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Enantioselective Construction of Quaternary Carbon Stereocenter via Palladium-Catalyzed Asymmetric Allylic Alkylation of Lactones

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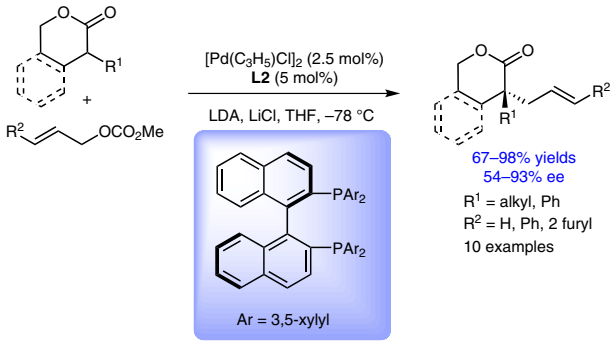

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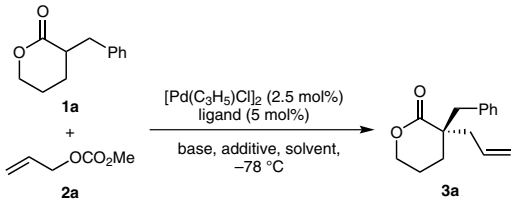
Abstract An efficient and practical method for the synthesis of α,α-disubstituted six-membered lactones was developed. Enantioselective construction of quaternary carbon centers by utilizing Pd-catalyzed asymmetric allylic alkylation proved its feasibility.

Key words palladium, allylic alkylation, asymmetric catalysis, lactones, quaternary carbon

The palladium-catalyzed asymmetric allylic alkylation (AAA) is among the most useful protocols for enantioselective construction of carbon–carbon and carbon–heteroatom bonds.[1] Different kinds of 'hard' carbanions have been used as nucleophile successfully.[2,3] In spite of the fact that the esters are very useful class of compounds in organic synthesis,[4] only a few reports appeared with the use of esters as the precursor of nucleophile in this reaction[2j–k,3e] and only one example was involved in the construction of α-chiral quaternary center with modest enantioselectivity.[2k] In the course of the research on the palladium-catalyzed AAA during recent years,[3,5] we have successfully developed many different types of enolates as nucleophile.[3] In this paper, we would like to report our further studies using α-substituted lactones as pre-nucleophile to construct chiral quaternary center by Pd-catalyzed AAA. Initially, the reaction of 3-benzyltetrahydro-2*H*-pyran-2-one (**1a**) and allyl methyl carbonate (**2a**) was carried out in the presence of catalytic amounts of $[Pd(C_3H_5)Cl]_2$ and (*R*)-BINAP, using LiHMDS as base and LiCl as additive in THF at –78 °C. The reaction afforded the product, 2,2-disubstituted tetrahydro-2*H*-pyran-2-one **3a**, in 79% yield with 77% ee (Table 1, entry 1). Encouraged by this result, influences of the reaction parameters were investigated (Table 1).

The screening of base showed that both yield and ee value significantly decreased when NaHMDS or KHMDS was the base (Table 1, entries 2, 3). The enantioselectivity was improved when LDA was used as base (entry 4 vs. entry 1). Thus, the effect of solvents was explored with LDA as base. It can be seen that THF gave the better results (entry 4) among the various solvents screened, including THF, Et_2O, methyl *tert*-butyl ether (MTBE), toluene, and CH_2Cl_2 (entries 4–8). The effect of additives was also studied (entries 9–15). Both yield and ee value decreased in the absence of LiCl (entry 9 vs. entry 4). In the presence of 2 equivalents of LiCl as additive, the yield increased with comparable ee value (entry 10 vs. entry 4). The yield decreased and the ee value remained the same if CuCl was the additive (entry 11 vs. entry 4). With Lewis base additive such as TMEDA or HMPA, inferior results were obtained (entries 12, 13). Mixed additives such as TMEDA and LiCl or HMPA and LiCl gave superior yields while the ee values were lower than that with LiCl as the only additive (entries 14, 15 vs. entry 4). Based upon these results, a series of chiral ligands (Figure 1) with different electronic and steric factors were screened in THF with LDA as base and LiCl as additive (entries 16–25). When **L2** with much more steric hindrance on P atom was used, both yield and enantioselectivity increased further (entry 16 vs. entry 4) while the reactions using ligands **L3**–**L9** with a biphenylene backbone afforded the product in good yields but with varied lower ee values (entries 17–23). It seems that the ligand **L3** has bigger dihedral angle than that of ligand **L1** and the ee value was lower

