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CONSTRUCTION OF CHIRAL QUATERNARY CARBON CENTERS *VIA* PALLADIUM-CATALYZED ASYMMETRIC DECONJUGATIVE ALLYLATION

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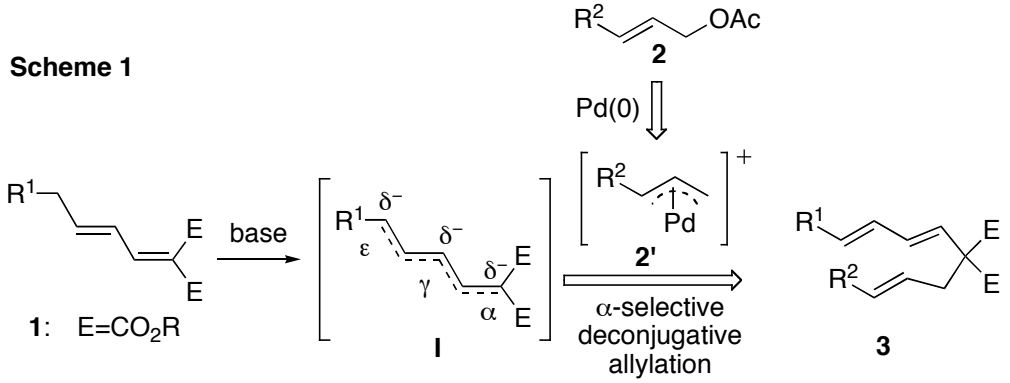
Abstract – A Pd(0)-catalyzed asymmetric deconjugative allylation of various Knoevenagel products and allylic compounds was investigated. It was found that various compounds, having a quaternary carbon center directly attached to sp^2-carbon centers including a 1,3-diene moiety, could be synthesized through this methodology, although the yield and enantiomeric excess varied from low to modest depending on the structure of substrates and the reaction conditions.

INTRODUCTION

Deconjugative alkylation of alkylidenemalonate[1] or alkenylidenemalonate[2] is a useful method for the synthesis of a compound having a quaternary carbon center that is attached to sp^2-carbon centers. We have recently reported a novel Pd(0)-catalyzed deconjugative allylation of alkenylidenemalonates **1** (Scheme 1).[3] That is, reactions of dimethyl 2-((*E*)-but-2-enylidene)malonate derivatives **1** with various allylic acetates **2** in the presence of a Pd(0) complex and a base proceeded to give the corresponding α-allylation products **3** in good yields in a stereoselective manner.

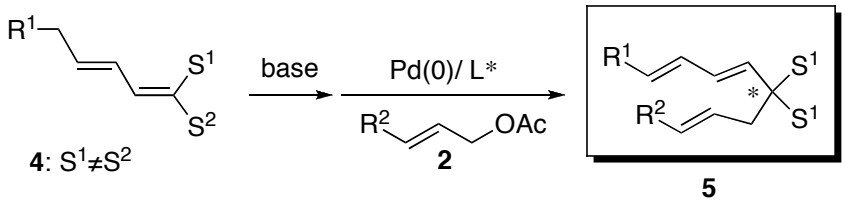
Scheme 1



This paper is dedicated to Prof. Dr. Ryoji Noyori on the occasion of his 70th birthday.

In this context, we envisaged that this reaction could be used in the synthesis of **5**, which has a chiral quaternary carbon center, if the reaction can proceed in the case of the substrate **4** ($S^1 \neq S^2$) using a Pd(0) complex in the presence of a chiral ligand (Scheme 2).

Scheme 2. Plan for Asymmetric Deconjugative Allylation

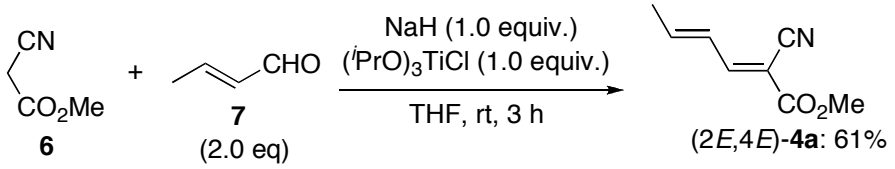


A number of biologically active substances occurring from nature contain various types of chiral quaternary carbon centers in their frameworks, and construction of those chiral centers has been important and challenging for synthetic organic chemists.[4,5] Herein we report a construction of chiral quaternary carbon centers via Pd(0)-catalyzed asymmetric deconjugative allylation of **4** with allylic acetates.

