions: (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-yl)-2-(thiophen-3-ylmethyl)propan-1,3-diol (1.0 g, 2.80 mmol), NaH (60%; 336 mg, 8.4 mmol), THF (9.3 mL), CH_3I (697 μL, 11.2 mmol) in THF (9.3 mL), rt, 1.5 h. Work up: sat. aq. NH_4Cl (10 mL), EtOAc (20 mL x 3), brine (50 mL), Na_2SO_4 (ca. 20 g) afforded a crude product (1.06 g). Purification: SiO_2-chromatography (100 g, 1:5 EtOAc–hexane eluent) afforded (*E*)-*tert*-butyl((6-methoxy-5-(methoxymethyl)-5-(thiophen-3-ylmethyl)hex-2-en-1-yl)oxy)dimethylsilane (1.06 g, 99%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.22 (m, 1H, ArH), 6.95 (m, 1H, ArH), 6.92 (d, *J* = 4.82 Hz, 1H, ArH), 5.69 (dt, *J* = 7.57, 15.15 Hz, 1H, CH=C*H*), 5.60 (dt, *J* = 4.82, 15.8 Hz, C*H*=CH), 4.16 (d, *J* = 4.82 Hz, 2H, CH_2O), 3.32 (s, 6H, OCH_3 x 2), 3.08 (d, *J* = 9.64 Hz, 2H, C*H*HOCH_3 x 2), 3.06 (d, *J* = 8.95 Hz, 2H, CH*H*OCH_3 x 2), 2.64 (s, 2H, $ArCH_2$), 2.02 (d, *J* = 6.89 Hz, 2H, CH_2CH=CH), 0.92 (s, 9H, $C(CH_3)_3$), 0.08 (s, 6H, $SiCH_3$ x 2).

Process (iv). Conditions: (*E*)-*tert*-Butyl((6-methoxy-5-(methoxymethyl)-5-(thiophen-3-ylmethyl)hex-2-en-1-yl)oxy)dimethylsilane (1.06 g, 2.76 mmol), THF (13.8 mL), TBAF (1.0 M in THF; 4.13 mL, 4.13 mmol), 0 °C, 2.5 h. Work up: sat. aq. NH_4Cl (20 mL), EtOAc (30 mL x 3), brine (200 mL), Na_2SO_4 (ca. 20 g) afforded a crude product (1.18 g). Purification: SiO_2-chromatography (100 g, 1:1 EtOAc–hexane eluent) afforded (*E*)-6-methoxy-5-(methoxymethyl)-5-(thiophen-3-ylmethyl)hex-2-en-1-ol (**3b**) (682 mg, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.23 (t, *J* = 3.45 Hz, 1H, ArH), 6.95 (s, 1H, ArH), 6.91 (d, *J* = 4.82 Hz, 1H, ArH), 5.76–5.69 (m, 2H, CH=CH), 4.14 (t, *J* = 5.51 Hz, 2H, CH_2OH), 3.33 (s, 6H, OCH_3 x 2), 3.07 (dd, *J* = 8.95, 10.3 Hz, 4H, CH_2OCH_3 x 2), 2.65 (s, 2H, $ArCH_2$), 2.06 (d, *J* = 6.20 Hz, 2H, CH_2CH=CH), 1.25 (t, *J* = 5.86 Hz, 1H, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 138.0, 132.4, 130.3, 128.4, 124.5, 122.9, 74.4, 63.8, 59.1, 42.7, 35.1, 32.3; HRMS (ESI) *m/z* $[M+Na]^+$ calcd. for $C_{14}H_{22}NaO_3S$ 293.1182, found 293.1182.

Figure S9 shows the ^{1}H- and ^{13}C-NMR spectra.

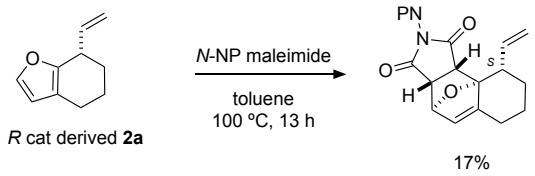
3. Products.

For catalytic asymmetric reaction, general procedure, results, and the physical properties were described in the manuscript. **Figures S10–S25** show ^{1}H- and ^{13}C-NMR spectra, and HPLC charts for each product.

Determination of absolute configuration of 2a.

The absolute configuration of **2a** was determined by X-ray crystallographic analysis with Flack parameter after conversion through Diels–Alder reaction as shown in **Scheme S10**. Procedures were described below.

Scheme S10



(*S*)-7-Vinyl-4,5,6,7-tetrahydrobenzofuran (**2a**) (50.9 mg, 0.343 mmol), *N*-(4-nitrophenyl)maleimide (74.8 mg, 0.343 mmol), and toluene (1.71 mL) were placed in 5-mL Young Shlenk. After 13-h stirring at 100 °C, the reaction mixture was added H_2O (2 mL) at rt. The organic layer was separated, and the aq. layer was extracted by EtOAc (5 mL x 2). The combined organic layers were washed by brine (10 mL) and dried over Na_2SO_4 (ca. 5 g). Filtration/evaporation process afforded a crude product (73.5 mg). This was purified by SiO_2-chromatography (10 g, 1:4 Et_2O–pentane eluent) to give (3a*R*,4*S*,9*S*,9a*S*,9b*S*)-2-(4-nitrophenyl)-9-vinyl-3a,6,7,8,9,9b-hexahydro-4,9a-epoxybenzo[*e*]isoindole-1,3(2*H*,4*H*)-dion (21.7 mg, 17%) as a white solid. This was placed in 10 mm x 50 mm test tube, and dissolved in $CHCl_3$ (0.5 mL), and hexane (2.0 mL) was carefully added. This was stored at 4 °C for 12 h to give colorless needle crystals (13.5 mg, 62%). **Figure S26** and **Table S1** shows molecular structure of Diels–Alder adduct of **2a** and structural parameter.

Determination of absolute configuration of 4a.

Absolute configuration of **4a** was determined after conversion to corresponding hydroxymethyl compound **4a'** via OsO_4–NMO/$NaIO_4$/$NaBH_4$ method (see manuscript) and compared optical rotation to the value previously reported.[10] Conditions: Reaction solution (7 mL), H_2O (1.4 mL), NMO (164 mg, 1.40 mmol),

OsO_4 (4% aq. solution, 35.0 mmol); $NaIO_4$ (180 mg, 0.840 mmol); $NaBH_4$ (81.3 mg, 2.10 mmol). Yield 72% (84.6 mg).

^{1}H NMR ($CDCl_3$) δ 7.12 (d, *J* = 4.80 Hz, 1H, ArH), 6.79 (d, *J* = 6.79 Hz, 1H, ArH), 3.79 (d, *J* = 4.86 Hz, 2H, HOC*H*$_2$CH), 3.06 (t, *J* = 6.18 Hz, 1H, C*H*CH$_2$), 2.67 (dt, *J* = 5.52, 15.8 Hz, 1H, CH$_2$CH*H*Ar), 2.60 (dt, *J* = 5.50, 17.2 Hz, 1H, CH$_2$C*H*HAr), 2.03–1.92 (m, 2H, CHC*H*$_2$CH$_2$), 1.57–1.74 (m, 3H, CH$_2$C*H*$_2$CH$_2$ and OH).

$[\alpha]_D^{19.8}$ –42.5 (*c* 0.995, $CHCl_3$) (ref: $[\alpha]_D^{23}$ –40.65 (*c* 1, $CHCl_3$) for *S*)

REFERENCES

(1) Hu, Y.; Yi, R.; Wu, F.; Wan, B. *J. Org. Chem.* **2013**, *78*, 7714–7726.

(2) Clair, L. J.; Lansbury, P.; Zhi, B.; Hoogsteen, K. *J. Org. Chem.* **1995**, *60*, 4822–4833.

(3) Baner*J*ee, S. T.; Paul, S.; Sinha, S.; Das, S. *Bioorg. Med. Chem.* **2014**, *22*, 6062–6070.

(4) Kotoku, N.; Fujioka, S.; Nakata, C.; Yamada, M.; Sumii, Y.; Kawachi, T.; Arai, M.; Kobayashi, M. *Tetrahedron* **2011**, *67*, 6673–6678.

(5) Yamada, K.; Kurokawa, T.; Tokuyama, H.; Fukuyama, T. *J. Am. Chem. Soc.* **2003**, *125*, 6630–6631. Yamada, K.; Kurokawa, T.; Tokuyama, H.; Fukuyama, T. *J. Am. Chem. Soc.* **2003**, *125*, 6630–6631.

(6) Nilson, G. M.; Funk, L. R. *Org. Lett.* **2006**, *8*, 3833–3836. Martins, A.; Lautens, M. *J. Org. Chem.* **2008**, *73*, 8705–8710.

(7) DeBoef, B.; Counts, R. W.; Gilbertson, R. S. *J. Org. Chem.* **2007**, *72*, 799–804.

(8) Martins, A.; Lautens, M. *J. Org. Chem.* **2008**, *73*, 8705–8710.

(9) Chuang, C.-P.; Wang, S.-F. *Synth. Commun.* **1994**, *24*, 1493–1505.

(10) Conrad. C. J.; Jongrock, K.; Brian, N. L.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 11640–11641.

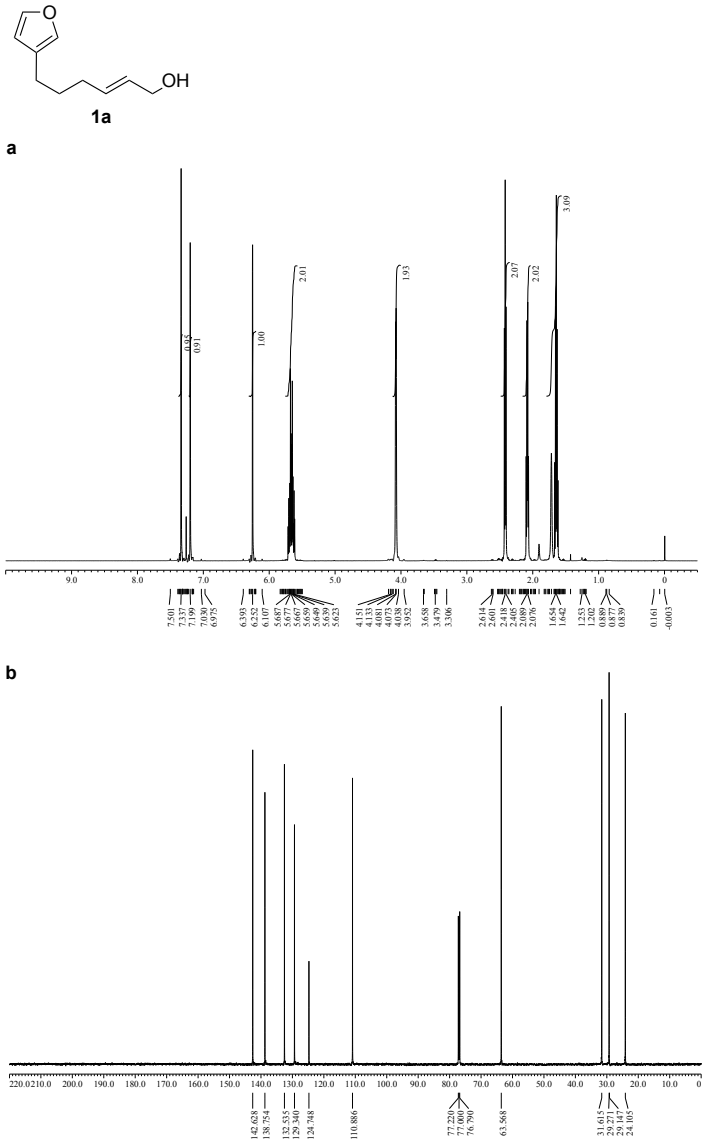


Figure S1. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-6-(furan-3-yl)hex-2-en-1-ol (**1a**) in $CDCl_3$.