Table 1 Optimization of Parameters for the Reaction of **1a** with **2a**[a]



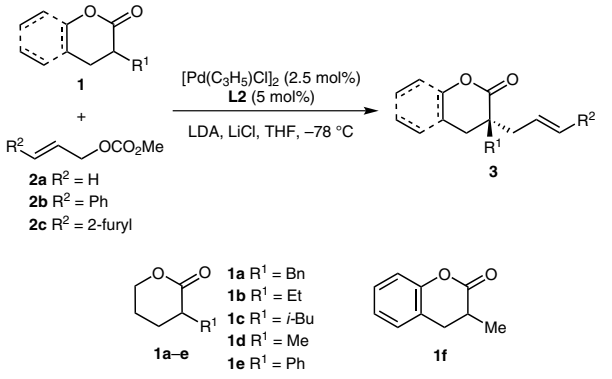
Entry	L*	Base	Solvent	Additive	Yield (%)[b]	ee (%)[c]
1	**L1**	LiHMDS	THF	LiCl	79	77
2	**L1**	NaHMDS	THF	LiCl	15	–6[d]
3	**L1**	KHMDS	THF	LiCl	trace	–
4	**L1**	LDA	THF	LiCl	78	85
5	**L1**	LDA	Et_2O	LiCl	63	50
6	**L1**	LDA	MTBE	LiCl	69	40
7	**L1**	LDA	toluene	LiCl	32	37
8	**L1**	LDA	CH_2Cl_2	LiCl	NP[e]	–
9	**L1**	LDA	THF	none	68	62
10	**L1**	LDA	THF	LiCl[f]	86	87
11	**L1**	LDA	THF	CuCl	69	85
12	**L1**	LDA	THF	TMEDA	49	77
13	**L1**	LDA	THF	HMPA	23	51
14	**L1**	LDA	THF	TMEDA + LiCl	86	80
15	**L1**	LDA	THF	HMPA + LiCl	85	67
16	**L2**	LDA	THF	LiCl	83	90
17	**L3**	LDA	THF	LiCl	82	57
18	**L4**	LDA	THF	LiCl	84	68
19	**L5**	LDA	THF	LiCl	79	81
20	**L6**	LDA	THF	LiCl	91	78
21	**L7**	LDA	THF	LiCl	89	69
22	**L8**	LDA	THF	LiCl	82	80
23	**L9**	LDA	THF	LiCl	82	81
24	**L10**	LDA	THF	LiCl	46	11
25	**L11**	LDA	THF	LiCl	18	67

[a] Reactions were carried out at –78 °C, molar ratio of **1a**/**2a**/$[Pd(C_3H_5)Cl]_2$/**L**/base/additive = 100:120:2.5:5:120:100.
[b] Isolated yields of **3a** is based on **1a**.
[c] Determined by chiral HPLC.
[d] The reversed sequence of peaks by HPLC.
[e] NP: No product.
[f] Two equivalents of LiCl were used as additive.

in the reaction with **L3** as ligand than that using **L1** (entry 17 vs. entry 4). The same trend was observed also in the reactions with ligand **L7** and **L9**; ligand **L7** with bigger dihedral angle than that of ligand **L9**, afforded the product with lower ee value (entry 21 vs. entry 23). By using ligand **L10**, the reaction could proceed only in moderate yield with low enantioselectivity (entry 24). By using Trost's ligand **L11**, the reaction could provide only in low yield with moderate enantioselectivity (entry 25).