RESULTS AND DISCUSSION

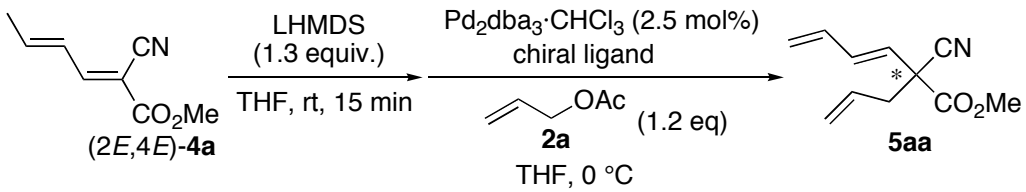
Initially, we investigated asymmetric deconjugative allylation of (2*E*,4*E*)-**4a**, which was stereoselectively synthesized via Knoevenagel condensation of methyl cyanoacetate **6** and aldehyde **7** using NaH and $(^i\text{PrO})_3\text{TiCl}$ according to the literature[6] (Scheme 3).

Scheme 3. Synthesis of Substrate (2*E*,4*E*)-**4a**



The reaction of lithium enolate of **4a**, which was prepared by treatment of **4a** with LHMDS at room temperature for 15 minutes, and allyl acetate **2a** using $Pd_2dba_3{\cdot}CHCl_3$ (2.5 mol%) and BINAPO[7a] (5 mol%) in THF at 0 °C gave the product **5aa** in 49% yield. The enantiomeric excess of **5aa** was determined by HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane-2-propanol, 95:5) to be 7% (Table 1, run 1). An asymmetric deconjugative allylation of **4a** utilizing DTBM-SEGPHOS[7b], ^{i}Pr-phox[7c], or BPPFA[7d] as a chiral ligand was investigated under similar conditions, but only low enantiomeric excesses were obtained (runs 2-4). On the other hand, the reaction of **4a** and **2a** using **8**[7e] as a chiral ligand produced **5aa** in 57% yield and 29% ee (run 5). The reaction using **9**[7e] or **10**[7f] as a chiral ligand was very slow, and the desired product **5aa** was obtained in 46% yield and 30% ee or in 27% yield and 9% ee after 48 or 121 hours, respectively (runs 6 and 7).

Table 1. Asymmetric Deconjugative Allylation of (2*E*,4*E*)-**4a** with Allyl Acetate Using Various Chiral Ligands



run	ligand	time (h)	yield (%)	ee (%)
1	BINAPO[a]	4	49	7
2	DTBM-SEGPHOS[b]	3	48	7
3	*i*Pr-phox[a]	85	48	1
4	BPPFA[a]	2	36	3
5	**8**[b]	3	57	29
6	**9**[a]	48	46[c]	30
7	**10**[a]	121	27	9

[a] 5 mol% of ligand was used.
[b] 7.5 mol% of ligand was used.
[c] **4a** was recovered in 6%.

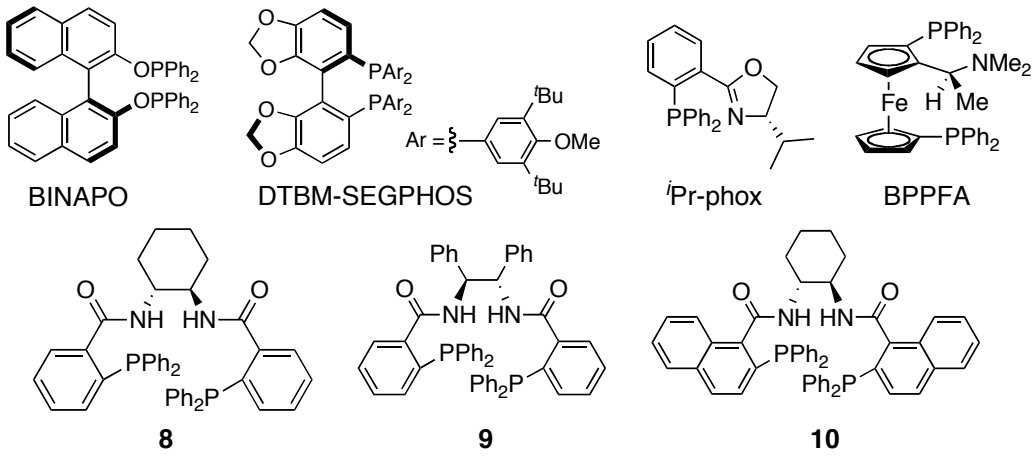
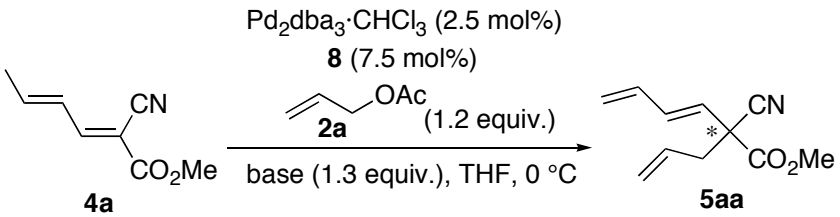