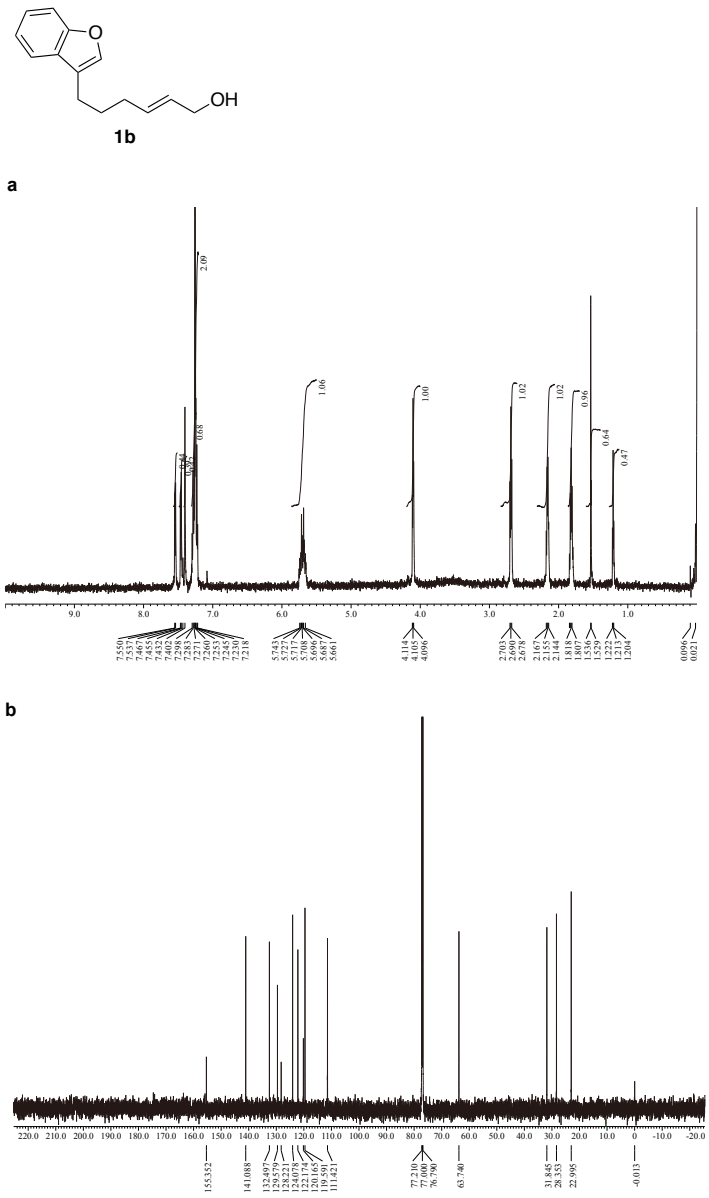


Figure S2. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-6-(benzofuran-3-yl)hex-2-en-1-ol (**1b**) in $CDCl_3$.

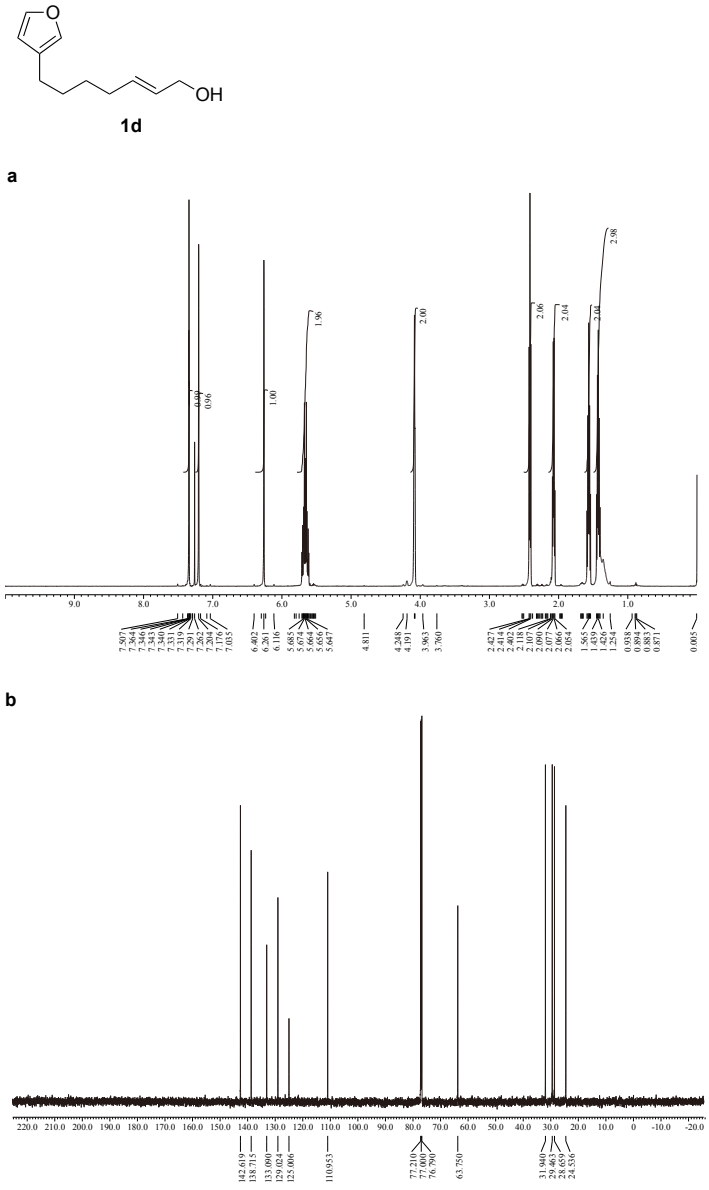


Figure S3. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-7-furan-3-ylhept-2-en-1-ol (**1d**) in $CDCl_3$.

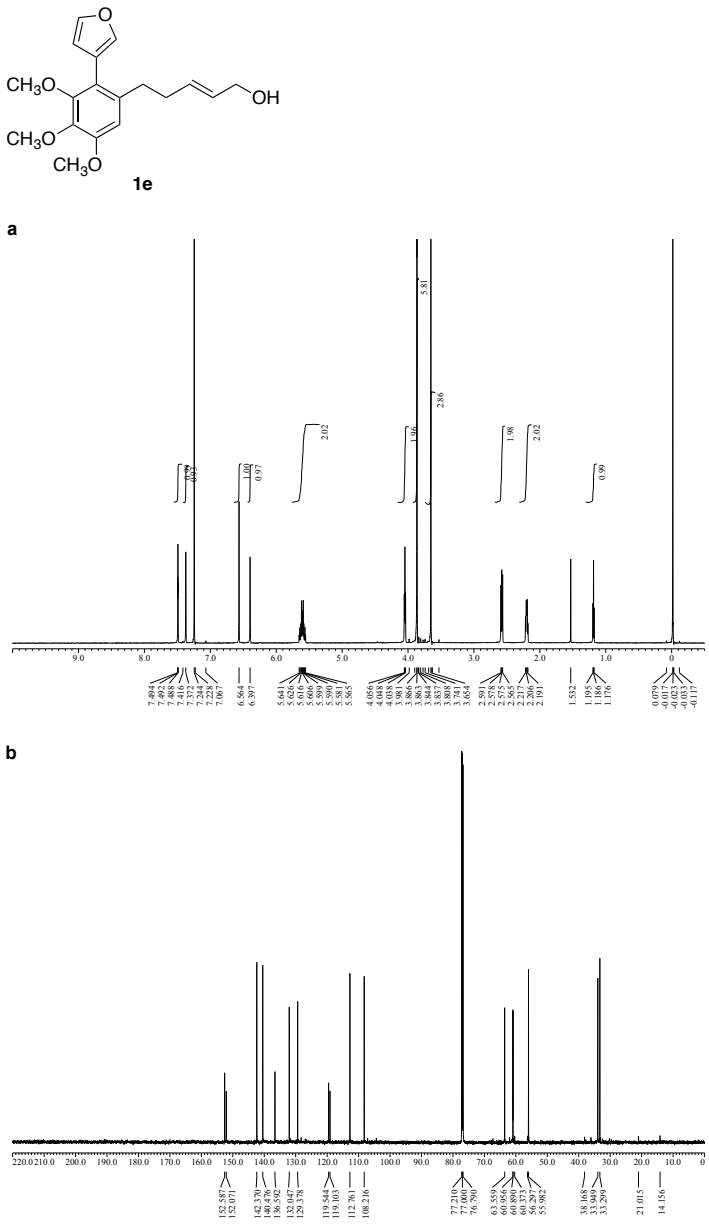


Figure S4. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-5-(2-(furan-3-yl)-3,4,5-trimethoxyphenyl)pent-2-en-1-ol (**1e**) in $CDCl_3$.