Under the optimized conditions, the substrate scope was explored and the results are summarized in Table 2. Generally the reactions proceeded smoothly for all α-substituted six-membered lactones to produce the corresponding lactones with α-chiral quaternary carbon in 67–98% yields with 54–94% ee, in spite of the substituent at α-position of carbonyl being benzyl (Table 2, entry 1), alkyl (entries 2–4), or phenyl (entry 5). The reaction was also suitable for 3-methylchroman-2-one (**1f**) (entry 6). With allyl substrate **2b**, it also afforded the corresponding products **3g** and **3j** with excellent ee values (entries 7, 10). Only reactions using **1e** with a phenyl as substituent at α-position delivered the products **3h** and **3i** with moderate ee values (entries 8, 9).

Table 2 Substrate Scope for Pd-Catalyzed AAA[a]



Entry	1	2	Product	Yield (%)[b]	ee (%)[c]
1	**1a**	**2a**	**3a**	83	90
2	**1b**	**2a**	**3b**	79	89
3	**1c**	**2a**	**3c**	82	75
4	**1d**	**2a**	**3d**	89	92
5	**1e**	**2a**	**3e**	80	48
6	**1f**	**2a**	**3f**	98	94
7	**1a**	**2b**	**3g**	78	87
8	**1e**	**2b**	**3h**	90	54
9	**1e**	**2c**	**3i**	88	59
10	**1d**	**2b**	**3j**	67	93

[a] Reactions were carried out at –78 °C, molar ratio of **1**/**2**/$[Pd(C_3H_5)Cl]_2$/**L2**/Base/Additive = 100:120:2.5:5:120:100.
[b] Isolated yields of **3** are based on **1**.
[c] Determined by chiral HPLC or GC.

The absolute configuration of **3a** was determined as *R* by comparing the sign of the optical rotation of the product with that reported in the literature.[6]

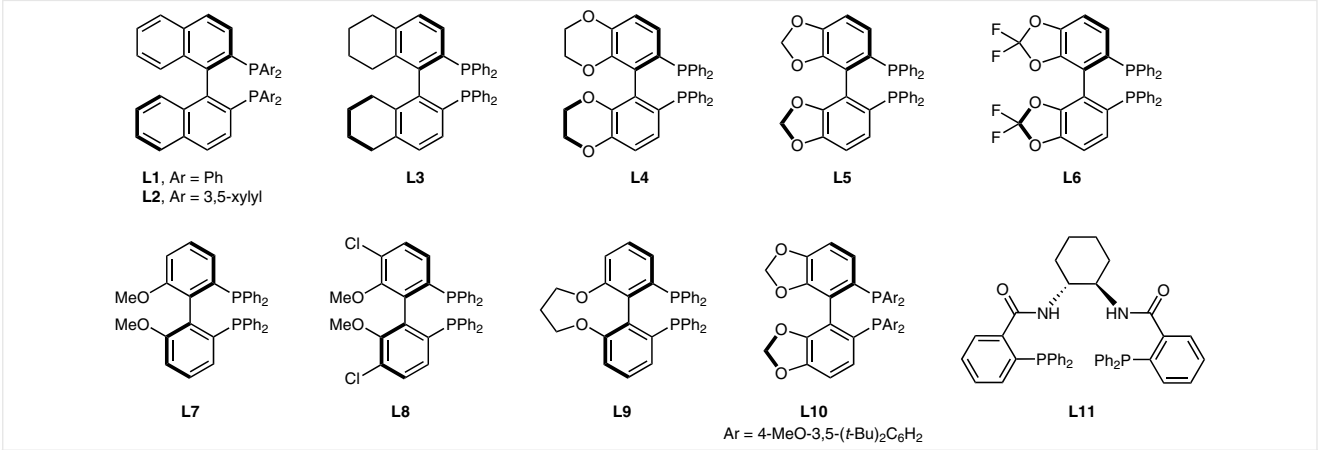


Figure 1 The structure of ligands **L1**–**L11**

In summary, we have realized the Pd-catalyzed asymmetric allylic alkylation of α-substituted six-membered lactones with allyl methyl carbonates in good yields with good enantioselectivities. The chiral quaternary carbon center has also been constructed successfully during the reaction. Further investigations to extend the reaction scope and applications in organic synthesis are in progress.

