Oxidative Kinetic Resolution–Claisen Rearrangement Sequence to Enantioenriched Arylcycloalkenes

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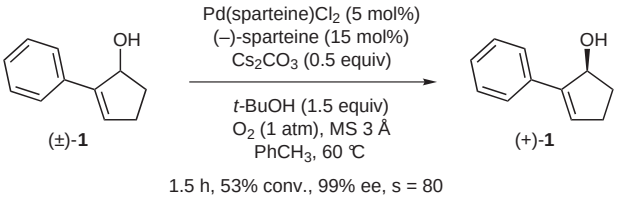
Abstract: The Pd-catalyzed oxidative kinetic resolution of secondary alcohols afforded enantioenriched allylic alcohols with high selectivity. These alcohols were transformed into arylcycloalkenes with enantioenriched tertiary and quaternary stereocenters through a two-step vinylation and Lewis acid promoted Claisen rearrangement. Subsequent Pd-catalyzed oxidative cyclization of a Claisen product afforded a 5,5-fused tetrahydrofuran.

Key words: oxidative kinetic resolution, Claisen rearrangement, oxidative cyclization, secondary alcohols, palladium catalysis



Scheme 1

As part of a general program directed toward the design of new synthetic methodology to facilitate the efficient construction of complex targets, we have developed a number of Pd(II)-catalyzed oxidative transformations.[1,2] These oxidations take advantage of the versatility of palladium to selectively perform a variety of processes and utilize molecular oxygen as an operationally simple and inexpensive stoichiometric oxidant. Recently, our group reported the oxidative kinetic resolution of secondary alcohols using a palladium dichloride catalyst precursor [Pd(nbd)Cl_2] in conjunction with the commercially available diamine (–)-sparteine.[1a,3] We subsequently made a number of improvements,[1b,c] rendering these methods more amenable to synthetic endeavors.[4,5]

While these developments greatly enhanced the reactivity and selectivity of this oxidative system, the explored substrate scope remained somewhat limited. In particular, allylic alcohols were a relatively unexplored class of compounds using our methodology.[3c,5] Due to their broad application in complex molecule synthesis, their successful resolution would be an important demonstration of the utility of the Pd-catalyzed oxidative kinetic resolution. Herein, we report the resolution of a number of secondary allylic alcohols, which can be further transformed into enantioenriched primary alcohols with tertiary and quaternary stereocenters through Claisen rearrangement.

Our exploration of the scope of the oxidative kinetic resolution of secondary alcohols led us to investigate a variety of 2-aryl allylic alcohols. These compounds were readily prepared by reported methods[6] and then subjected to our enantioselective oxidation conditions (Scheme 1). To our delight, our system was exceptionally effective in resolving these substrates, affording allylic alcohols with outstanding selectivity and unprecedented reactivity (Table 1).

Allylic alcohols with both electron-rich and electron-poor benzene substituents led to excellent selectivities (entries 1–5), as did substrates containing other aromatic rings (entries 6 and 7), including a heteroaromatic furan. Importantly, a 3-substituted allylic alcohol (entry 8) and a cyclohexenyl alcohol (entry 9) were also obtained in high ee with very short reaction times. For comparison, an alkylcyclopentenol was resolved much less successfully, affording modest selectivity after prolonged reaction times (entry 10).

Next, we looked to further elaborate these resolved arylalcohols into other synthetically useful building blocks. To this end, alcohol (–)-**8** was subjected to Claisen rearrangement conditions. While both Ireland–Claisen[7] and Johnson orthoester Claisen conditions[8] were unsuccessful in our hands, a two-step protocol involving Hg-promoted vinylation followed by Claisen rearrangement proved effective. The vinyl ether was prone to 1,3-rearrangement in the presence of various Lewis acids and under thermal conditions. However, we found that treatment of vinyl ether (+)-**11** with DIBAL-H in CH_2Cl_2 at –40 °C led to clean Claisen rearrangement followed by reduction of the intermediate aldehyde (Scheme 2).

We then applied this two-step sequence to other resolved alcohols. Though the vinylation gave modest yields, the majority of the mass balance was recovered starting material. The DIBAL-H promoted Claisen rearrangement afforded good to excellent yields of the desired primary alcohol (Table 2). Allylic alcohols bearing a variety of aromatic groups were successfully transformed to enantioenriched arylcyclopentenes. This sequence also allowed access to a cyclohexene (entry 9) and a primary alcohol containing a quaternary stereocenter (entry 8) in high ee.

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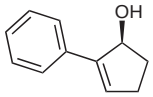
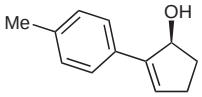
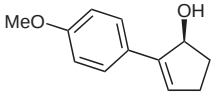
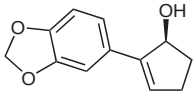
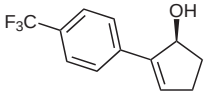
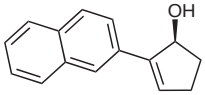
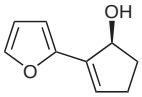
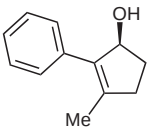
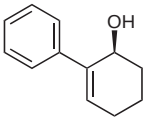
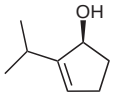
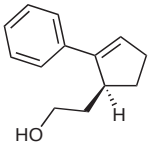
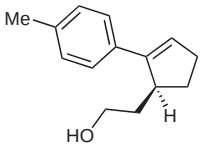
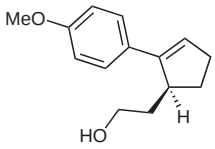
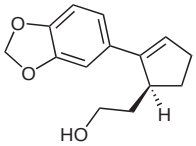
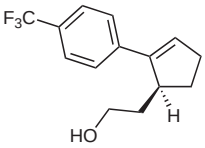
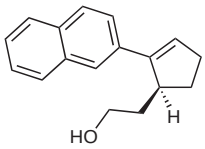
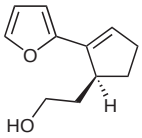
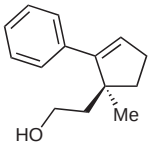
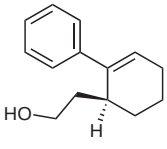
Table 1 Oxidative Kinetic Resolution of Allylic Alcohols[a]