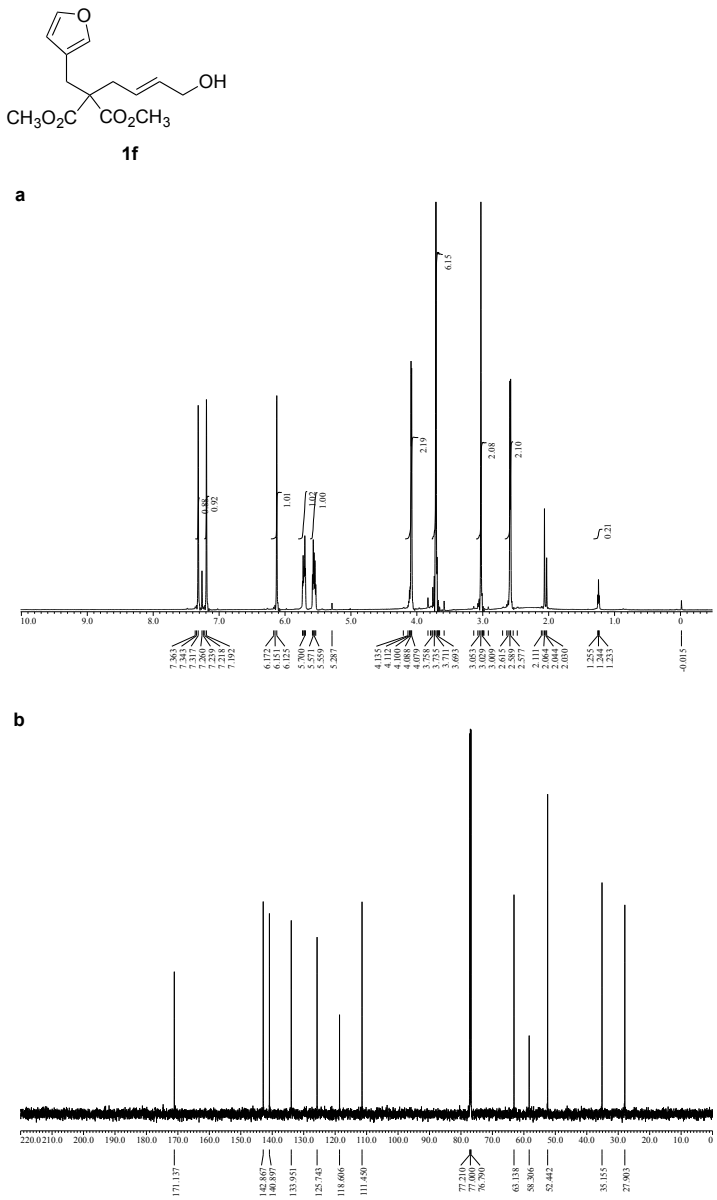


Figure S5. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of dimethyl (*E*)-2-(furan-3-ylmethyl)-2-(4-hydroxybut-2-en-1-yl)malonate (**1f**) in $CDCl_3$.

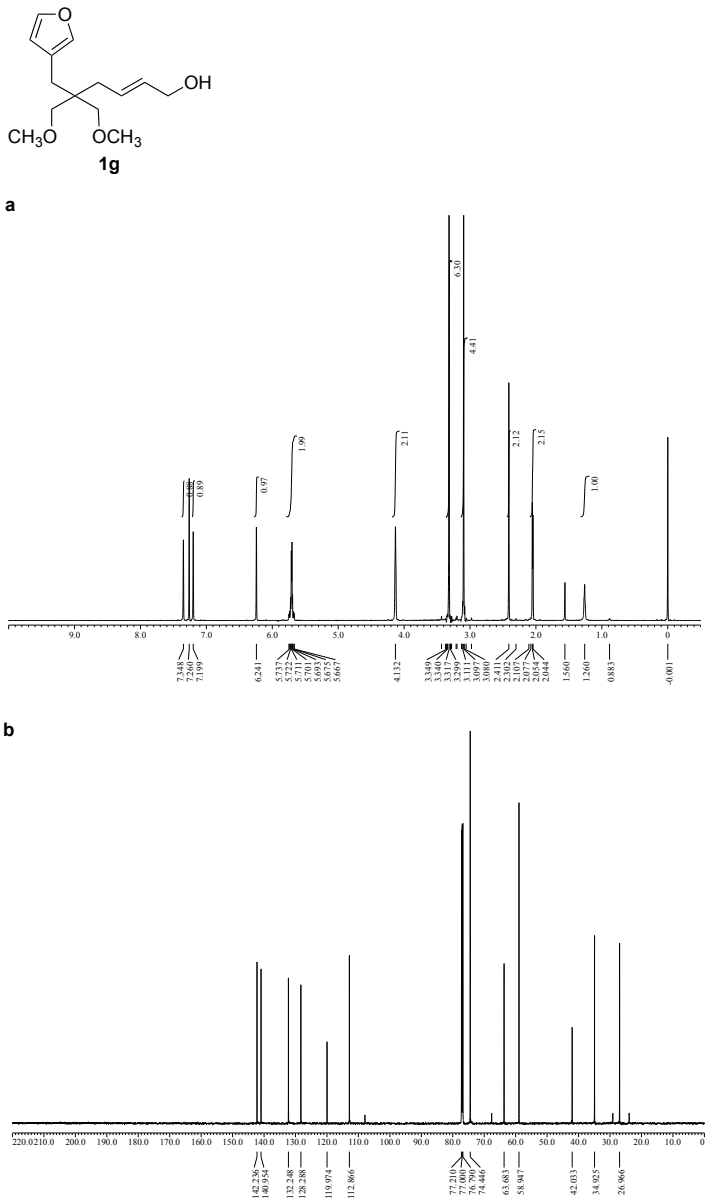


Figure S6. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-6-(furan-3-yl)-5,5-di(methoxymethyl)hex-2-en-1-ol (**1g**) in $CDCl_3$.

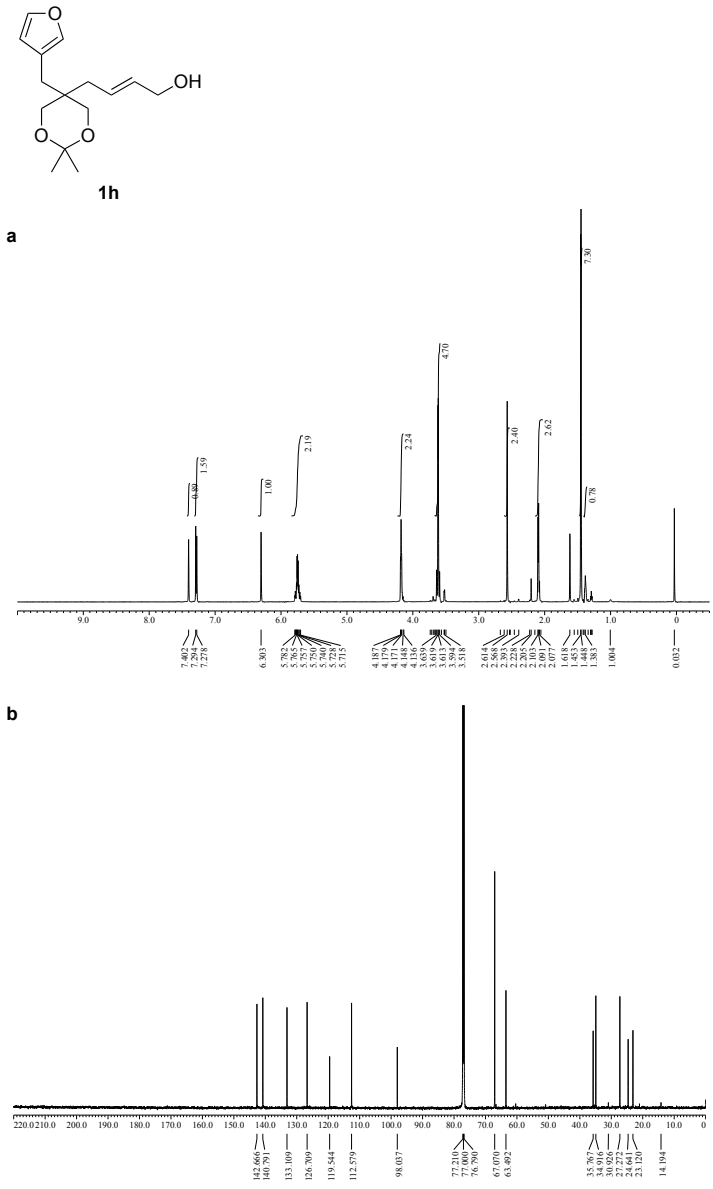


Figure S7. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-4-(5-(furan-3-ylmethyl)-2,2-dimethyl-1,3-dioxan-5-yl)but-2-en-1-ol (**1h**) in $CDCl_3$.

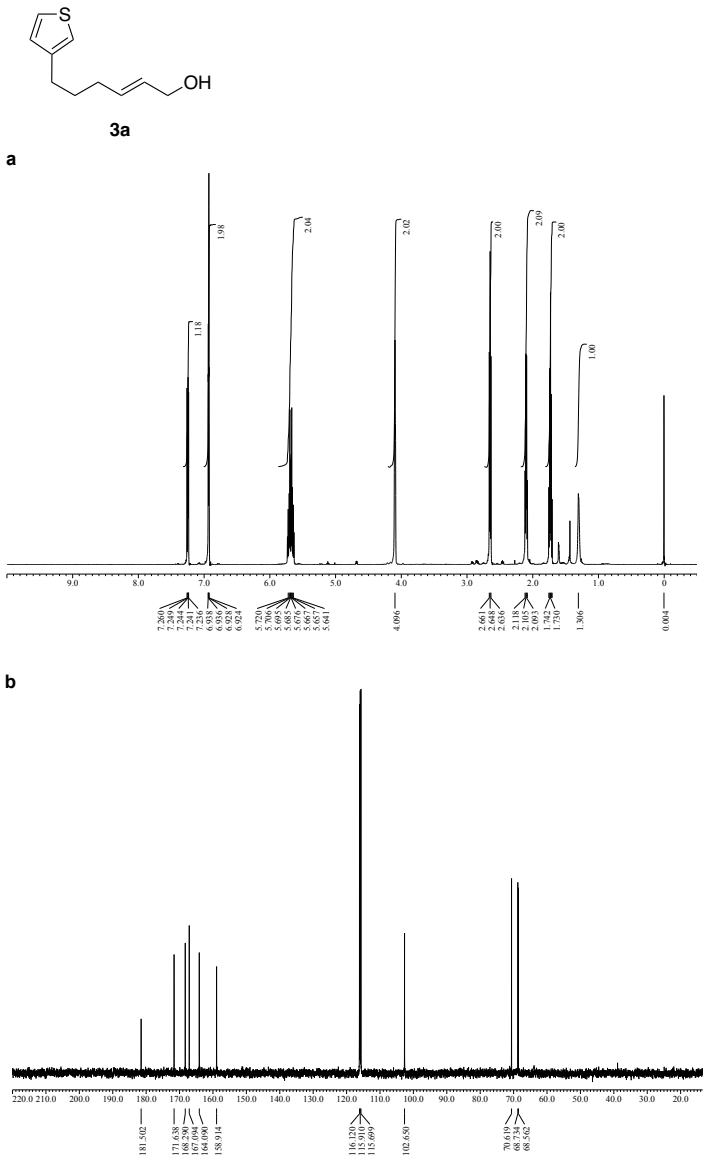


Figure S8. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-6-(thiophen-3-yl)hex-2-en-1-ol (**3a**) in $CDCl_3$.