Table 2. Asymmetric Deconjugative Allylation of **4a** Using Various Bases



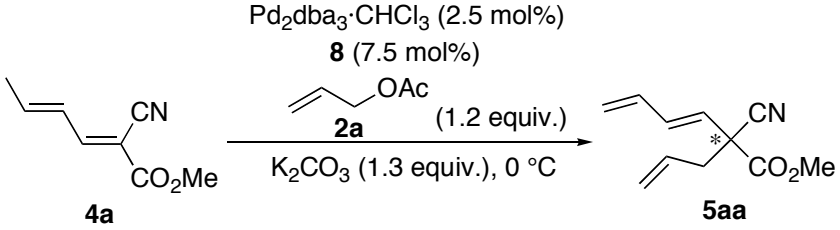
run	base	time (h)	yield (%)	ee (%)
1[a]	NaHMDS	3	25	35
2[a]	KHMDS	5	12	36
3	DBU	1.5	38	25
4	K_2CO_3	20	60	28
5[a]	Cs_2CO_3	15	59	28
6	none	120	57	27

[a] 5 mol% of **8** was used.

Thus, effects of bases were investigated in the reaction of **4a** and **2a** using **8** as a ligand, and the results are summarized in Table 2. The reaction using NaHMDS or KHMDS as a base slightly improved the enantiomeric excess of **5aa**, compared to that using LHMDS (Table 1, run 5), but the yield of **5aa** was decreased (Table 2, runs 1 and 2). The use of an organic base such as DBU was not so effective (run 3), while both the yield and enantiomeric excess of **5aa** in the reaction using inorganic bases such as K_2CO_3 and Cs_2CO_3 were comparable to those in the reaction using LHMDS (runs 4 and 5), although the reaction rate was relatively slow. It is interesting that the reaction of **4a** and **2a** without bases also occurred under similar conditions to give **5aa** in 57% yield and 27% ee, although the reaction rate was very slow (run 6).

The fact that inorganic bases instead of LHMDS could be used in this reaction enabled us to carry out the reaction in various solvents. Thus, solvent effects were investigated in the reaction of **4a** and **2a** using **8** in the presence of K_2CO_3 as a base, and the results are summarized in Table 3.

Table 3. Solvent Effects in Asymmetric Deconjugative Allyaltion of **4a**



run	solvent	time (h)	yield (%)	ee (%)
1	MeCN	70	2	1
2	CH_2Cl_2	20	52	23
3	CPME	52	60	39
4	Et_2O	72	46	43
5	toluene	24	68	48

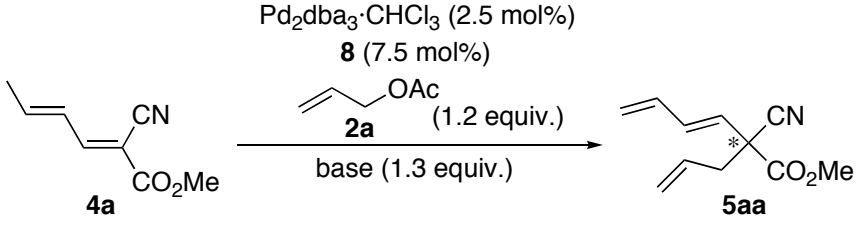
CPME=cyclopentyl methy ether

Polar solvents such as MeCN retarded the reaction, giving a trace amount of **5aa** as an almost racemic form (run 1). The use of CH_2Cl_2 was tolerated in the reaction to give **5aa** in 52% yield and 23% ee (run 2). Ethers such as CPME and Et_2O were more effective than THF, and the enantiomeric excesses of **5aa** were increased to 39% and 43%, respectively (runs 3 and 4). Finally, we found that the use of toluene gave the best result, producing **5aa** in 68% yield and 48% ee (run 5).