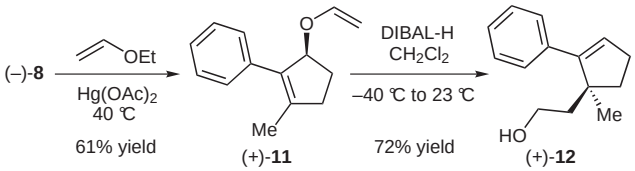
Entry	Alcohol	Reaction time (h)	Conversion[b]	ee[c]	s[d]
1	 (+)-**1**	1.5	53	99	89
2	 (+)-**2**	3.5	58	99	31
3	 (+)-**3**	1.5	54	97	46
4	 (+)-**4**	1.5	61	99	22
5	 (+)-**5**	1.5	63	99	19
6	 (+)-**6**	1.5	53	94	36
7	 (+)-**7**	10	64	99	19
8	 (–)-**8**	1	53	98	64
9	 (–)-**9**	3	57	97	27
10	 **10**	21	72	93	6.5

[a] Reaction conditions: Pd(sparteine)Cl_2 (5 mol%), (–)-sparteine (15 mol%), Cs_2CO_3 (0.5 equiv), *t*-BuOH (1.5 equiv), O_2 (1 atm), 3 Å MS in toluene (0.25 M allylic alcohol), 60 °C.
[b] Percent conversion (%) determined by GC relative to internal standard.
[c] Alcohol percent ee determined by chiral HPLC.
[d] $s = k_{fast}/k_{slow} = \ln[(1 - conv)(1 - ee_{alc})]/\ln[(1 - conv)(1 + ee_{alc})]$.

Table 2 Vinylation and Claisen Rearrangement of Allylic Alcohols[12]

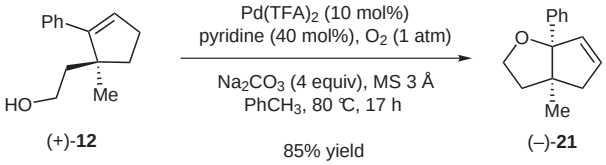
Entry	Alcohol[a]	Vinyl ether yield (%)[b]	Claisen product[c]	Claisen product yield (%)[b]
1	(+)-**1**	55	 (+)-**13**	36
2	(+)-**2**	42	 (+)-**14**	77
3	(+)-**3**	36	 (+)-**15**	91
4	(+)-**4**	56	 (+)-**16**	76
5	(+)-**5**	37	 (+)-**17**	82
6	(+)-**6**	47	 (+)-**18**	86
7	(+)-**7**	31	 (+)-**19**	87
8	(–)-**8**	61	 (+)-**12**	72
9	(–)-**9**	16	 (+)-**20**	83

[a] Reaction conditions: $Hg(OAc)_2$ (0.28 equiv) in ethyl vinyl ether (0.08 M allylic alcohol), 40 °C, 120 h.
[b] Isolated yield.
[c] Reaction conditions: DIBAL-H (1.1 equiv, 1 M in PhMe) in CH_2Cl_2 (0.08 M vinyl ether), –40 °C to 23 °C, 2 h.



Scheme 2

These primary alcohols seemed to be ideal substrates for a Pd-catalyzed oxidative cyclization recently developed by our laboratories.[2] Thus, phenylcyclopentene (+)-**12** was exposed to our reported aerobic conditions (Scheme 3).[2d] Clean cyclization to 5,5-fused bicycle (–)-**21** was observed. The absence of alcohol oxidation under these conditions accentuates the exquisite selectivity that can be obtained in these Pd-catalyzed oxidations by slight modifications to the system.



Scheme 3

In conclusion, we have employed the Pd-catalyzed oxidative kinetic resolution to obtain allylic alcohol intermediates in high ee, which can subsequently yield compounds bearing enantioenriched tertiary and quaternary stereocenters through Claisen rearrangement. These Claisen products can then undergo a second Pd-catalyzed aerobic oxidation to afford 5,5-fused tetrahydrofurans. Application of the oxidative kinetic resolution of secondary alcohols to other transformations in the context of complex molecule synthesis is ongoing in our laboratories.

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References and Notes

(1) For oxidative kinetic resolutions, see: (a) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2001**, *123*, 7725. (b) Bagdanoff, J. T.; Ferreira, E. M.; Stoltz, B. M. *Org. Lett.* **2003**, *5*, 835. (c) Bagdanoff, J. T.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 353. (d) Trend, R. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 4482. (e) Nielson, R. J.; Keith, J. M.; Stoltz, B. M.; Goddard, W. A. III *J. Am. Chem. Soc.* **2004**, *126*, 7967.

(2) For oxidative cyclizations, see: (a) Trend, R. M.; Ramtohul, Y. K.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2003**, *42*, 2892. (b) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578. (c) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 6144. (d) Trend, R. M.; Ramtohul, Y. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 17778.

(3) Simultaneous to our publication, a related system was reported, see: (a) Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Am. Chem. Soc.* **2001**, *123*, 7475. (b) Mueller, J. A.; Jensen, D. R.; Sigman, M. S. *J. Am. Chem. Soc.* **2002**, *124*, 8202. (c) Mandal, S. K.; Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Org. Chem.* **2003**, *68*, 4600. (d) Mandal, S. K.; Sigman, M. S. *J. Org. Chem.* **2003**, *68*, 7535. (e) Mueller, J. A.; Sigman, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 7005. (f) Jensen, D. R.; Sigman, M. S. *Org. Lett.* **2003**, *5*, 63. (g) Mueller, J. A.; Cowell, A.; Chandler, B. D.; Sigman, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 14817. (h) Sigman, M. S.; Jensen, D. R. *Acc. Chem. Res.* **2006**, *39*, 221.

