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Pd-catalyzed asymmetric allylic aminations with aromatic amine nucleophiles using chiral diaminophosphine oxides: DIAPHOXs

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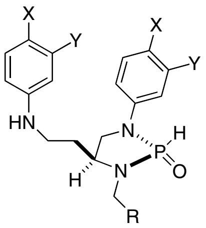
ABSTRACT

Asymmetric allylic aminations with aromatic amine nucleophiles using Pd–DIAPHOX catalyst systems are described. The asymmetric allylic aminations of various allylic carbonates proceeded using 2–5 mol % of the catalyst and BSA, providing the corresponding *N*-aryl chiral allylic amines in up to 99% ee for cyclic substrates, and in up to 97% ee for acyclic substrates.

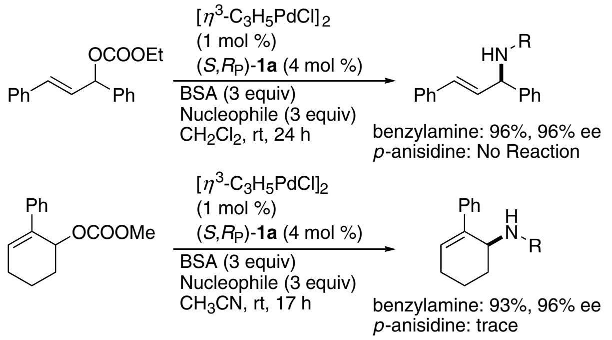
1. Introduction

Considerable effort has been directed toward the catalytic asymmetric synthesis of α-chiral amines because chiral amine units are ubiquitous in biologically active compounds. Transition metal-catalyzed asymmetric allylic amination is one of the most useful methods for synthesizing chiral allylic amines.[1] Several transition metal-catalyzed asymmetric allylic aminations using Pd,[2] Ir,[3] or other transition metal catalysts[4] have been reported. We recently developed aspartic acid-derived pentavalent chiral phosphorus preligands: P-chirogenic diaminophosphine oxides (DIAPHOXs) (Fig. 1).[5] These preligands are activated in situ by *N*,*O*-bis(trimethylsilyl)acetamide (BSA)-induced P(V) to P(III) transformations to afford trivalent phosphorus ligands. DIAPHOXs have been successfully applied to a Pd-catalyzed asymmetric allylic amination of cyclic and acyclic allylic alcohol derivatives using aliphatic amine nucleophiles, and various chiral allylic amines were obtained in good yield with high enantiomeric purity.[6,7] In contrast to aliphatic amine nucleophiles, asymmetric allylic amination with aromatic amine nucleophiles did not proceed using the Pd–DIAPHOX catalyst system (Scheme 1). This is probably due to the lower nucleophilicities of the aromatic amines compared with those of aliphatic amines, or stabilized anionic nitrogen nucleophiles derived from aromatic amines.[8,9] We attempted to overcome this drawback by tuning the reaction conditions. Herein, we describe a general and highly enantioselective allylic amination with aromatic amine nucleophiles using Pd–DIAPHOX catalyst systems.



1a: X = H, Y = H, R = phenyl
1b: X = H, Y = H, R = 1-naphthyl
1c: X = H, Y = H, R = 2-naphthyl
1d: X = H, Y = H, R = *t*-Bu
1e: X = H, Y = H, R = 3-biphenyl
1f: X = *t*-Bu, Y = H, R = phenyl
1g: X = OMe, Y = OMe, R = phenyl

Figure 1. (S,R_P)-DIAPHOX **1**.



Scheme 1. Asymmetric allylic amination with *p*-anisidine under the previous reaction conditions.

2. Results and discussion

2.1. Asymmetric allylic amination of 2-substituted cycloalkenyl carbonates using the Pd–DIAPHOX catalyst system

We previously reported that cyclic substrate **2**, bearing a methyl ester at the 2-position on the cyclohexenol framework, exhibits a much higher reactivity toward aromatic amine nucleophiles in comparison to other electrophiles.[6b] Therefore, the asymmetric