All the experiments were carried out in flame-dried glassware under a dry argon atmosphere. The solvents were purified and dried over appropriate drying agents and distilled under argon prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as internal standard on a Bruker Avance 300 MHz, 400 MHz, or 600 MHz spectrometers at r.t. HRMS analyses were carried out using the Finnigan MAT 8430 spectrometer.

The synthesis of 3-substituted tetrahydro-2*H*-pyran-2-ones **1a**–**e** is provided in the Supporting Information.

α,α-Disubstituted Esters 3; General Procedure

α-Substituted ester **1** (0.2 mmol), LiCl (8.4 mg, 0.2 mmol), and THF (1.0 mL) were added to a dry Schlenk tube. LDA (1.0 M in THF, 0.24 mL, 0.24 mmol) was then added dropwise and the contents were stirred for 0.5 h at –78 °C. In a separate flask, $[Pd(C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol) and ligand **L2** (7.3 mg, 0.01 mmol) were dissolved in THF (1.0 mL) and stirred at r.t. for 0.5 h, which was then added to the above enolate solution at –78 °C, followed by the addition of respective allyl methyl carbonate **2** (28 mg, 0.2 mmol). The resulting mixture was stirred at –78 °C. After completion (monitored by TLC), the reaction mixture was quenched by sat. aq NH_4Cl and extracted with Et_2O (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, PE–EtOAc, 10:1) to afford the desired product.

3-Allyl-3-benzyltetrahydro-2*H*-pyran-2-one (3a)

Yield: 38.2 mg (83%); slightly yellow oil; $[\alpha]_D^{26}$ +13.2 (*c* = 0.94 in $CHCl_3$).

HPLC: Chiralpak AD-H; hexane–*i*-PrOH (95:5), flow rate = 0.7 mL/min, 230 nm, t_R = 11.5 min, 12.3 min; ee = 90%.

IR (film): 2963 (w), 1718 (m), 1454 (w), 1260 (m), 1098 (s), 1018 (s), 798 (s), 703 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38–1.47 (m, 1 H), 1.64–1.73 (m, 1 H), 1.79–1.82 (m, 2 H), 2.18 (dd, *J* = 13.2, 8.4 Hz, 1 H), 2.60 (d, *J* = 13.2 Hz, 1 H), 2.68 (dd, *J* = 13.2, 6.4 Hz, 1 H), 3.30 (d, *J* = 13.2 Hz, 1 H), 3.90–3.95 (m, 1 H), 4.11–4.17 (m, 1 H), 5.12–5.19 (m, 2 H), 5.75–5.85 (m, 1 H), 7.17–7.31 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 27.8, 45.0, 45.5, 47.5, 70.05, 119.4, 126.8, 128.3, 130.3, 133.1, 137.0, 175.2.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{19}O_2$: 231.1385; found: 231.1383.

3-Allyl-3-ethyltetrahydro-2*H*-pyran-2-one (3b)

Yield: 26.5 mg (79%); slightly yellow oil; $[\alpha]_D^{26}$ +3.0 (*c* = 0.95 in $CHCl_3$).

Chiral GC: RESTEK Rt-βDEX$_{cst}$ column, 30 m × 0.25 mm × 0.12 μm [carrier gas: N_2, injector temperature: 250 °C, split ratio: 30, constant column flow: 10 psi, column temperature 60 °C (5 min), 60–150 °C (2 °C/min), 150 °C (5 min), 150–180 °C (3 °C/min), FID detector temperature: 250 °C], t_R = 56.0 min, 56.4 min; ee = 89%.