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(5) For application to the synthesis of pharmaceutical intermediates, see: Caspi, D. D.; Ebner, D. C.; Bagdanoff, J. T.; Stoltz, B. M. *Adv. Synth. Catal.* **2004**, *346*, 185.

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(11) The decreased ee for this substrate is presumably due to competing 1,3-rearrangement, leading to partial racemization.

(12) **General Procedure for the Oxidative Kinetic Resolution of Allylic Alcohols**[1b]
To an oven-dried reaction tube with stir bar was added oven-dried powdered 3 Å MS (500 mg). After cooling, $Pd(nbd)Cl_2$ (13.5 mg, 0.05 mmol), followed by toluene (2 mL) and then (–)-sparteine (46.9 mg, 46 μL, 0.20 mmol) were added. The reaction vessel was then cooled to –78 °C, vacuum evacuated, and purged with O_2 (3×). The reaction was then heated to 60 °C with vigorous stirring under O_2 (1 atm) for 20 min. Finely powdered anhyd Cs_2CO_3 (162.9 mg, 0.50 mmol) was added, followed by a solution of allylic alcohol (1.0 mmol), *t*-BuOH (111.2 mg, 143 mL, 1.5 mmol) and toluene (2 mL). Reaction progress was monitored by GC analysis of an aliquot filtered through silica gel (Et_2O as eluent). When the reaction was complete, the reaction was cooled to r.t., filtered through silica gel (Et_2O as eluent), concentrated under reduced pressure, and purified by flash chromatography to afford enantioenriched alcohol and ketone.
2-Phenylcyclopent-2-enol [(+)-1]
R_f = 0.20 (4:1 hexane–EtOAc). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.54 (comp. m, 2 H), 7.39–7.22 (comp. m, 3 H), 6.32 (t, *J* = 2.5 Hz, 1 H), 5.29–5.21 (m, 1 H), 2.74–2.60 (m, 1 H), 2.51–2.34 (m, 2 H), 2.02–1.90 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.8, 135.1, 130.2, 128.8, 127.8, 126.4, 77.4, 34.3, 30.7. IR (thin film/NaCl): 3220, 2883, 1496, 1322, 1050, 759, 691 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{11}H_{12}O]^+$: 160.0888; found: 160.0881. $[\alpha]_D^{25}$ +14.0 (*c* 1.4, $CHCl_3$; 99% ee). HPLC: Chiralcel OD-H column, 3% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 21.1 min, minor peak t_R = 16.9 min.

2-(4-Methylphenyl)cyclopent-2-enol [(+)-2]
R_f = 0.35 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.0 Hz, 2 H), 7.16 (d, *J* = 8.1 Hz, 2 H), 6.26 (t, *J* = 2.5 Hz, 1 H), 5.22 (m, 1 H), 2.73–2.59 (m, 1 H), 2.49–2.32 (m, 2 H), 2.34 (s, 3 H), 2.01–1.88 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7, 137.3, 132.2, 129.5, 129.2, 126.3, 77.4, 34.2, 30.7, 21.4. IR (thin film/NaCl): 3337, 2921, 1512, 1043, 813 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{12}H_{14}O]^+$: 174.1045; found: 174.1042. $[\alpha]_D^{25}$ +4.5 (*c* 1.6, $CHCl_3$; 98.5% ee). HPLC: Chiralcel OB-H column, 8% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 15.3 min, minor peak t_R = 7.8 min.

2-(4-Methoxyphenyl)cyclopent-2-enol [(+)-3]
R_f = 0.30 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.8 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 6.18 (t, *J* = 2.4 Hz, 1 H), 5.19 (m, 1 H), 3.81 (s, 3 H), 2.72–2.56 (m, 1 H), 2.48–2.31 (m, 2 H), 2.00–1.87 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 144.2, 128.1, 127.8, 127.6, 114.2, 77.5, 55.5, 34.3, 30.6. IR (thin film/NaCl): 3249, 2958, 2892, 2846, 1052, 1033, 824 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{12}H_{14}O_2]^+$: 190.0994; found: 190.0995. $[\alpha]_D^{25}$ +10.6 (*c* 1.9, $CHCl_3$; 99% ee); HPLC: Chiralpak AS column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 11.5 min, minor peak t_R = 15.9 min.

2-{Benzo[1,3]dioxol-5-yl}cyclopent-2-enol [(+)-4]
R_f = 0.27 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08–7.03 (comp. m, 2 H), 6.82–6.76 (m, 1 H), 6.16 (t, *J* = 2.5, 1 H), 5.95 (s, 2 H), 5.15 (m, 1 H), 2.71–2.57 (m, 1 H), 2.47–2.30 (m, 2 H), 1.99–1.87 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.1, 147.1, 144.3, 129.5, 128.8, 120.0, 108.5, 106.8, 101.2, 77.5, 34.3, 30.6. IR (thin film/NaCl): 3354, 2894, 1490, 1503, 1226, 1041, 937 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{12}H_{12}O_3]^+$: 204.0787; found: 204.0793. $[\alpha]_D^{25}$ +9.6 (*c* 1.6, $CHCl_3$; 99% ee). HPLC: Chiralcel OB-H column, 10% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 27.1 min, minor peak t_R = 12.0 min.