Next, the reaction of **4a** and **2a** was carried out at a lower temperature with the intention of improving the enantiomeric excess of the product. As expected, the reaction of **4a** and **2a** using K_2CO_3 as a base at -20 °C gave **5aa** in 46% and 56% ee (Table 4, run 1). When the reaction was carried out at -50 °C, the enantiomeric excess of **5aa** was slightly improved to 60%, but the yield was greatly decreased,

presumably due to the insolubility of K_2CO_3 at a lower temperature (run 2). Thus, the addition of 18-crown-6 to the reaction mixture at -50 °C, which might help K_2CO_3 dissolve in toluene at a lower temperature, improved the enantiomeric excess up to 68%, although the yield was still low (run 3). On the other hand, since the reaction of **4a** and **2a** using LHMDS as a base in toluene gave no products (run 4), THF was used as a solvent in these reaction conditions. When the reaction was carried out at -20 °C, the yield and enantiomeric excess of **5aa** were improved to 71% and 36% (run 5), compared to those in the above-mentioned reaction at 0 °C (cf. Table 1, run 5). Further lowering of the temperature did not affect the yield and enantiomeric excess, and the reaction at -50 °C gave **5aa** in almost the same yield and enantiomeric excess as those when the reaction was carried out at -20 °C (run 6).

Table 4. Asymmetric Deconjugative Allylation of **4a** at Lower Temperature

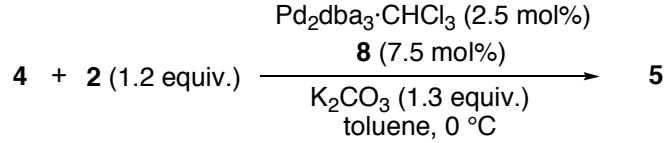


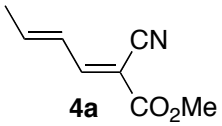
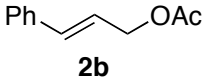
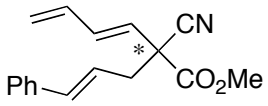
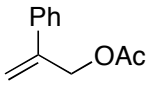
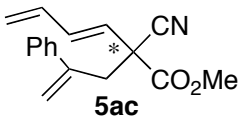
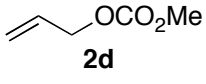
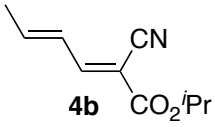
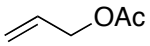
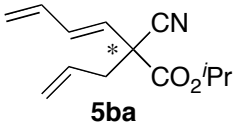
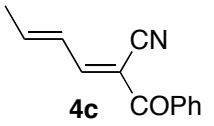
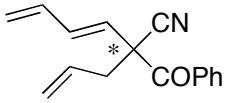
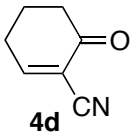
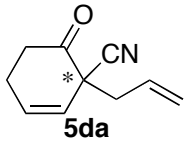
run	base	solvent	temp. (°C)	time (h)	yield (%)	ee (%)
1	K_2CO_3	toluene	-20	120	46	56
2	K_2CO_3	toluene	-50	75	3[a]	60
3	K_2CO_3[b]	toluene	-50	48	16	68
4	LHMDS	toluene	0	17	—	—
5	LHMDS	THF	-20	3	71	36
6	LHMDS	THF	-50	3	71	37

[a] **4a** was recovered in 22%.
[b] 18-Crown-6 (1.3 equiv.) was added.

Thus, the scope and limitations for substrates **4** and allylic compounds **2** were investigated in the reaction in toluene using K_2CO_3 as a base at 0 °C, and the results are summarized in Table 5. The reaction of **4a** and **2b**, having a phenyl group at the C-3 position, gave the corresponding product **5ab** in 19% yield and 24% ee (run 1), while the reaction of **4a** and **2c**, having a phenyl group at the C-2 position, gave the corresponding product **5ac** in 45% yield and 7% ee (run 2), indicating that the structure of the allylic compound affected the yield and enantiomeric excess of the product. Allyl carbonate **2d** was applicable in the reaction, and **5aa** was obtained in 25% yield and 43% ee in the reaction with **4a** (run 3). In this reaction, bases are not necessary because MeO^- would be formed via oxidative addition of **2d** to Pd(0) complex and operate as a base. Thus, it is noteworthy that **5aa** was obtained in almost the same enantiomeric excess with that in the reaction of **4a** and **2a** in the presence of K_2CO_3 (cf. Table 3, run 5), although the yield was lower. The reaction of (2*E*,4*E*)-**4b** and **2a** gave the corresponding product **5ba** in 67% yield and 39% ee (run 4).