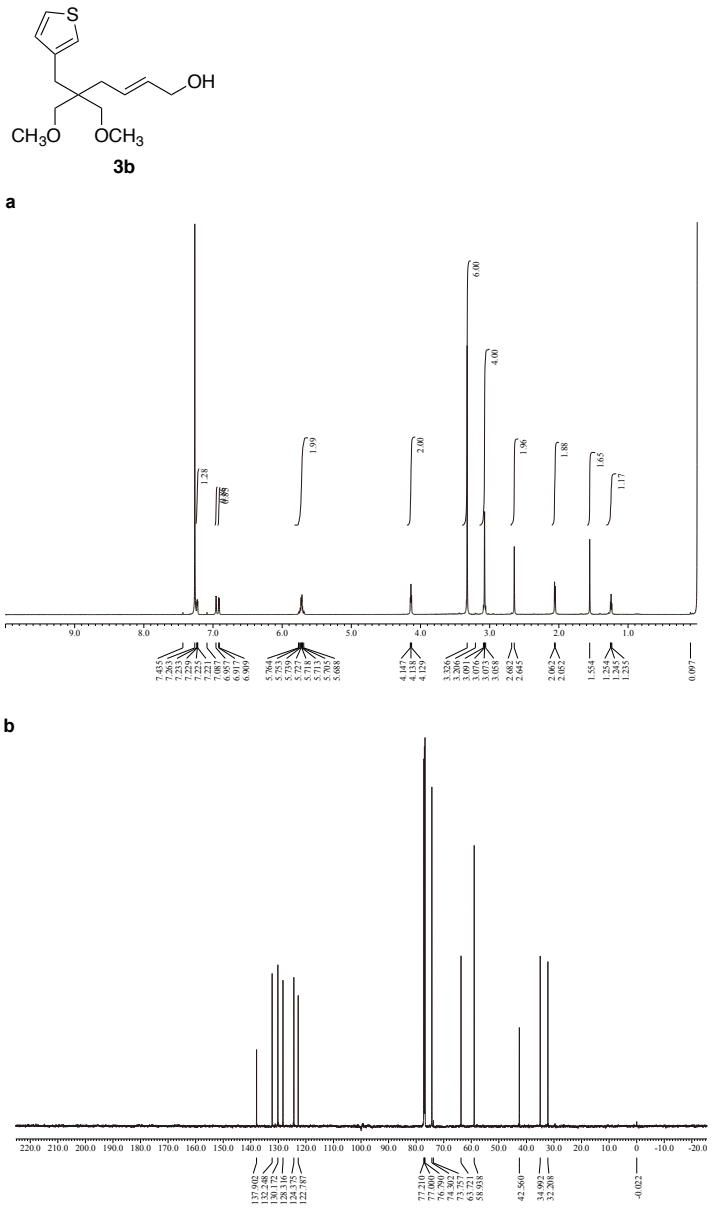


Figure S9. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*E*)-6-Methoxy-5-(methoxymethyl)-5-(thiophen-3-ylmethyl)hex-2-en-1-ol (**3b**) in $CDCl_3$.

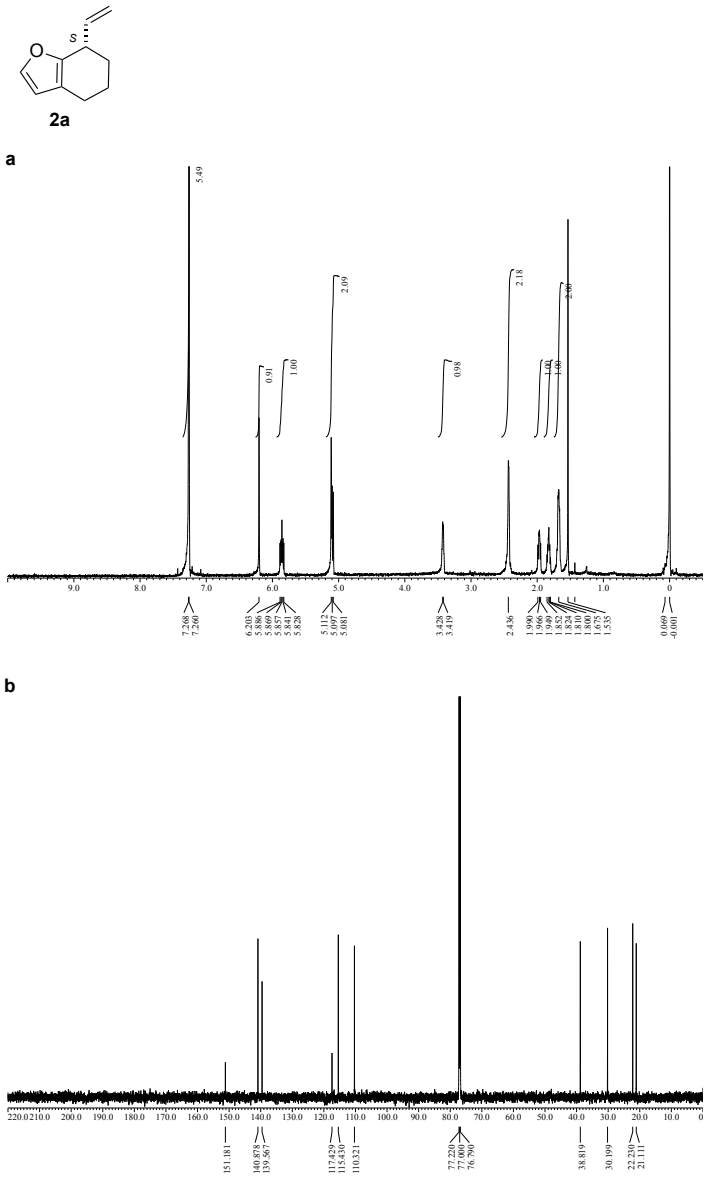


Figure S10. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*S*)-7-vinyl-4,5,6,7-tetrahydrofuran (**2a**) in $CDCl_3$.

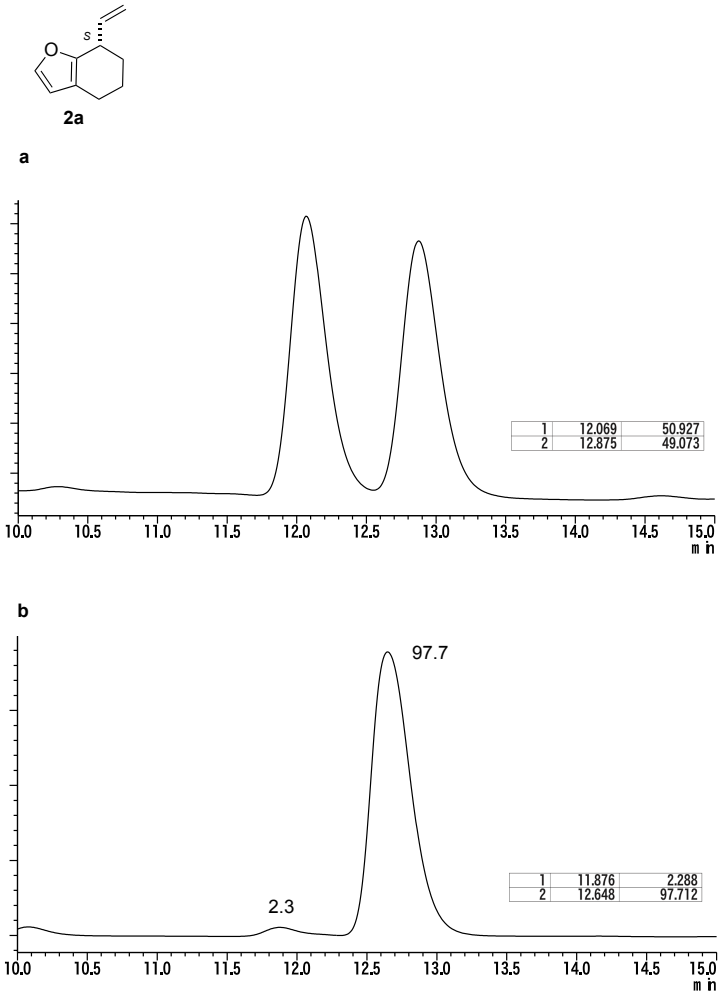


Figure S11. HPLC charts for determination of the er of (*S*)-7-vinyl-4,5,6,7-tetrahydrofuran (**2a**). (**a**) Racemic product. (**b**) Product **2a** obtained in the *R* cat-catalyzed cyclization of **1a**. HPLC conditions: CHIRALCEL OJ-3 (0.46 cmϕ x 250 mm); 0.5:99.5 *i*-PrOH–hexane eluent; 0.4 mL/min flow rate; 210-nm detection; 25 °C; t_R 11.9 min (*R*) and 12.6 min (*S*).

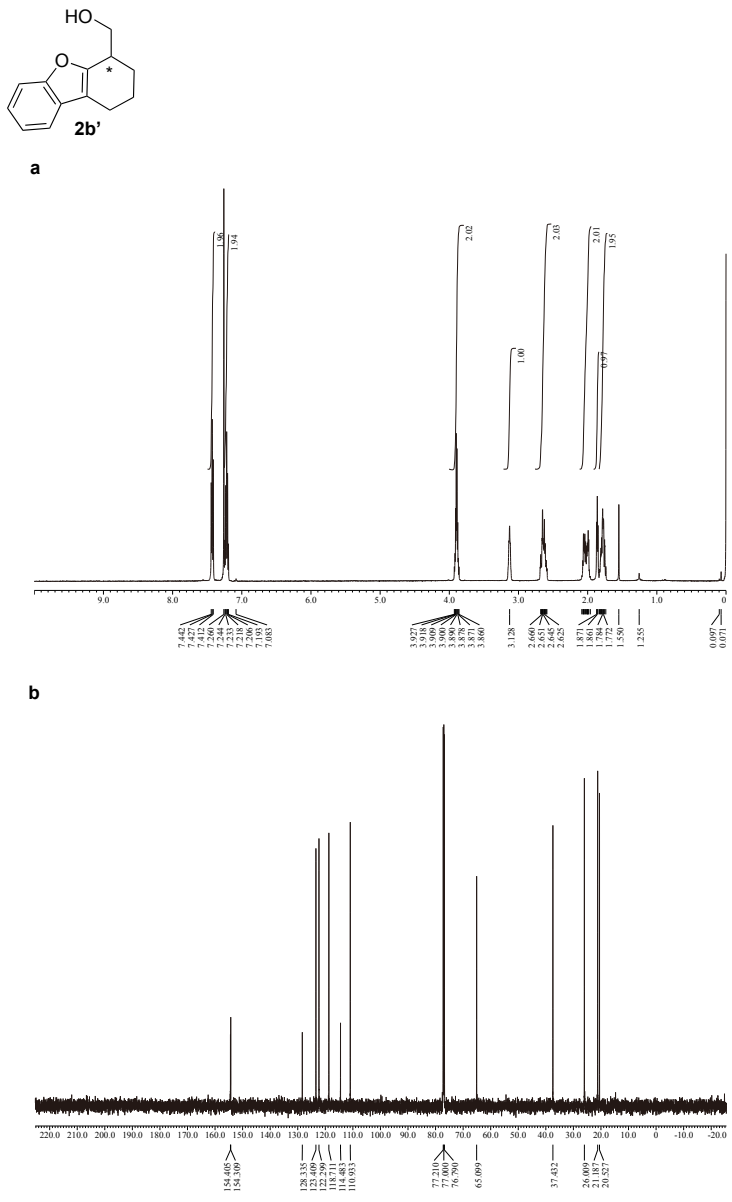


Figure S12. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of 4-(hydroxymethyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan (**2b'**) in $CDCl_3$.