2-[4-(Trifluoromethyl)phenyl]cyclopent-2-enol [(+)-5]
R_f = 0.34 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.5 Hz, 2 H), 7.58 (d, *J* = 8.5 Hz, 2 H), 6.43 (t, *J* = 2.6 Hz, 1 H), 5.24 (m, 1 H), 2.77–2.62 (m, 1 H), 2.54–2.37 (m, 2 H), 2.02–1.86 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.4, 138.4, 132.6, 127.7, 126.3, 125.4 (q, J_F = 3.8 Hz), 77.1, 34.1, 30.5. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –63.5. IR (thin film/NaCl): 3239, 1326, 1112, 827 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{12}H_{11}OF_3]^+$: 228.0762; found: 228.0752. $[\alpha]_D^{25}$ +16.0 (*c* 2.5, $CHCl_3$; 99% ee). HPLC: Chiralcel OD-H column, 2% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 15.0 min, minor peak t_R = 13.7 min.

2-(2-Naphthyl)cyclopent-2-enol [(+)-6]
R_f = 0.37 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (s, 1 H), 7.87–7.67 (comp. m, 4 H), 7.50–7.40 (comp. m, 2 H), 6.45 (t, *J* = 2.5 Hz, 1 H), 5.37 (m, 1 H), 2.80–2.65 (m, 1 H), 2.56–2.38 (m, 2 H), 2.07–1.95 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7, 133.9, 133.0, 132.4, 130.9, 128.5, 128.4, 127.9, 126.4, 126.1, 125.0, 124.8, 77.4, 34.4, 30.9. IR (thin film/NaCl): 3385, 1044, 819, 476 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{15}H_{14}O]^+$: 210.1045; found: 210.1043. $[\alpha]_D^{25}$ +46.4 (*c* 2.0, $CHCl_3$; 99% ee); HPLC: Chiralpak AS column, 3% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 11.5 min, minor peak t_R = 13.3 min.

2-(2-Furyl)cyclopent-2-enol [(+)-7]
R_f = 0.26 (7:3 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 1.6 Hz, 1 H), 6.43 (d, *J* = 3.4 Hz, 1 H), 6.40 (dd, *J* = 3.3, 1.7 Hz, 1 H), 5.11 (m, 1 H), 2.74–2.60 (m, 1 H), 2.49–2.30 (m, 2 H), 1.95–1.84 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.2, 142.0, 135.7, 128.4, 111.4, 106.8, 77.3, 55.9, 30.8. IR (thin film/NaCl): 3344, 2934, 2849, 1044, 928, 733 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_9H_{10}O_2]^+$: 150.0681; found: 150.0680. $[\alpha]_D^{25}$ +30.9 (*c* 1.1, $CHCl_3$; 99% ee). HPLC: Chiralcel OB-H column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 17.0 min, minor peak t_R = 10.5 min.

3-Methyl-2-phenylcyclopent-2-enol [(–)-8]
R_f = 0.24 (4:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.22 (comp. m, 5 H), 5.16 (br d, *J* = 5.5 Hz, 1 H), 2.74–2.58 (m, 1 H), 2.44–2.30 (m, 2 H), 1.87–1.75 (m, 1 H), 1.85 (d, *J* = 1.1 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 138.5, 136.7, 128.6, 128.5, 126.9, 80.5, 36.9, 32.7, 15.9. IR (thin film/NaCl): 3370, 2930, 1442, 699 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{12}H_{14}O]^+$: 174.1045; found: 174.1037. $[\alpha]_D^{25}$ –2.4 (*c* 1.2, $CHCl_3$; 99% ee). HPLC: Chiralcel OB-H column, 2% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 13.2 min, minor peak t_R = 10.4 min.

2-Phenylcyclohex-2-enol [(–)-9]
Characterization data matched that in the literature;[9] $[a]_D^{25}$ –109.5 (*c* 1.3, $CHCl_3$; 99% ee) {lit.[10] $[\alpha]_D$ +114.5 (*c* 1.6, $CHCl_3$)}. HPLC: Chiralpak AD column, 3% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 22.5 min, minor peak t_R = 17.3 min.

General Procedure for the Vinylation of Allylic Alcohols
To a flame-dried 1-dram vial was added allylic alcohol (0.23 mmol), freshly distilled ethyl vinyl ether (3 mL), and then $Hg(OAc)_2$ (20.3 mg, 0.64 mmol, 0.28 equiv). The reaction mixture was stirred at 40 °C for 120 h. After cooling to 23 °C, K_2CO_3 (173 mg, 1.25 mmol, 5.4 equiv) was added, and the suspension was stirred for 30 min. Then, the mixture was filtered, and the solution was concentrated under reduced pressure. Purification by preparative TLC (10:1 hexane–EtOAc as eluent) afforded the vinyl ether and starting allylic alcohol.

3-Methyl-2-phenyl-1-vinyloxy-2-cyclopentene [(+)-11]
R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.36 (comp. m, 4 H), 7.31–7.24 (m, 1 H), 6.45 (dd, *J* = 13.8, 6.3 Hz, 1 H), 5.25 (br d, *J* = 6.9 Hz, 1 H), 4.31 (dd, *J* = 14.4, 1.8 Hz, 1 H), 4.04 (dd, *J* = 6.6, 1.5 Hz, 1 H), 2.79–2.68 (m, 1 H), 2.48–2.22 (m, 2 H), 2.06–1.97 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 142.3, 136.4, 134.7, 128.2, 128.1, 126.6, 88.0, 87.1, 37.1, 28.9, 15.7. IR (thin film/NaCl): 3055, 3029, 2975, 2938, 2912, 2845, 1631, 1608, 1492, 1444, 1379, 1350, 1317, 1189, 1099, 1058, 1016, 989, 964, 872, 816 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O]^+$: 200.1201; found: 200.1213. $[\alpha]_D^{26}$ +6.1 (*c* 0.80, CH_2Cl_2).