Table 5. Scope and Limitations of Asymmetric Deconjugative Allylation



run	substrate **4**	allylic compound **2**	time (h)	product	yield (%)	ee (%)
1	 **4a**	 **2b**	66	 **5ab**	19	24[a]
2	**4a**	 **2c**	63	 **5ac**	45	7[a]
3[b]	**4a**	 **2d**	164	**5aa**	25	43
4	 **4b**	 **2a**	24	 **5ba**	67	39[c]
5	 **4c**	**2a**	6	 **5ca**	19	2[a]
6	 **4d**	**2a**	9	 **5da**	40	5[a]

[a] The ees of the products **5ab**, **5ac**, **5ca**, and **5da** were determined by HPLC analysis (**5ab**: DAICEL CHIRALPAK AD-H, hexane-2-propanol, 95:5; **5ac**: DAICEL CHIRALCEL OJ-H, hexane-2-propanol, 9:1; **5ca**: DAICEL CHIRALCEL OJ-H, hezane-2-propanol, 95:5; **5da**: DAICEL CHIRALPAK AS-H, hexane-2-propanol, 95:5).

[b] The reaction was carried out without K_2CO_3.

[c] The ee of **5ba** was determined after conversion to **5aa**.

The substrate (2*E*,4*E*)-**4c**, having a ketone moiety, was not suitable for the reaction, giving **5ca** in a low yield as an almost racemic form. Cyclic substrate **4d**[8] was tolerated in the reaction, and the reaction with **2a** gave the corresponding product **5da** in 40% yield, although the enantiomeric excess was relatively low.

In summary, a Pd(0)-catalyzed asymmetric deconjugative allylation of various Knoevenagel products and allylic compounds was investigated. It was found that various compounds, having a quaternary carbon center directly attached to sp^2-carbon centers including a 1,3-diene moeity, could be synthesized through

this methodology, although the yield and enantiomeric excess varied from low to modest depending on the structure of substrates and the reaction conditions.

EXPERIMENTAL

All manipulations were performed under an argon atmosphere. THF and toluene were purified using Glass Contour Solvent Purification System. Solvents were distilled from sodium-benzophenone (Et_2O and CPME) CaH_2 (DMF and CH_2Cl_2), or P_2O_5-CaH_2 (MeCN), respectively. All other solvents and reagents were purified when necessary by standard procedures. Column chromatography was performed on silica gel 60 (Merck, 70-230 mesh), and flash chromatography on silica gel (Meck, 230-400 mesh) with the indicated solvent as eluent. IR spectra were obtained on a Jasco FT/IR-460 plus, and ^{1}H NMR and ^{13}C NMR spectroscopy were carried out on Jeol EX270, Jeol AL400 NMR spectromerter, or Jeol ECA500 NMR. Mass spectra were obtained on Shimadzu GCMS-QP5050A, Jeol JMS-FAB mate, or JMS-HX110. Optical rotation was measured on a JASCO P-1030.

(2*E*,4*E*)-Methyl 2-cyanohexa-2,4-dienoate (4a) and (2*E*,4*E*)-Isopropyl 2-cyanohexa-2,4-dienoate (4b).

To a suspension of NaH (60% dispersion in mineral oil, 720 mg, 18 mmol) in THF (50 mL) was added methyl cyanoacetate (**6**) (1.6 mL, 18 mmol) at 0 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added (^{i}PrO)$_3$TiCl (1.0 *M* hexane solution, 18.0 mL, 18 mmol) at -78 °C, and the mixture was stirred at the same temperature for 1 h. To the mixture was added aldehyde **7** (3.0 mL, 36 mmol) at -78 °C, and the mixture was warmed to rt and stirred for 3 h. To the mixture was added 10% HCl aq. at 0 °C, and the mixture was extracted with Et_2O. The combined organic layer was washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/CPME, 10:1, 5:1) to afford **4a** (1.65 g, 61%) as a colorless solid along with **4b** (585 mg, 15%) as a colorless oil.