IR (film): 2962 (w), 2927 (w), 1729 (m), 1462 (w), 1260 (s), 1092 (s), 1019 (s), 798 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.6 Hz, 3 H), 1.52–1.61 (m, 1 H), 1.77–1.88 (m, 5 H), 2.20 (dd, *J* = 13.6, 5.6 Hz, 1 H), 2.54 (dd, *J* = 13.6, 8.4 Hz, 1 H), 4.29–4.32 (m, 2 H), 5.10–5.14 (m, 2 H), 5.71–5.82 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.7, 21.2, 28.6, 32.2, 43.6, 46.2, 70.1, 118.9, 133.5, 175.4.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{17}O_2$: 169.1229; found: 169.1225.

3-Allyl-3-isobutyltetrahydro-2*H*-pyran-2-one (3c)

Yield: 32.1 mg (82%); slightly yellow oil; $[\alpha]_D^{26}$ +7.1 (*c* = 0.85 in $CHCl_3$).

Chiral GC: VARIAN CHIRASIL- DEXCB column, 30 m × 0.25 mm × 0.12 μm [carrier gas: N_2, injector temperature: 250 °C, split ratio: 30, constant column flow: 10 psi, column temperature 60 °C (5 min), 60–150 °C (2 °C/min), 150 °C (2 min), 150–180 °C (3 °C/min), FID detector temperature: 250 °C], t_R = 47.6 min, 47.9 min; ee = 75%.

IR (film): 2956 (m), 2927 (w), 2871 (w), 1723 (s), 1396 (w), 1240 (m), 1135 (s), 917 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.4 Hz, 3 H), 0.93 (d, *J* = 6.4 Hz, 3 H), 1.41–1.47 (m, 1 H), 1.73–1.93 (m, 6 H), 2.18 (dd, *J* = 13.6, 8.0 Hz, 1 H), 2.52 (dd, *J* = 13.6, 6.4 Hz, 1 H), 4.32–4.35 (m, 2 H), 5.09–5.15 (m, 2 H), 5.71–5.81 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 23.3, 24.6, 24.8, 28.5, 45.1, 45.4, 47.6, 70.1, 119.1, 133.4, 175.8.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{21}O_2$: 197.1542; found: 197.1540.

3-Allyl-3-methyltetrahydro-2*H*-pyran-2-one (3d)

Yield: 27.4 mg (89%); colorless oil; $[\alpha]_D^{26}$ +3.3 (*c* = 1.00 in $CHCl_3$).

Chiral GC: VARIAN CHIRASIL-DEXCB column, 30 m × 0.25 mm × 0.12 µm [carrier gas: N_2, injector temperature: 250 °C, split ratio: 30, constant column flow: 10 psi, column temperature 60 °C (5 min), 60–150 °C (3 °C/min), 150 °C (5 min), 150–180 °C (3 °C/min), FID detector temperature: 250 °C], t_R = 31.2 min, 31.5 min; ee = 92%.

HPLC: Chiralpak AD-H; *i*-PrOH–hexane (3:97), flow rate: 0.7 mL/min, 214 nm, t_R (minor) = 12.8 min, t_R (major) = 13.5 min; ee = 91%.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H), 1.57–1.66 (m, 1 H), 1.84–1.97 (m, 3 H), 2.20 (dd, *J* = 13.6, 8.0 Hz, 1 H), 2.54 (dd, *J* = 13.2, 6.8 Hz, 1 H), 4.25–4.39 (m, 2 H), 5.10–5.16 (m, 2 H), 5.70–5.81 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 26.3, 31.6, 42.2, 44.5, 70.4, 102.5, 119.1, 133.2, 176.1.

3-Allyl-3-phenyltetrahydro-2*H*-pyran-2-one (3e)

Yield: 34.6 mg (80%); colorless oil; $[\alpha]_D^{26}$ +81.4 (*c* = 0.99 in $CHCl_3$).