2-Phenyl-1-vinyloxy-2-cyclopentene
R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.46 (comp. m, 2 H), 7.35–7.22 (comp. m, 3 H), 6.50–6.43 (m, 2 H), 5.37 (dt, *J* = 6.9, 2.4 Hz, 1 H), 4.35 (dd, *J* = 14.4, 1.8 Hz, 1 H), 4.11 (dd, *J* = 6.6, 1.5 Hz, 1 H), 2.76–2.64 (m, 1 H), 2.54–2.26 (m, 2 H), 2.15–2.12 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 141.1, 134.6, 132.0, 128.4, 127.3, 125.9, 88.3, 83.1, 31.0, 30.1. IR (thin film/NaCl): 3057, 2934, 2846, 1632, 1610, 1496, 1447, 1358, 1318, 1188, 1048, 1032, 962, 822 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{13}H_{14}O]^+$: 186.1045; found: 186.1042. $[\alpha]_D^{25}$ +32.5 (*c* 0.38, CH_2Cl_2).

2-(4-Methylphenyl)-1-vinyloxy-2-cyclopentene
R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 6.3 Hz, 2 H), 7.17 (d, *J* = 8.1 Hz, 2 H), 6.52 (dd, *J* = 14.4, 6.9 Hz, 1 H), 6.42 (t, *J* = 2.4 Hz, 1 H), 5.37 (dt, *J* = 7.2, 2.4 Hz, 1 H), 4.37 (dd, *J* = 14.4, 1.8 Hz, 1 H), 4.12 (dd, *J* = 6.6, 1.8 Hz, 1 H), 2.74–2.65 (m, 1 H), 2.54–2.43 (m, 1 H), 2.36 (s, 3 H), 2.39–2.27 (m, 1 H), 2.16–2.09 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 141.0, 137.0, 131.8, 131.0, 129.1, 125.9, 88.3, 83.1, 31.0, 30.1, 21.2. IR (thin film/NaCl): 2921, 2849, 1631, 1609, 1513,

1449, 1352, 1317, 1187, 1048, 1030, 963, 813 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O]^+$: 200.1201; found: 200.1201. $[\alpha]_D^{25}$ +20.8 (*c* 0.16, CH_2Cl_2).

2-(4-Methoxyphenyl)-1-vinyloxy-2-cyclopentene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.7 Hz, 2 H), 6.89 (d, *J* = 9.0 Hz, 2 H), 6.51 (dd, *J* = 14.4, 6.9 Hz, 1 H), 6.33 (t, *J* = 2.7 Hz, 1 H), 5.37 (dt, *J* = 7.2, 2.1 Hz, 1 H), 4.36 (dd, *J* = 14.4, 2.1 Hz, 1 H), 4.11 (dd, *J* = 6.6, 1.8 Hz, 1 H), 3.81 (s, 3 H), 2.75–2.62 (m, 1 H), 2.52–2.42 (m, 1 H), 2.38–2.56 (m, 1 H), 2.14–2.05 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 150.1, 140.5, 129.9, 127.4, 127.2, 113.8, 88.3, 83.3, 55.2, 30.9, 30.1. IR (thin film/NaCl): 2918, 2848, 2359, 2340, 1632, 1609, 1512, 1463, 1353, 1317, 1269, 1257, 1180, 1112, 1036, 963, 891, 824 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O_2]^+$: 216.1150; found: 216.1155. $[\alpha]_D^{26}$ +18.8 (*c* 0.43, CH_2Cl_2).

2-{Benzo[1,3]dioxol-5-yl}-1-vinyloxy-2-cyclopentene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.00 (d, *J* = 1.8 Hz, 1 H), 6.97 (dd, *J* = 13.8, 1.5 Hz, 1 H), 6.79 (d, *J* = 7.8 Hz, 1 H), 6.49 (q, *J* = 6.9 Hz, 1 H), 6.30 (t, *J* = 2.4 Hz, 1 H), 5.94 (s, 2 H), 5.29 (dt, *J* = 7.2, 2.4 Hz, 1 H), 4.35 (dd, *J* = 14.4, 2.1 Hz, 1 H), 4.11 (dd, *J* = 6.9, 1.8 Hz, 1 H), 2.73–2.61 (m, 1 H), 2.51–2.40 (m, 1 H), 2.37–2.25 (m, 1 H), 2.13–2.04 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0, 147.7, 146.9, 140.6, 130.6, 119.7, 108.2, 106.4, 100.9, 88.4, 83.2, 30.9, 30.0. IR (thin film/NaCl): 2898, 2849, 2359, 2340, 1632, 1610, 1503, 1490, 1447, 1366, 1317, 1227, 1187, 1106, 1040, 969, 936, 889, 808 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{14}O_3]^+$: 230.0943; found: 230.0933. $[\alpha]_D^{26}$ +20.8 (*c* 0.075, CH_2Cl_2).

2-[4-(Trifluoromethyl)phenyl]-1-vinyloxy-2-cyclopentene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (m, 4 H), 6.58 (t, *J* = 2.7 Hz, 1 H), 6.50 (dd, *J* = 14.4, 6.6 Hz, 1 H), 5.37 (dt, *J* = 7.2, 2.1 Hz, 1 H), 4.37 (dd, *J* = 14.1, 1.8 Hz, 1 H), 4.15 (dd, *J* = 6.6, 1.8 Hz, 1 H), 2.80–2.67 (m, 1 H), 2.58–2.47 (m, 1 H), 2.42–2.30 (m, 1 H), 2.17–2.08 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9, 140.2, 134.6, 126.2, 125.5, 125.4, 125.3, 125.3, 88.8, 82.9, 31.2, 30.0. IR (thin film/NaCl): 2917, 2846, 2141, 1731, 1660, 1633, 1614, 1507, 1414, 1365, 1317, 1246, 1190, 1164, 1122, 1071, 1033, 1016, 963, 829, 733 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{13}OF_3]^+$: 254.0919; found: 254.0913. $[\alpha]_D^{26}$ +31.0 (*c* 0.32, CH_2Cl_2).