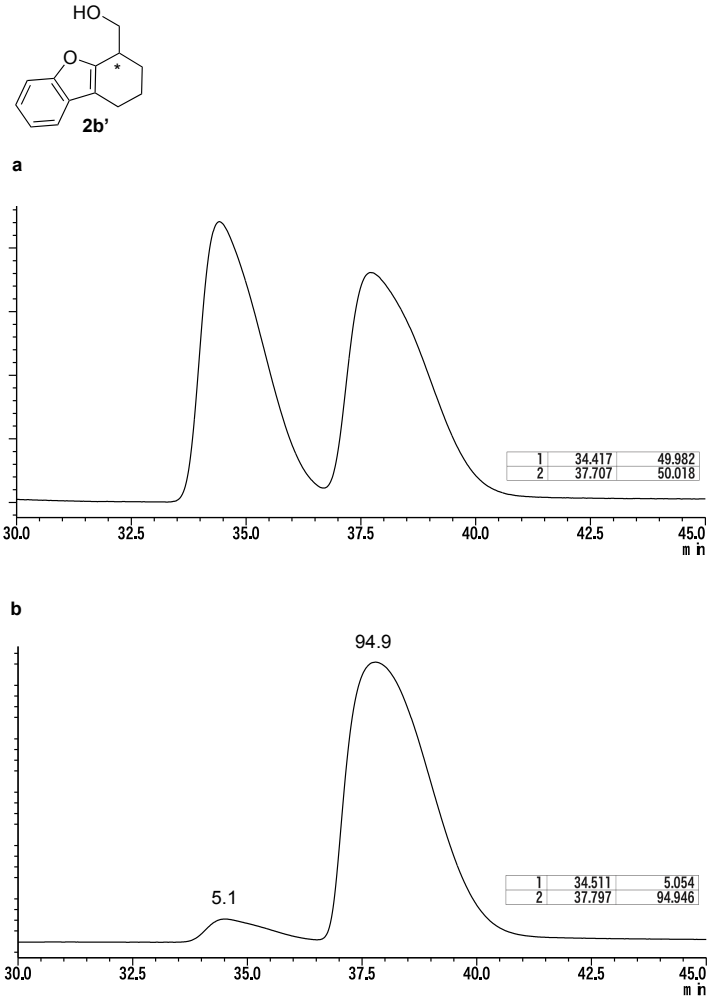


Figure S13. HPLC charts for determination of the er of 4-(hydroxymethyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan (**2b'**). (**a**) Racemic product. (**b**) Synthetic compound **2b'** derived from product **2b** obtained in the *R* cat-catalyzed cyclization of **1b**. HPLC conditions: CHIRALCEL OJ-H (0.46 cmϕ x 250 mm); 5:95 *i*-PrOH–hexane eluent; 0.5 mL/min flow rate; 254-nm detection; 25 °C; t_R 34.5 min (minor) and 37.8 min (major).

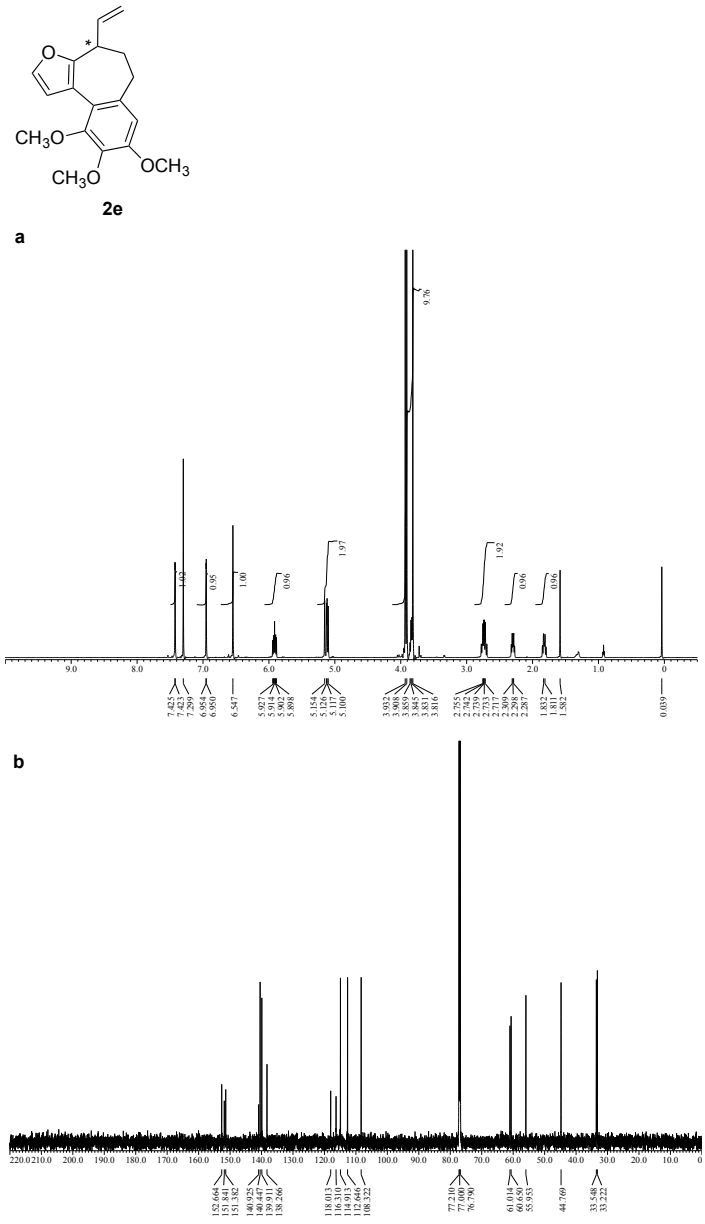


Figure S14. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of 8,9,10-trimethoxy-4-vinyl-5,6-dihydro-4*H*-benzo[3,4]cyclohepta[1,2-*b*]furan (**2e**) in $CDCl_3$.

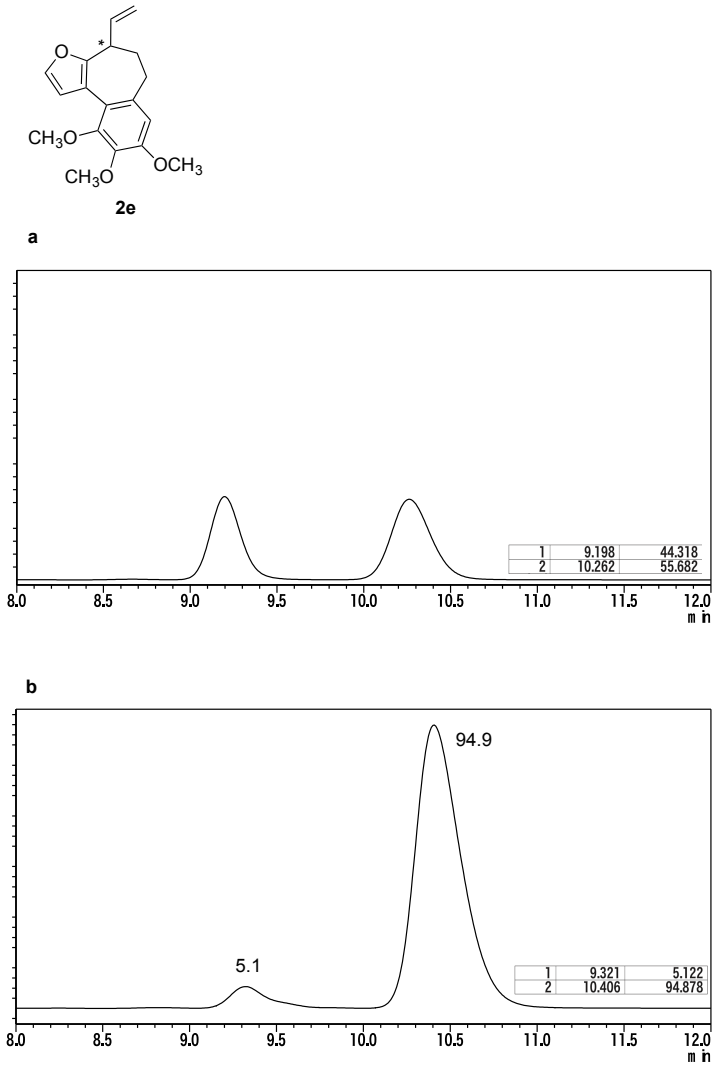


Figure S15. HPLC charts for determination of the er of 8,9,10-trimethoxy-4-vinyl-5,6-dihydro-4*H*-benzo[3,4]cyclohepta[1,2-*b*]furan (**2e**). (**a**) Racemic product. (**b**) Product **2e** obtained in the *R* cat-catalyzed cyclization of **1e**. HPLC conditions: CHIRALPAK IG (0.46 cmϕ x 250 mm); 1:99 *i*-PrOH–hexane eluent; 1.0 mL/min flow rate; 254-nm detection; 25 ºC; t_R 9.2 min (minor) and 10.3 min (major).