HPLC: Chiralpak OJ-H; hexane–*i*-PrOH (90/10), flow rate = 0.7 mL/min, 214 nm, t_R = 18.3 min, 20.0 min; ee = 48%.

IR (film): 2963 (w), 1729 (s), 1446 (w), 1261 (m), 1151 (m), 1094 (s), 798 (m), 701 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.69–1.88 (m, 1 H), 1.93–2.01 (m, 1 H), 2.33–2.39 (m, 1 H), 2.47 (dd, *J* = 13.6, 7.6 Hz, 1 H), 2.69 (dd, *J* = 13.6, 6.8 Hz, 1 H), 3.90–3.96 (m, 1 H), 4.09–4.15 (m, 1 H), 4.94–5.00 (m, 2 H), 5.54–5.65 (m, 1 H), 7.19–7.31 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 27.9, 45.9, 51.1, 67.8, 118.8, 126.0, 127.3, 128.8, 133.7, 140.4, 174.2.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{17}O_2$: 217.1229; found: 217.1228.

3-Allyl-3-methylchroman-2-one (3f)

Yield: 39.6 mg (98%); slightly yellow oil; $[\alpha]_D^{26}$ –6.9 (*c* = 0.05 in $CHCl_3$).

HPLC: Chiralpak OJ-H; hexane–*i*-PrOH (95/5), flow rate = 0.5 mL/min, 214 nm, t_R = 13.4 min, 14.5 min; ee = 94%.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (s, 3 H), 2.28–2.40 (m, 2 H), 2.75 (d, *J* = 16.0 Hz, 1 H), 2.91 (d, *J* = 16.0 Hz, 1 H), 5.03 (d, *J* = 16.8 Hz, 1 H), 5.14 (d, *J* = 10.4 Hz, 1 H), 5.73–5.84 (m, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 7.07 (d, *J* = 7.2 Hz, 1 H), 7.14 (d, *J* = 6.4 Hz, 1 H), 7.23–7.27 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2, 35.4, 40.4, 40.8, 116.0, 119.6, 121.6, 124.3, 128.1, 128.5, 132.2, 151.2, 172.6.

3-Benzyl-3-cinnamyltetrahydro-2*H*-pyran-2-one (3g)

Yield: 47.7 mg (78%); colorless oil; $[\alpha]_D^{26}$ –5.2 (*c* = 0.97 in $CHCl_3$).

HPLC: Chiralpak PA-2; hexane–*i*-PrOH (95/5), flow rate = 0.7 mL/min, 214 nm, t_R = 42.2 min, 46.3 min; ee = 87%.

IR (film): 2959 (m), 1719 (s), 1451 (m), 1263 (m), 1115 (s), 972 (m), 801 (m), 700 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.45–1.49 (m, 1 H), 1.65–1.69 (m, 1 H), 1.84–1.87 (m, 2 H), 2.31–2.37 (m, 1 H), 2.68 (d, *J* = 13.2 Hz, 1 H), 2.86–2.92 (m, 1 H), 3.32 (d, *J* = 13.6 Hz, 1 H), 3.92–3.94 (m, 1 H), 4.10–4.14 (m, 1 H), 6.18–6.21 (m, 1 H), 6.47 (d, *J* = 15.6 Hz, 1 H), 7.19–7.35 (m, 10 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 28.0, 44.4, 45.8, 48.1, 70.2, 124.7, 126.2, 126.9, 127.5, 128.4, 128.6, 130.4, 134.3, 136.9, 137.0, 175.5.

HRMS: *m*/*z* $[M + NH_4]^+$ calcd for $C_{21}H_{26}NO_2$: 324.1958; found: 324.1961.

3-Cinnamyl-3-phenyltetrahydro-2*H*-pyran-2-one (3h)

Yield: 52.6 mg (90%); colorless oil; $[\alpha]_D^{26}$ +85.8 (*c* = 0.98 in $CHCl_3$).