2-(2-Naphthyl)-1-vinyloxy-2-cyclopentene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.80 (comp. m, 4 H), 7.70–7.67 (m, 1 H), 7.51–7.43 (comp. m, 2 H), 6.61 (t, *J* = 2.7 Hz, 1 H), 6.58 (dd, *J* = 14.4, 6.9 Hz, 1 H), 5.51 (dt, *J* = 7.2, 2.7 Hz, 1 H), 4.43 (dd, *J* = 14.1, 1.8 Hz, 1 H), 4.18 (dd, *J* = 6.9, 1.8 Hz, 1 H), 2.83–2.71 (m, 1 H), 2.60–2.49 (m, 1 H), 2.44–2.32 (m, 1 H), 2.23–2.13 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 141.1, 133.5, 1327, 131.9, 128.3, 127.9, 127.5, 126.0, 125.8, 124.7, 124.3, 88.5, 83.1, 31.2, 30.1. IR (thin film/NaCl): 3282, 3055, 2929, 2848, 1632, 1610, 1507, 1449, 1317, 1187, 1048, 1030, 963, 947, 894, 815, 746, 665 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{17}H_{16}O]^+$: 236.1201; found: 236.1207. $[\alpha]_D^{26}$ +48.7 (*c* 0.53, CH_2Cl_2).

2-(2-Furyl)-1-vinyloxy-2-cyclopentene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 1.8 Hz, 1 H), 6.49 (q, *J* = 6.6 Hz, 1 H), 6.39 (dd, *J* = 3.6, 2.1 Hz, 1 H), 6.36 (t, *J* = 3.0 Hz, 1 H), 6.30 (d, *J* = 3.3 Hz, 1 H), 5.23 (dt, *J* = 7.2, 2.7 Hz, 1 H), 4.34 (dd, *J* = 14.4, 1.8 Hz, 1 H), 4.10 (dd, *J* = 6.9, 1.8 Hz, 1 H), 2.75–2.63 (m, 1 H), 2.53–2.42 (m, 1 H), 2.37–2.25 (m, 1 H), 2.09–1.99 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 150.2, 141.9, 132.2, 130.1, 111.1, 106.9, 88.5, 83.3, 31.1, 30.1. IR (thin film/NaCl): 2924, 2850, 1633, 1611, 1487, 1349, 1317, 1189, 1153, 1051, 1028, 962, 916, 884, 806 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{11}H_{12}O_2]^+$: 176.0837; found: 176.0842. $[\alpha]_D^{25}$ +39.1 (*c* 0.35, CH_2Cl_2).

2-Phenyl-1-vinyloxy-2-cyclohexene

R_f = 0.75 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.22 (comp. m, 5 H), 6.43 (dd, *J* = 14.1, 6.6 Hz, 1 H), 6.35 (t, *J* = 3.3 Hz, 1 H), 4.78 (t, *J* = 3.0 Hz, 1 H), 4.41 (dd, *J* = 14.1, 1.5 Hz, 1 H), 4.08 (dd, *J* = 6.6, 1.8 Hz, 1 H), 2.40–2.30 (m, 1 H), 2.25–2.14 (m, 2 H), 1.91–1.64 (comp. m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 140.4, 135.6, 130.6, 128.3, 126.9, 125.6, 88.5, 72.5, 27.6, 25.9, 16.8. IR (thin film/NaCl): 3023, 2933, 2865, 2829, 2359, 2340, 1632, 1610, 1496, 1445, 1376, 1355, 1330, 1312, 1260, 1185, 1094, 1062, 1011, 977, 946, 917, 870, 813, 756, 695 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O]^+$: 200.1201; found: 200.1207. $[\alpha]_D^{25}$ –115.8 (*c* 0.17, CH_2Cl_2).

General Procedure for Claisen Rearrangement of Vinyl Ethers

To a flame-dried 1-dram vial was added vinyl ether (0.041 mmol) and CH_2Cl_2 (0.5 mL). The solution was cooled to –40 °C, and DIBAL-H (1 M in toluene, 45 μL, 0.045 mmol) was added dropwise. The reaction mixture was allowed to warm to 23 °C and stir for 2 h, after which it was quenched with excess $Na_2SO_4 \cdot 10H_2O$. After 30 min stirring, the cloudy suspension was filtered, and the solution was concentrated under reduced pressure. Purification by preparative TLC (9:2 hexane–EtOAc as eluent) afforded the primary alcohol.

1-(2-Hydroxyethyl)-1-methyl-2-phenyl-2-cyclopentene [(+)-12]

R_f = 0.16 (10:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.20 (comp. m, 5 H), 5.80 (t, *J* = 2.4 Hz, 1 H), 3.75–3.58 (m, 2 H), 2.42–2.35 (m, 2 H), 2.10–2.01 (m, 1 H), 1.89–1.77 (comp. m, 3 H), 1.34 (s, 1 H), 1.25 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.6, 137.9, 128.9, 128.1, 127.3, 126.6, 60.7, 48.7, 48.5, 39.2, 30.1, 26.8. IR (thin film/NaCl): 3369, 3054, 2951, 2866, 1598, 1492, 1453, 1376, 1099, 1054, 1020, 759, 700 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{18}O]^+$: 202.1358; found: 202.1355. $[\alpha]_D^{25}$ +27.5 (*c* 0.66, CH_2Cl_2; 87% ee). HPLC: Chiralcel OD-H column, 3% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 13.1 min, minor peak t_R = 10.7 min.