4a: mp 56-57 °C (recrystallized from hexane, white needles); Ir (Nujol) 2226, 1739, 1635, 1590, 1250 cm^{-1}; ^{1}H NMR (270 MHz, C_6D_6) δ 1.18 (dd, *J* = 6.9, 1.3 Hz, 3 H), 3.27 (s, 3 H), 5.57 (dq, *J* = 14.9, 6.9 Hz, 1 H), 6.39 (ddq, *J* = 14.9, 11.9, 1.3 Hz, 1 H), 7.50 (d, *J* = 11.9 Hz, 1 H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 19.4, 52.9, 102.9, 114.1, 127.8, 150.1, 155.9, 162.7; LRMS (EI) *m/z* 151 (M^+), 136, 119, 92, 65, 39; HRMS (EI) calcd for $C_8H_9NO_2$ 151.0633, found 151.0636. Anal. Calcd for $C_8H_9NO_2$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.55; H, 5.83; N, 9.22.

4b: Ir (neat) 2225, 1719, 1634, 1587, 1251 cm^{-1}: ^{1}H NMR (500 MHz, C_6D_6) δ 0.99 (d, *J* = 6.3 Hz, 6 H), 1.16 (dd, *J* = 6.9, 1.7 Hz, 3 H), 4.98 (qq, *J* = 6.3, 6.3 Hz, 1 H), 5.54 (dq, *J* = 14.9, 6.9 Hz, 1 H), 6.41 (ddq, *J* = 14.9, 11.5, 1.7 Hz, 1 H), 7.57 (d, *J* = 11.5 Hz, 1 H): ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 19.5, 21.7, 70.2,

104.0, 114.3, 127.9, 149.5, 155.5, 161.8; LRMS (EI) *m/z* 179 (M^+), 137, 120, 93, 66, 43, 39; HRMS (EI) calcd for $C_{10}H_{13}NO_2$ 179.0946, found 179.0948.

(2*E*,4*E*)-2-Benzoylhexa-2,4-dienenitrile (4c).

A solution of benzoylacetonitrile (500 mg, 3.4 mmol), aldehdye **7** (0.28 mL, 3.4 mmol),, and piperidine (6.8 mL, 0.068 mmol) in benzene (3.4 mL) was stirred at rt for 4 h. The mixture was diluted with Et_2O, and the solution was washed with 10% HCl aq. and brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/AcOEt, 9:1) to afford **4c** as a colorless solid, which was recrystallized from CH_2Cl_2/hexanane to give **4c** (71 mg, 11%) as a yellowish needles: mp 86-87 °C; Ir (Nujol) 2212, 1664, 1617, 1595, 1551, 715 cm^{-1}; ^1H NMR (270 MHz, C_6D_6) δ 1.20 (dd, *J* = 6.9, 1.6 Hz, 3 H), 5.54 (dq, *J* = 14.5, 6.9 Hz, 1 H), 6.52 (ddq, *J* = 14.5, 11.2, 1.6 Hz, 1 H), 6.95-7.09 (m, 3 H), 7.35 (d, *J* = 11.2 Hz, 1 H), 7.73-7.77 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 110.3, 115.6, 128.3, 128.5, 128.9, 133.1, 136.0, 150.7, 156.6, 188.2.; LRMS (EI) *m/z* 197 (M^+), 182, 105, 77, 51; HRMS (EI) calcd for $C_{13}H_{11}NO$ 197.0841, found 197.0840.

General procedure for asymmetric deconjugative allylation in toluene by Pd_2dba_3·$CHCl_3$ in the presence of chiral ligand 8 using K_2CO_3 as a base.

A suspension of Pd_2dba_3·$CHCl_3$ (2.5 mol% to the substrate **4**), ligand **8** (7.5 mol% to **4**), and K_2CO_3 (1.3 equiv. to **4**) in degassed toluene (0.016 *M* to Pd complex) was stirred at rt for 15 min. To the mixture was added a solution of **4** and **2** (1.2 equiv. to **4**) in toluene (0.12 *M* to **4**) at 0 °C, and the mixture was stirred at the same temperature. After the reaction was completed, sat. aqueous NH_4Cl was added to the reaction mixture, and the mixture was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel to give the product.

Typical procedure for asymmetric deconjugative allylation of 4a and 2a in THF using LHMDS as a base at lower temperature (Table 4, run 6).