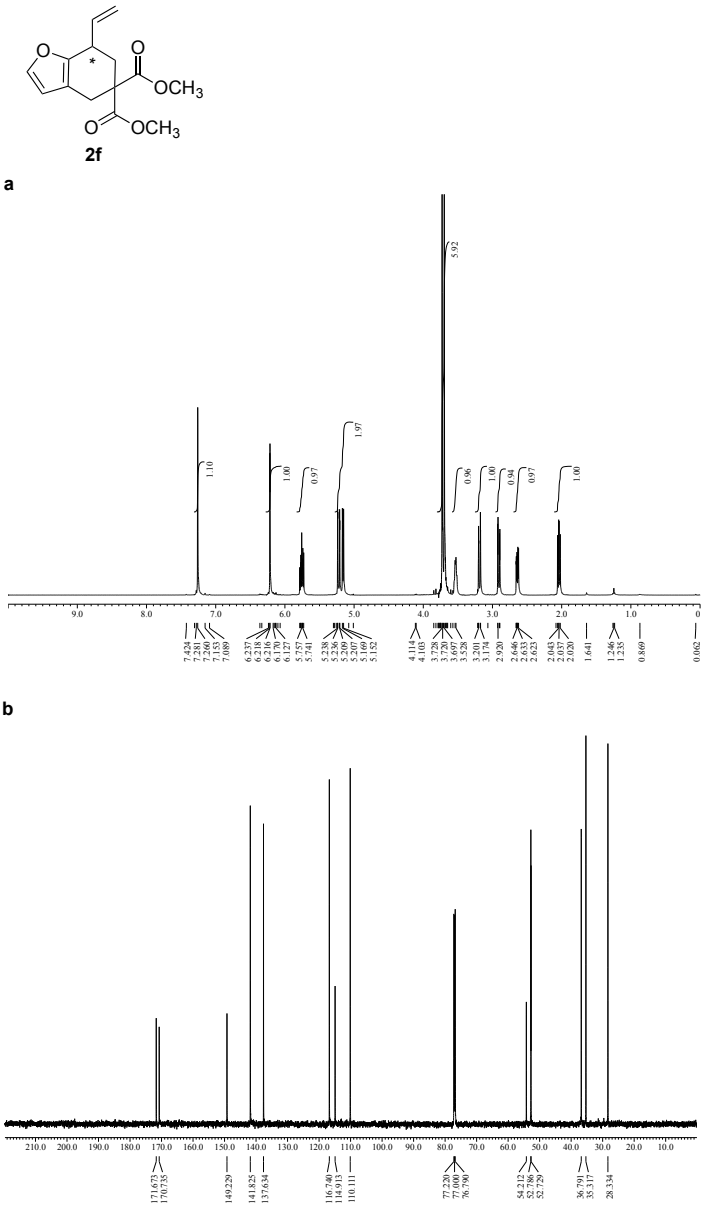


Figure S16. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of dimethyl 7-vinyl-6,7-dihydrobanzofuran-5,5(4*H*)-dicarboxylate (**2f**) in $CDCl_3$.

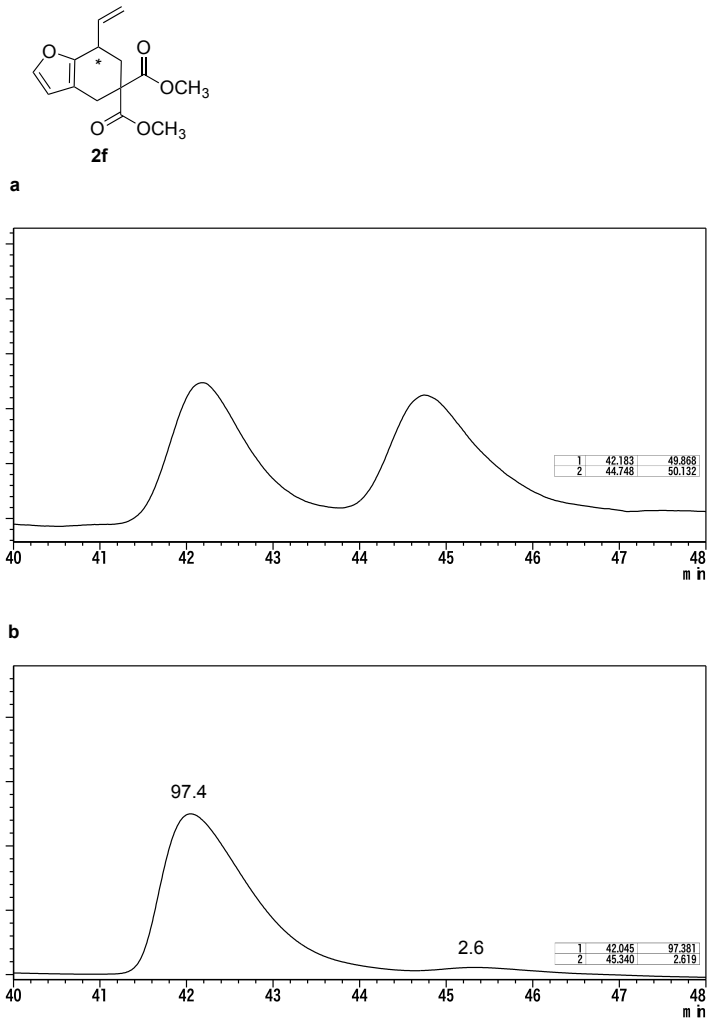


Figure S17. HPLC charts for determination of the er of dimethyl 7-vinyl-6,7-dihydrobanzofuran-5,5(4*H*)-dicarboxylate (**2f**). (**a**) Racemic product. (**b**) Product **2f** obtained in the *R* cat-catalyzed cyclization of **1f**. HPLC conditions: CHIRALCEL OJ-H (2.0 cmϕ x 250 mm); 1:99 *i*-PrOH–hexane eluent; 5.0 mL/min flow rate; 210-nm detection; 25 ºC; t_R 42.2 min (minor) and 44.7 min (major).

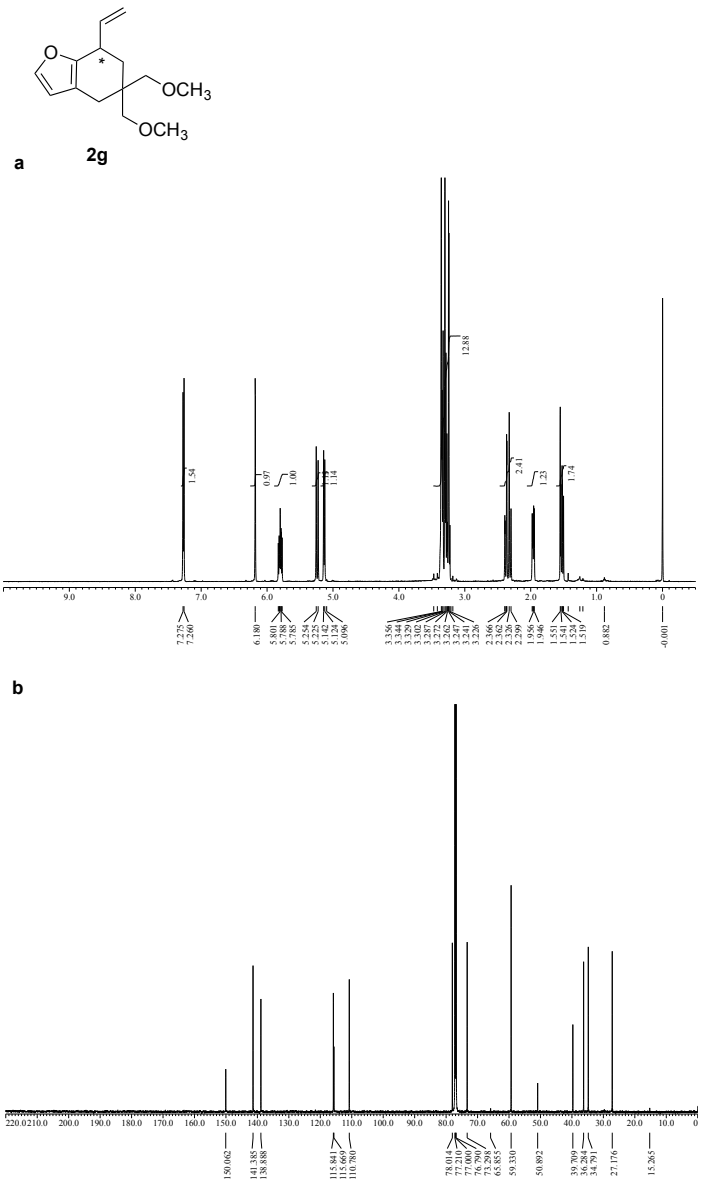


Figure S18. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of 5,5-bis(methoxymethyl)-7-vinyl-4,5,6,7-tetrahydrofuran (**2g**) in $CDCl_3$.

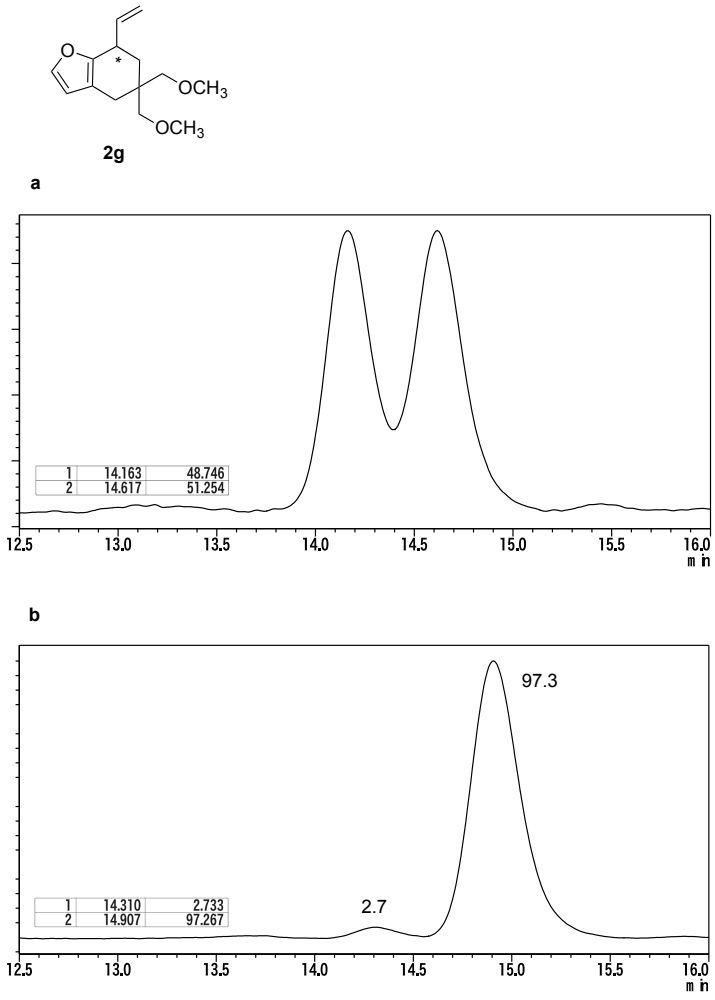


Figure S19. HPLC charts for determination of the er of 5,5-bis(methoxymethyl)-7-vinyl-4,5,6,7-tetrahydrofuran (**2g**). (**a**) Racemic product. (**b**) Product **2g** obtained in the *R* cat-catalyzed cyclization of **1g**. HPLC conditions: CHIRALCEL OD-H (2.0 cmϕ x 250 mm)); 1:99 *i*-PrOH–hexane eluent; 5.0 mL/min flow rate; 210-nm detection; 25 ºC; t_R 14.3 min (minor) and 14.9 min (major).