HPLC: Chiralpak PC-2; hexane–*i*-PrOH (60/40), flow rate = 0.5 mL/min, 230 nm, t_R = 16.1 min, 17.1 min; ee = 54%.

IR (film): 2964 (m), 1714 (m), 1448 (w), 1262 (s), 1094 (s), 1023 (s), 802 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.02–1.89 (m, 2 H), 2.03–2.12 (m, 1 H), 2.44–2.50 (m, 1 H), 2.63–2.69 (m, 1 H), 2.90–2.96 (m, 1 H), 3.97–4.00 (m, 1 H), 4.16–4.20 (m, 1 H), 6.06–6.10 (m, 1 H), 6.36 (d, *J* = 16.0 Hz, 1 H), 7.19–7.31 (m, 10 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 27.9, 45.2, 51.7, 67.9, 125.4, 126.0, 126.2, 127.3, 127.4, 128.5, 129.0, 133.9, 137.2, 140.4, 174.3.

HRMS: *m*/*z* $[M + NH_4]^+$ calcd for $C_{20}H_{24}NO_2$: 310.1802; found: 310.1805.

(*E*)-3-[3-(Furan-2-yl)allyl]-3-phenyltetrahydro-2*H*-pyran-2-one (3i)

Yield: 49.6 mg (88%); slightly yellow oil; $[\alpha]_D^{26}$ +62.2 (*c* = 0.99 in $CHCl_3$).

HPLC: Chiralpak PC-2; hexane–*i*-PrOH (60/40), flow rate = 0.5 mL/min, 230 nm, t_R = 12.9 min, 14.1 min; ee = 59%.

IR (film): 2963 (m), 2906 (s), 1411 (s), 1259 (m), 1081 (s), 1014 (s), 794 (s), 701 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.80–1.92 (m, 2 H), 2.06–2.11 (m, 2 H), 2.44–2.50 (m, 1 H), 2.63 (dd, *J* = 14.0, 7.2 Hz, 1 H), 2.63 (dd, *J* = 14.0, 8.4 Hz, 1 H), 3.97–4.00 (m, 1 H), 4.16–4.23 (m, 1 H), 5.99–6.05 (m, 1 H), 6.13–6.21 (m, 2 H), 6.32–6.34 (m, 1 H), 7.29–7.40 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.5, 27.9, 45.0, 51.7, 67.9, 106.9, 111.1, 122.4, 124.1, 126.0, 127.4, 129.0, 140.3, 141.6, 152.7, 174.2.

HRMS: *m*/*z* $[M + NH_4]^+$ calcd for $C_{18}H_{22}NO_3$: 300.1594; found: 300.1596.

3-Cinnamyl-3-methyltetrahydro-2*H*-pyran-2-one (3j)

Yield: 30.8 mg (67%); colorless oil; $[\alpha]_D^{26}$ +0.58 (*c* = 1.07 in $CHCl_3$).

HPLC: Chiralpak AD-H; *i*-PrOH–hexane (5:95); flow rate: 0.7 mL/min, 214 nm, t_R = 15.7 min, 17.7 min; ee = 93%.

HPLC: Chiralpak PC-2; hexane–*i*-PrOH (60/40), flow rate = 0.5 mL/min, 230 nm, t_R = 15.7 min, 17.7 min.

IR (film): 2962 (m), 1725 (w), 1258 (s), 1076 (s), 1011 (s), 789 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 3 H), 1.64–1.68 (m, 1 H), 1.87–1.99 (m, 3 H), 2.36 (dd, *J* = 14.0, 7.2 Hz, 1 H), 2.74 (dd, *J* = 13.6, 8.4 Hz, 1 H), 4.28–4.36 (m, 2 H), 6.15–6.18 (m, 1 H), 6.46 (d, *J* = 16.0 Hz, 1 H), 7.22–7.35 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 26.5, 31.8, 42.8, 43.8, 70.5, 124.9, 126.2, 127.4, 128.5, 134.1, 137.1, 176.2.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{19}O_2$: 231.1380; found: 231.1385.

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Supporting Information

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