A suspension of Pd_2dba_3·$CHCl_3$ (8.6 mg, 0.0083 mmol) and ligand **8** (18.3 mg, 0.025 mmol) in degassed THF (0.5 mL) was stirred at rt for 15 min. To a solution of **4a** (50 mg, 0.33 mmol) in THF (1.5 mL) was added LHMDS (1.9 *M* in THF, 0.43 mL) at 0 °C, and the mixture was stirred at rt for 15 min. To the solution of lithium salt of **4a** were added the above-mentioned catalyst mixture and **2a** (0.043 mL, 0.4 mmol) at -50 °C, and the mixture was stirred at the same temperature for 3 h. To the mixture was added sat. aqueous NH_4Cl, and the mixture was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash

column chromatography on silica gel (hexane/Et_2O, 10:1) to give **5aa** (45 mg, 71%, 37% ee) as a yellowish oil.

Spectral data of deconjugative allylation products.

(*E*)-Methyl 2-allyl-2-cyanohexa-3,5-dienoate (5aa): Ir (neat) 2248, 1743, 1643, 1602, 1228 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.61 (dd, *J* = 13.9, 6.6 Hz, 1 H), 2.80 (dd, *J* = 13.9, 7.9 Hz, 1 H), 3.82 (s, 3 H), 5.23-5.29 (m, 3 H), 5.38 (d, *J* = 16.5 Hz, 1 H), 5.66 (d, *J* = 15.2 Hz, 1 H), 5.70-5.85 (m, 1 H), 6.34 (ddd, *J* = 16.5, 9.9, 9.9 Hz, 1 H), 6.57 (dd, *J* = 15.2, 9.9 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 42.0, 51.8, 53.7, 116.9, 120.8, 121.2, 126.2, 130.1, 134.4, 134.5, 167.5; LRMS (EI) *m/z* 191 (M^+), 132, 65, 59, 41, 39; HRMS (EI) calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0949. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.18; H, 7.00; N, 7.24. $[\alpha]_D^{27}$ -49.9 (*c* 0.99, $CHCl_3$) (48% ee).

(3*E*)-Methyl 2-cinnamyl-2-cyanohexa-3,5-dienoate (5ab): Ir (neat) 2247, 1742, 1652, 1601, 1577, 1257 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.78 (dd, *J* = 13.6, 6.8 Hz, 1 H), 2.95 (dd, *J* = 13.6, 7.7 Hz, 1 H), 3.82 (s, 3 H), 5.27 (d, *J* = 10.4 Hz, 1 H), 5.39 (d, *J* = 16.8 Hz, 1 H), 5.72 (d, *J* = 15.4 Hz, 1 H), 6.13 (ddd, *J* = 15.9, 7.7, 6.8 Hz, 1 H), 6.35 (ddd, *J* = 16.8, 10.4, 10.4 Hz, 1 H), 6.57 (d, *J* = 15.9 Hz, 1 H), 6.59 (dd, *J* = 15.4, 10.4 Hz, 1 H), 7.22-7.38 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.6, 52.1, 53.8, 117.0, 121.0, 121.1, 126.2, 126.5, 127.9, 128.6, 134.50, 134.52, 136.0, 136.3, 167.6; LRMS (FAB) *m/z* 268 (M^++H), 236, 117; HRMS (FAB) calcd for $C_{17}H_{18}NO_2$ (M^++H) 268.1338, found 268.1337. $[\alpha]_D^{19}$ -13.7 (*c* 0.54, $CHCl_3$) (24% ee).

(*E*)-Methyl 2-cyano-2-(2-phenylallyl)hexa-3,5-dienoate (5ac): Ir (neat) 2248, 1742, 1628, 1601, 1575, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.01 (dd, *J* = 14.0, 0.9 Hz, 1 H), 3.32 (dd, *J* = 14.0, 0.9 Hz, 1 H), 3.43 (s, 3 H), 5.21 (d, *J* = 10.0 Hz, 1 H), 5.33 (d, *J* = 16.8 Hz, 1 H), 5.34 (d, *J* = 0.9 Hz, 1 H), 5.43 (d, *J* = 0.9 Hz, 1 H), 5.65 (d, *J* = 15.0 Hz, 1 H), 6.23 (ddd, *J* = 16.8, 10.4, 10.0 Hz, 1 H), 6.52 (dd, *J* = 15.0, 10.4 Hz, 1 H), 7.25-7.33 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.8, 52.2, 53.4, 116.7, 119.4, 120.6, 126.8, 126.9, 127.9, 128.2, 133.7, 134.5, 140.0, 142.4, 167.4; LRMS (FAB) *m/z* 268 (M^++H), 226, 208; HRMS (FAB) calcd for $C_{17}H_{18}NO_2$ (M^++H) 268.1338, found 268.1342. $[\alpha]_D^{20}$ +6.2 (*c* 0.98, $CHCl_3$) (7% ee).