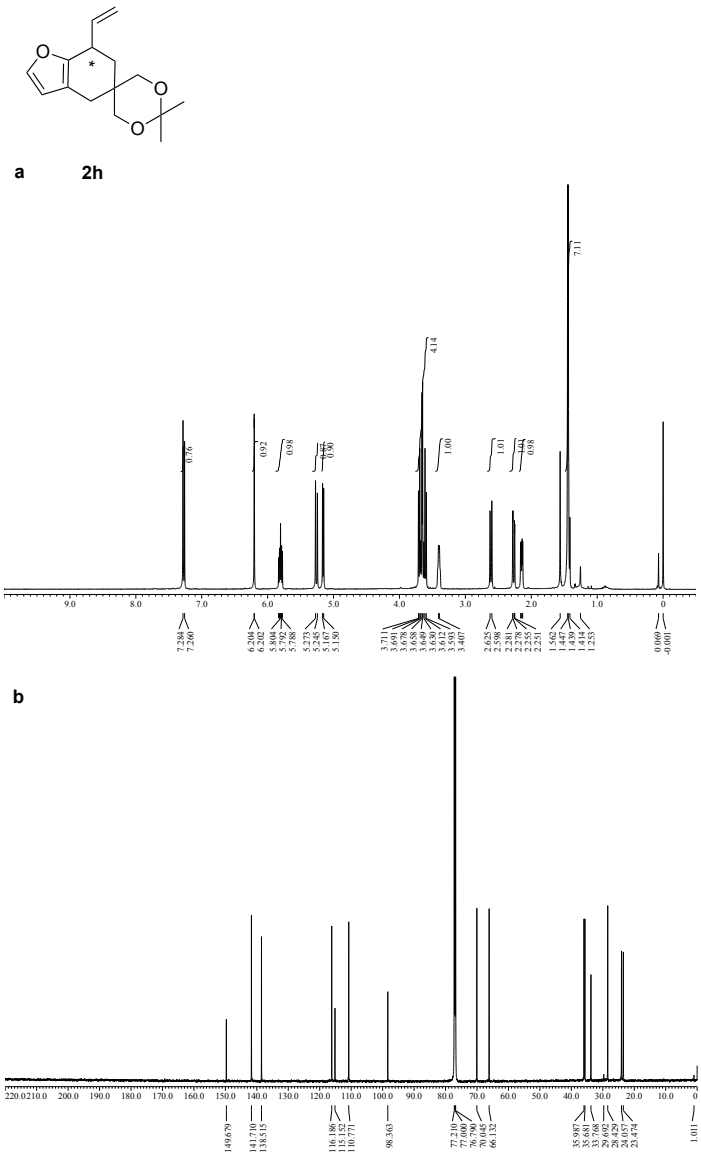


Figure S20. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of 2',2'-dimethyl-7-vinyl-6,7-dihydro-4*H*-spiro[benzofuran-5,5'-[1,3]dioxane] (**2h**) in $CDCl_3$.

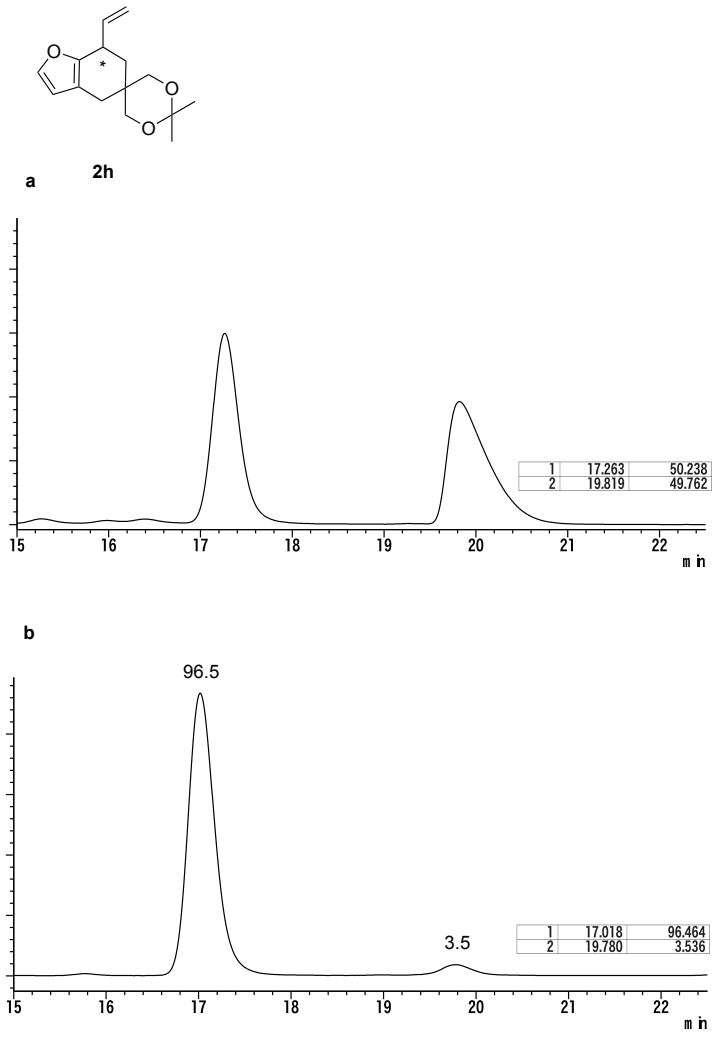


Figure S21. HPLC charts for determination of the er of 2',2'-dimethyl-7-vinyl-6,7-dihydro-4*H*-spiro[benzofuran-5,5'-[1,3]dioxane] (**2h**). (**a**) Racemic product. (**b**) Product **2h** obtained in the *R* cat-catalyzed cyclization of **1h**. HPLC conditions: CHIRALPAK IG (0.46 cmϕ x 250 mm); 10:90 *i*-PrOH–hexane eluent; 0.5 mL/min flow rate; 210-nm detection; 25 ºC; t_R 17.1 min (major) and 19.8 min (minor).

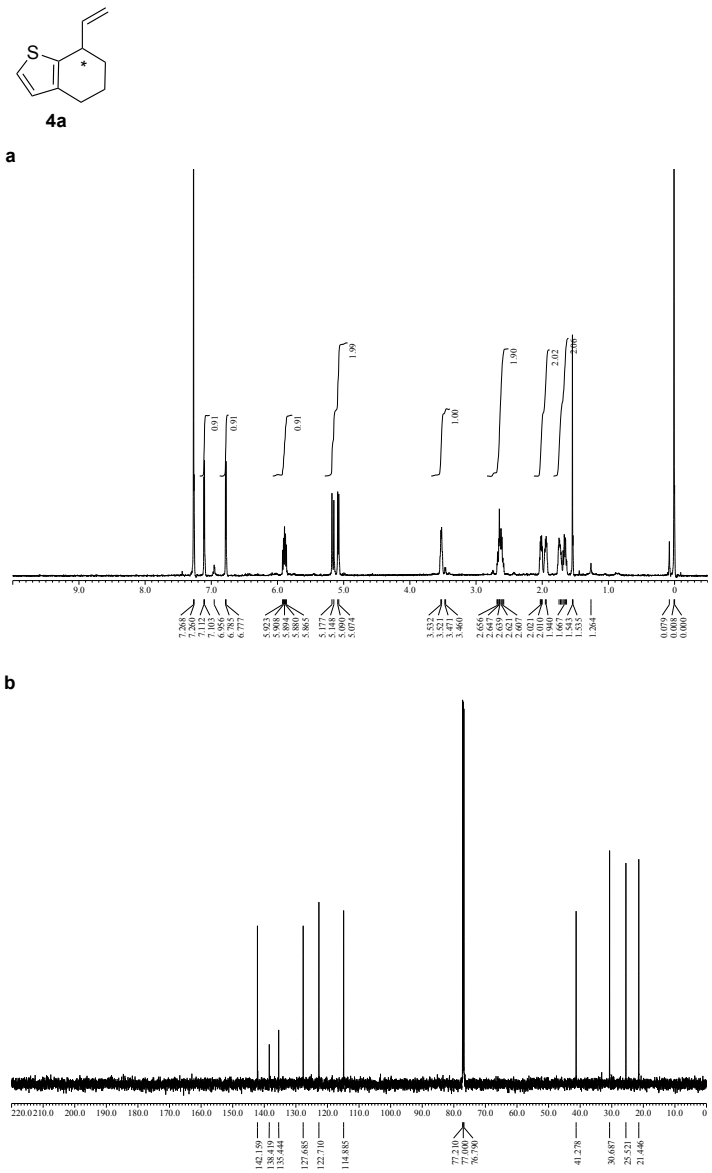


Figure S22. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of (*S*)-7-vinyl-4,5,6,7-tetrahydrobenzo[*b*]thiophen (**4a**) in $CDCl_3$.

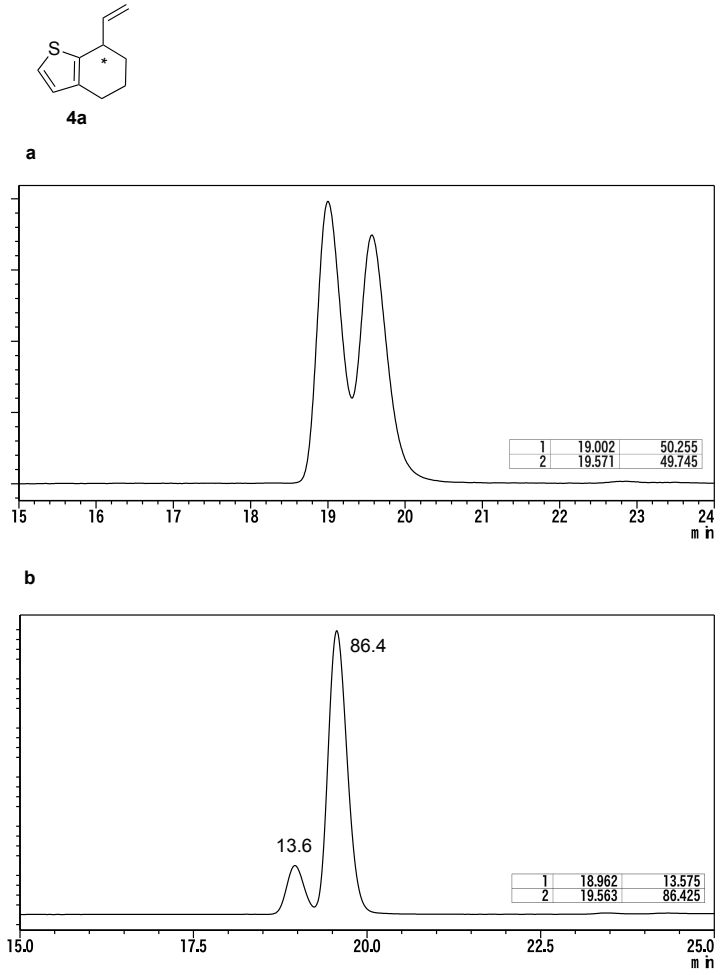


Figure S23. HPLC charts for determination of the er of (*S*)-7-vinyl-4,5,6,7-tetrahydrobenzo[*b*]thiophen (**4a**). (**a**) Racemic product. (**b**) Product **4a** obtained in the *R* cat-catalyzed cyclization of **3a**. HPLC condition: CHIRALCEL OJ-H (0.46 cmϕ x 250 mm x 2); 0.1:99.9 *i*-PrOH-hexane eluent; 0.5 mL/min flow rate; 254-nm detection; 25 ºC; t_R 19.0 min (*R*) and 19.6 min (*S*).