1-(2-Hydroxyethyl)-2-phenyl-2-cyclopentene [(+)-13]

R_f = 0.13 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.19 (comp. m, 5 H), 6.07–6.05 (m, 1 H), 3.75–3.63 (m, 2 H), 3.29 (m, 1 H), 2.53–2.21 (m, 2 H), 2.20–2.14 (m, 1 H), 1.94–1.75 (m, 2 H), 1.55–1.45 (m, 1 H), 1.42 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3, 136.2, 128.4, 126.9, 126.7, 126.1, 61.7, 41.5, 36.5, 31.5, 29.8. IR (thin film/NaCl): 3350, 3053, 2935, 2847, 1598, 1494, 1445, 1330, 1055, 755, 694 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{13}H_{16}O]^+$: 188.1201; found: 188.1208. $[\alpha]_D^{24}$ +62.3 (*c* 0.27, CH_2Cl_2; 97.9% ee). HPLC: Chiralcel OJ column, 2% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 32.6 min, minor peak t_R = 22.8 min.

1-(2-Hydroxyethyl)-2-(4-methylphenyl)-2-cyclopentene [(+)-14]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 7.8 Hz, 2 H), 7.14 (d, *J* = 8.1 Hz, 2 H), 6.02–6.00 (m, 1 H), 3.73–3.65 (m, 2 H), 3.26 (m, 1 H), 2.52–2.44 (m, 2 H), 2.34 (s, 3 H), 2.26–2.13 (m, 1 H), 1.94–1.74 (m, 2 H), 1.55–1.43 (m, 1 H), 1.34 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1, 136.6, 129.1, 126.0, 125.8, 61.7, 41.5, 36.5, 31.5, 29.8, 21.1. IR (thin film/NaCl): 3337, 3048, 3023, 2936, 2844, 1901, 1617, 1566, 1511, 1437, 1379, 1335, 1307, 1185, 1111, 1056, 1019, 981, 879, 803 cm^{-1}.

HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{18}O]^+$: 202.1358; found: 202.1353. $[\alpha]_D^{24}$ +51.5 (*c* 0.075, CH_2Cl_2; 96.8% ee). HPLC: Chiralcel OJ column, 2% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 13.4 min, minor peak t_R = 15.3 min.

1-(2-Hydroxyethyl)-2-(4-methoxyphenyl)-2-cyclopentene [(+)-15]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.94 (s, 1 H), 3.80 (s, 3 H), 3.72–3.64 (m, 2 H), 3.26 (br s, 1 H), 2.50–2.44 (m, 2 H), 2.24–2.11 (m, 1 H), 1.92–1.73 (m, 2 H), 1.54–1.42 (m, 1 H), 1.44 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5, 145.6, 128.9, 127.2, 124.7, 113.7, 61.7, 55.2, 41.6, 36.4, 31.4, 29.8. IR (thin film/NaCl): 3392, 2934, 2836, 1607, 1510, 1462, 1441, 1294, 1252, 1178, 1037, 804 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{18}O_2]^+$: 218.1307; found: 218.1299. $[\alpha]_D^{25}$ +66.9 (*c* 0.27, CH_2Cl_2; 98.6% ee). HPLC: Chiralcel OJ column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 13.6 min, minor peak t_R = 16.2 min.

1-(2-Hydroxyethyl)-2-{2-Benzo[1,3]dioxol-5-yl}-2-cyclopentene [(+)-16]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.92 (s, 1 H), 6.89 (dd, *J* = 8.4, 1.2 Hz, 1 H), 6.78 (d, *J* = 8.4 Hz), 5.94 (s, 2 H), 5.93 (s, 1 H), 3.72–3.64 (m, 2 H), 3.32 (br s, 1 H), 2.49–2.43 (m, 2 H), 2.23–2.11 (m, 1 H), 1.92–1.73 (m, 2 H), 1.54–1.42 (m, 1 H), 1.49 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 146.5, 145.8, 130.6, 125.4, 119.6, 108.1, 106.6, 100.9, 61.6, 41.7, 36.3, 31.3, 29.7. IR (thin film/NaCl): 3350, 3041, 2935, 2888, 2777, 2063, 1850, 1604, 1503, 1489, 1443, 1356, 1223, 1126, 1104, 1040, 986, 937, 862, 806 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O_3]^+$: 232.1100; found: 232.1091. $[\alpha]_D^{24}$ +62.2 (*c* 0.27, CH_2Cl_2; 93.1% ee). HPLC: Chiralcel OJ column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 17.8 min, minor peak t_R = 21.1 min.

1-(2-Hydroxyethyl)-2-[4-(trifluoromethyl)phenyl]-2-cyclopentene [(+)-17]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (dd, *J* = 8.4, 21.6 Hz, 4 H), 6.17 (s, 1 H), 3.72–3.67 (m, 2 H), 3.30 (br s, 1 H), 2.52–2.50 (m, 2 H), 2.29–2.16 (m, 1 H), 1.90–1.78 (m, 2 H), 1.52–1.42 (m, 1 H), 1.37 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.3, 139.8, 129.4, 126.3, 125.4, 125.4, 125.3, 61.5, 41.5, 36.3, 31.6, 29.7. IR (thin film/NaCl): 3368, 2937, 2846, 1615, 1412, 1326, 1164, 1123, 1110, 1069, 1015, 850, 831, 815 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{15}OF_3]^+$: 256.1075; found: 256.1073. $[\alpha]_D^{26}$ +48.5 (*c* 0.20, CH_2Cl_2; 97.1% ee). HPLC: Chiralcel OJ column, 2% *i*-PrOH–hexane, 1 mL/min flow rate, major peak t_R = 21.6 min, minor peak t_R = 18.5 min.