(*E*)-Isopropyl 2-allyl-2-cyanohexa-3,5-dienoate (5ba): Ir (neat) 2248, 1740, 1644, 1603, 1234 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.6 Hz, 3 H), 1.30 (d, *J* = 6.6 Hz, 3 H), 2.60 (dd, *J* = 13.9, 6.9 Hz, 1 H), 2.78 (dd, *J* = 13.9, 7.9 Hz, 1 H), 5.07 (qq, *J* = 6.6, 6.6 Hz, 1 H), 5.22-5.29 (m, 3 H), 5.37 (d, *J* = 17.2 Hz, 1 H), 5.67 (d, *J* = 15.2 Hz, 1 H), 5.70-5.85 (m, 1 H), 6.34 (ddd, *J* = 17.2, 10.2, 10.2 Hz, 1 H), 6.56 (dd, *J* = 15.2, 10.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 21.6, 42.1, 52.0, 71.3, 117.1, 120.6,

121.2, 126.5, 130.2, 134.2, 134.7, 166.5; LRMS (EI) *m/z* 219 (M^+), 132, 43, 41; HRMS (EI) calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1258. $[\alpha]_D^{20}$ -33.9 (*c* 1.05, $CHCl_3$) (39% ee).

(*E*)-2-Allyl-2-benzoylhexa-3,5-dienenitrile (5ca): Ir (neat) 2239, 1693, 1643, 1597, 1580, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.69 (dd, *J* = 13.8, 7.2 Hz, 1 H), 2.98 (dd, *J* = 13.8, 7.0 Hz, 1 H), 5.20-5.29 (m, 3 H), 5.41 (dd, *J* = 17.0, 0.6 Hz, 1 H), 5.69 (d, *J* = 15.5 Hz, 1 H), 5.74-5.85 (m, 1 H), 6.35 (ddd, *J* = 17.0, 10.4, 10.4 Hz, 1 H), 6.67 (dd, *J* = 15.5, 10.4 Hz, 1 H), 7.45-7.49 (m, 2 H), 7.58-7.61 (m, 1 H), 8.02-8.04 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.4, 54.6, 118.9, 120.9, 121.2, 127.6, 128.5, 129.5, 130.7, 133.8, 134.4, 134.6, 134.8, 191.5; LRMS (EI) *m/z* 236 (M^+-H), 105, 77, 51; HRMS (EI) calcd for $C_{16}H_{15}NO$ 237.1154, found 237.1157. $[\alpha]_D^{18}$ +6.0 (*c* 0.58, $CHCl_3$) (2% ee).

1-Allyl-6-oxocyclohex-2-enecarbonitrile (5da): Ir (neat) 2242, 1724, 1642 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.51-1.68 (m, 2 H), 1.83 (ddd, *J* = 14.3, 7.2, 7.2 Hz, 1 H), 2.13 (ddd, *J* = 14.3, 6.6, 6.6 Hz, 1 H), 2.21 (dd, *J* = 13.7, 7.9 Hz, 1 H), 2.31 (dd, *J* = 13.7, 6.8 Hz, 1 H), 4.88 (d, *J* = 16.9 Hz, 1 H), 4.93 (d, *J* = 10.2 Hz, 1 H), 5.18 (ddd, *J* = 9.6, 1.7, 1.5 Hz, 1 H), 5.25 (ddd, *J* = 9.6, 4.0, 3.8 Hz, 1 H), 5.59 (dddd, *J* = 16.9, 10.2, 7.9, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 35.8, 41.5, 49.4, 117.9, 121.2, 125.5, 130.2, 130.7, 201.3; LRMS (EI) *m/z* 161 (M^+), 132, 118, 104, 91, 41, 39; HRMS (EI) calcd for $C_{10}H_{11}NO$ 161.0841, found 161.0851. $[\alpha]_D^{17}$ -5.2 (*c* 0.67, $CHCl_3$) (5% ee).

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