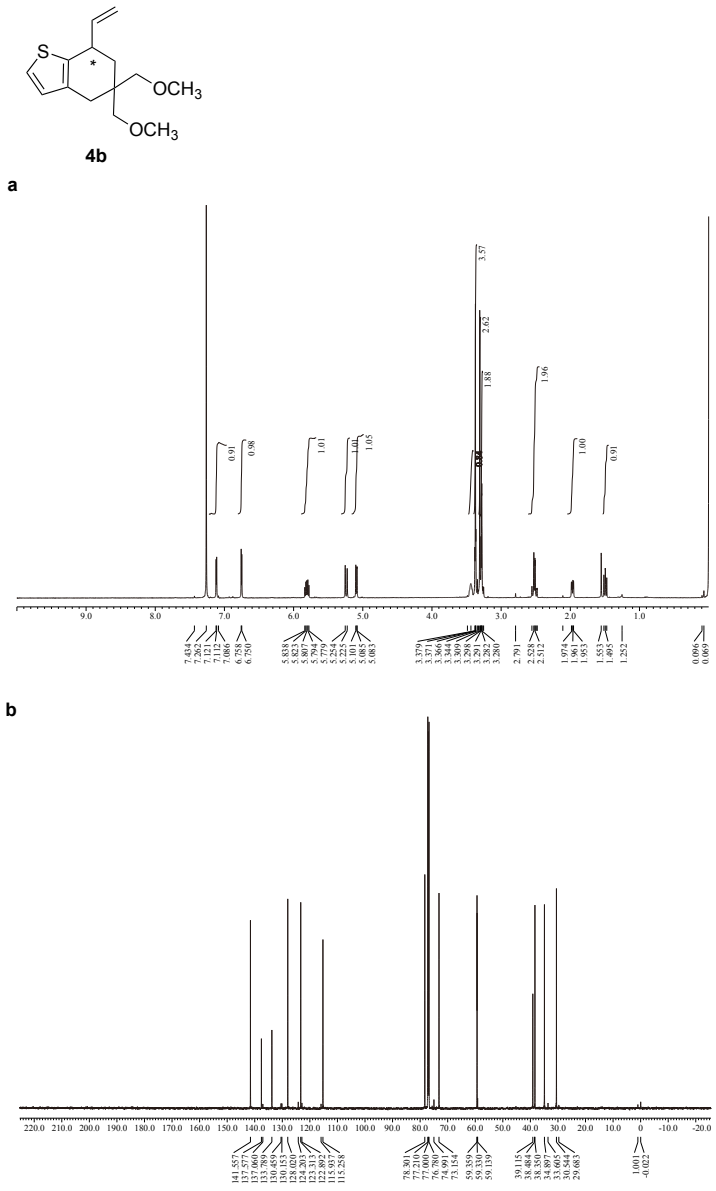


Figure S24. ^{1}H-NMR (**a**, 600 MHz) and ^{13}C-NMR (**b**, 152 MHz) spectra of 5,5-bis(methoxymethyl)-7-vinyl-4,5,6,7-tetrahydrobenzo[*b*]thiphene (**4b**) in $CDCl_3$.

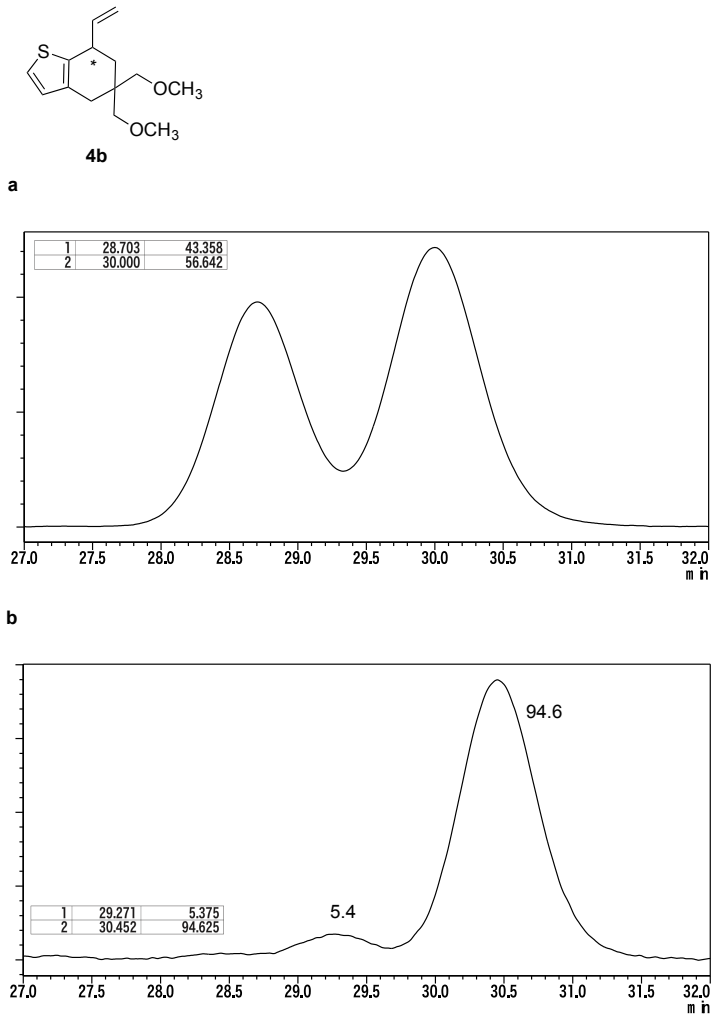


Figure S25. HPLC charts for determination of the er of 5,5-bis(methoxymethyl)-7-vinyl-4,5,6,7-tetrahydrobenzo[*b*]thiphen (**4b**). (**a**) Racemic product. (**b**) Product **4b** obtained in the *R* cat-catalyzed cyclization of **3b**. HPLC conditions: CHIRALCEL OD-H ((0.46 cmϕ x 250 mm) x 2); 0.1:99.9 *i*-PrOH–hexane eluent; 0.5 mL/min flow rate; 254-nm detection; 25 ºC; t_R 29.3 min (minor) and 30.5 min (major).

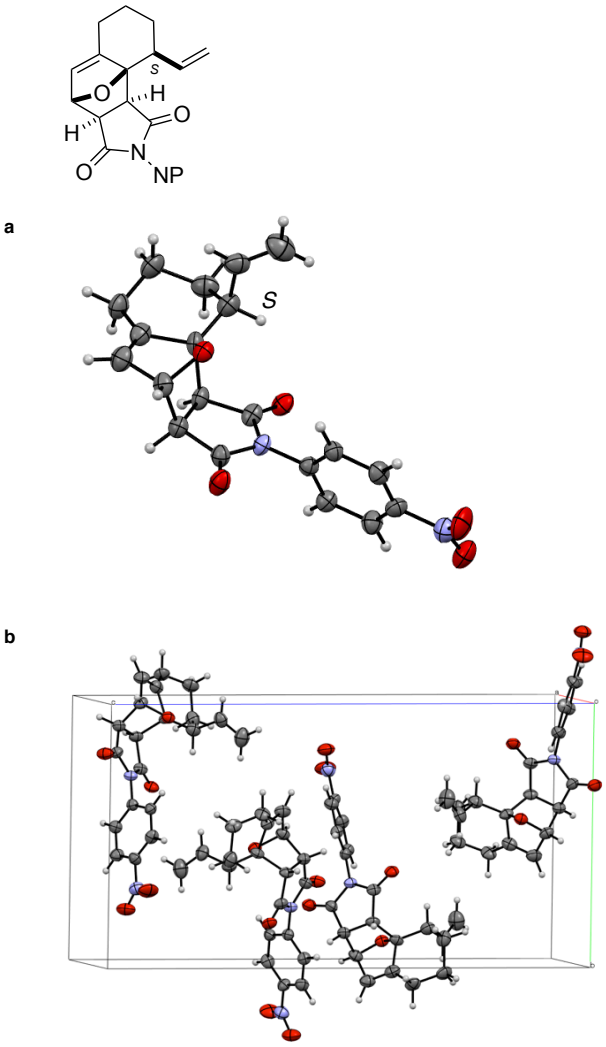


Figure S26. Molecular Structure of 1*S*-camphorsultam imide of (3aR,4S,9S,9aS,9bS)-2-(4-nitrophenyl)-9-vinyl-3a,6,7,8,9,9b-hexahydro-4,9a-epoxy benzo[*e*]isoindole-1,3(2*H*,4*H*)-dione in the crystalline state. (**a**) Ellipsoid structure drawn in 50% probability level. (**b**) Packing diagram.

Table S1. Crystallographic data and parameters for (3a*R*,4*S*,9*S*,9a*S*,9b*S*)-2-(4-nitrophenyl)-9-vinyl-3a,6,7,8,9,9b-hexahydro-4,9a-epoxybenzo[*e*]isoindole-1,3(2*H*,4*H*)-dione

mol formula	$C_{20}H_{18}N_2O_5$
mol wt	366.37
crystal color, habit	colorless, needle
crystal size, mm^3	0.100 x 0.100 x 0.100
crystal system	orthorhombic
lattice type	primitive
space group	$P2_12_12_1$ (#19)
cell dimens	
a, Å	6.4589(4)
b, Å	12.0159(7)
c, Å	22.7820(15)
vol, $Å^3$	1768.10(19)
Z	4
ρ calcd, g cm^{-3}	1.376
diffractometer	R-AXIS RAPID
radiation	CuKα (λ = 1.54187 Å)
graphite monochromated	
$2\theta_{max}$, deg	136.2°
no. of reflections measured	total: 4103
corrections	Lorentz-polarization
structure solution	direct methods (SIR92)
function minimized by	$\Sigma\omega(F_0^2-F_c^2)^2$
refinement	Full-matrix least-squares on F^2
R	0.0950
wR^2	0.1742
goodness-of-fit indicator	0.950
Flack Parameter	-0.0(3)