1-(2-Hydroxyethyl)-2-(2-naphthyl)-2-cyclopentene [(+)-18]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.78 (comp. m, 4 H), 7.63 (d, *J* = 8.7 Hz, 1 H), 7.49–7.41 (m, 1 H), 6.22 (s, 1 H), 3.80 (s, 3 H), 3.72 (t, *J* = 5.1 Hz, 2 H), 3.41 (br s, 1 H), 2.62–2.46 (m, 2 H), 2.31–2.18 (m, 1 H), 2.10–1.81 (m, 2 H), 1.61–1.49 (m, 1 H), 1.44 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.2, 133.6, 133.5, 132.5, 128.0, 127.9, 127.52, 127.46, 126.1, 125.6, 124.8, 124.5, 61.7, 41.5, 36.4, 31.6, 29.8. IR (thin film/NaCl): 3369, 3055, 2933, 2847, 1627, 1595, 1505, 1435, 1354, 1273, 1197, 1145, 1128, 1056, 989, 962, 946, 893, 858, 812, 747 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{17}H_{18}O]^+$: 238.1358; found: 238.1354. $[\alpha]_D^{25}$ +25.4 (*c* 0.47, CH_2Cl_2; 98.8% ee). HPLC: Chiralcel OJ column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 12.7 min, minor peak t_R = 14.1 min.

1-(2-Hydroxyethyl)-2-(2-furyl)-2-cyclopentene [(+)-19]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 1.5 Hz, 1 H), 6.38 (dd, *J* = 3.3, 1.8 Hz, 1 H), 6.26 (d, *J* = 3.3 Hz, 1 H), 6.07 (s, 1 H), 3.77–3.67 (m, 2 H), 3.09 (br s, 1 H), 2.60–2.37 (m, 2 H), 2.19–2.09 (m, 1 H), 2.02–1.91 (m, 1 H), 1.83–1.74 (m, 1 H), 1.68–1.54 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.9, 141.4, 136.6, 125.4, 110.9, 105.8, 61.6, 41.6, 36.7, 31.3, 29.8. IR (thin film/NaCl): 3368, 2938, 2873, 1654, 1487, 1459, 1329, 1056, 1008, 920, 885, 800, 733, 681 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{11}H_{14}O_2]^+$: 178.0994; found: 178.0995. $[\alpha]_D^{24}$ +23.4 (*c* 0.29, CH_2Cl_2; 48.6% ee).[11] HPLC: Chiralcel OJ column, 4% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 12.3 min, minor peak t_R = 10.9 min.

1-(2-Hydroxyethyl)-2-phenyl-2-cyclohexene [(+)-20]

R_f = 0.15 (5:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.21 (comp. m, 5 H), 5.92 (t, *J* = 4.2 Hz, 1 H), 3.59 (t, *J* = 6.0 Hz, 2 H), 2.89 (br s, 1 H), 2.21–2.15 (m, 2 H), 1.87–1.43 (comp. m, 7 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6, 141.7, 128.3, 126.5, 126.5, 126.2, 61.2, 36.5, 30.0, 27.3, 26.0, 18.5. IR (thin film/NaCl): 3351, 3021, 2930, 2861, 2832, 1639, 1598, 1493, 1443, 1430, 1058, 1032, 1013, 986, 757, 698 cm^{-1}. HRMS-ES: *m/z* $[M]^+$ calcd for $[C_{14}H_{18}O]^+$: 202.1358; found: 202.1358. $[\alpha]_D^{25}$ +107.2 (*c* 0.050, CH_2Cl_2; 97.0% ee). HPLC: Chiralcel OJ column, 2% EtOH–hexane, 1 mL/min flow rate, major peak t_R = 14.2 min, minor peak t_R = 19.2 min.

Tetrahydrofuran (–)-21

To an oven-dried reaction tube with stir bar was added oven-dried powdered 3 Å MS (120 mg). After cooling, $Pd(TFA)_2$ (4.1 mg, 0.012 mmol), anhyd Na_2CO_3 (52.6 mg, 0.50 mmol), followed by toluene (2.5 mL), pyridine (3.9 mg, 4.0 μL, 0.050 mmol), and alcohol (+)-**12** (25.1 mg, 0.12 mmol). The reaction vessel was then cooled to –78 °C, vacuum evacuated, and purged with O_2 (3×). The reaction was then heated to 80 °C with vigorous stirring under O_2 (1 atm). After 15.5 h, the reaction was complete by TLC analysis. The reaction was cooled to r.t., filtered through silica gel (EtOAc as eluent), and concentrated under reduced pressure to afford tetrahydrofuran (–)-**21** (21.0 mg, 85% yield) as a colorless oil. Further purification by preparative TLC (4:1 hexane–EtOAc as eluent) afforded an analytically pure sample: R_f = 0.62 (4:1 hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.20 (comp. m, 5 H), 6.07 (ddd, *J* = 5.8, 2.4, 2.4 Hz, 1 H), 5.65 (ddd, *J* = 5.8, 2.1, 2.1 Hz, 1 H), 4.07 (ddd, *J* = 8.6, 6.8, 4.3 Hz, 1 H), 3.82 (ddd, *J* = 8.6, 8.6, 6.2 Hz, 1 H), 2.53 (ddd, *J* = 17.3, 2.2, 2.2 Hz, 1 H), 2.34 (ddd, *J* = 17.3, 2.2, 2.2 Hz, 1 H), 1.96 (ddd, *J* = 12.0, 6.1, 4.4 Hz, 1 H), 1.89 (ddd, *J* = 11.9, 8.6, 6.8 Hz, 1 H), 0.69 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.7, 134.6, 133.4, 128.0, 127.0, 126.2, 100.0, 65.9, 51.4, 47.6, 43.6, 25.5. IR (thin film/NaCl): 2956, 1722, 1492, 1448, 1047 cm^{-1}. HRMS-EI: *m/z* $[M]^+$ calcd for $[C_{14}H_{16}O]^+$: 200.1201; found: 200.1203. $[\alpha]_D^{26}$ –16.1 (*c* 1.6, CH_2Cl_2; 86% ee). Chiral GC: G-TA column, 100 °C initial temperature, ramp 1 °C/min, 1 mL/min carrier gas flow, major peak t_R = 28.8 min, minor peak t_R = 29.2 min.