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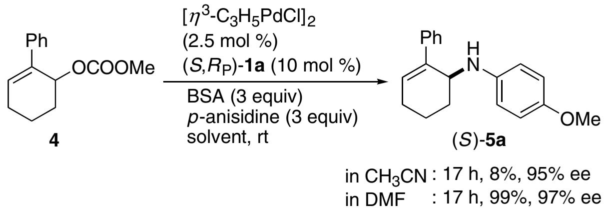
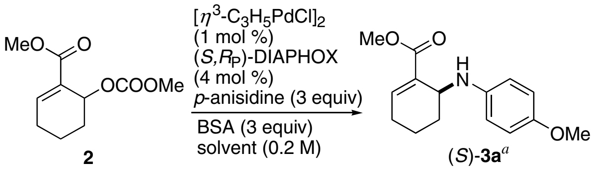
allylic amination of **2** using *p*-anisidine was selected for the initial optimization of the reaction conditions (Table 1). The effect of the ligand structure was first examined using 2 mol % of Pd catalyst, 4 mol % of (S,R_P)-DIAPHOX, and 3 equiv of BSA in CH_3CN at 4 °C, revealing that the catalyst prepared from **1a** or **1g** gave the product (*S*)-**3a** in excellent yield with over 90% ee (entries 1–7). Although the use of **1g** as the preligand produced (*S*)-**3a** with slightly higher enantioselectivity, the catalyst prepared from **1a** exhibited higher reactivity. Based on these results, **1a** was used for further optimization. Examination of the solvent effect revealed that the best reactivity was obtained when DMF was used as the solvent (entry 10). Although an enhanced reactivity in DMF was not observed at a lower temperature, the reaction proceeded in 48 h to afford (*S*)-**3a** in 99% yield with 95% ee (entry 12). These results led us to examine the asymmetric allylic amination of 2-phenylcyclohexenyl alcohol derivative **4** with *p*-anisidine using DMF as solvent (Scheme 2). The reaction rate was remarkably enhanced when the reaction was performed in DMF using 5 mol % of Pd catalyst and 10 mol % of **1a**, and the corresponding product (*S*)-**5a** was obtained in 99% yield with 97% ee.[10,11]

We next examined the scope and limitations of different cyclic substrates (Table 2). Both CH_3CN and DMF were used as solvents, and the better results are listed in the Table. Using 2 mol % of Pd catalyst and 4 mol % of **1a**, the asymmetric allylic amination of **2** was performed using various aromatic amines as nucleophiles. Primary aromatic amines with an electron-donating functional group, as well as an electron-withdrawing functional group, and



Scheme 2. Asymmetric allylic amination of **4**.

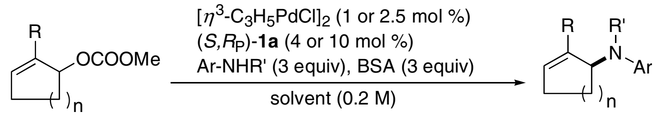
Table 1
Optimization of the reaction conditions



Entry	DIAPHOX	Solvent	Temperature (°C)	Time (h)	Yield[b] (%)	ee[c] (% ee)
1	**1a**	CH_3CN	4	7	99	90
2	**1b**	CH_3CN	4	48	42	42
3	**1c**	CH_3CN	4	50	78	71
4	**1d**	CH_3CN	4	51	55	48
5	**1e**	CH_3CN	4	64	99	88
6	**1f**	CH_3CN	4	65	99	89
7	**1g**	CH_3CN	4	24	99	91
8	**1a**	C_2H_5CN	4	16	99	73
9	**1a**	CH_2Cl_2	4	24	98	78
10	**1a**	DMF	4	4	99	90
11	**1a**	CH_3CN	−30	47	99	94
12	**1a**	DMF	−30	48	99	95

[a] For the determination of the absolute configuration, see Scheme 4.
[b] Isolated yield.
[c] Determined by HPLC analysis.

Table 2
Scope and limitations



Entry	Substrates		Ar–NHR′	Pd cat. (mol %)	Solvent	Temperature (°C)	Product	Time (h)	Yield[a] (%)	ee[b] (% ee)
1	**2**	R = COOMe (*n* = 2)	4-MeO–$C_6H_4NH_2$	2	DMF	−30	**3a**	48	99	95 (*S*)[c]
2	**2**	R = COOMe (*n* = 2)	$C_6H_4NH_2$	2	CH_3CN	0	**3b**	15	99	93
3	**2**	R = COOMe (*n* = 2)	4-*t*-Bu–$C_6H_4NH_2$	2	CH_3CN	0	**3c**	18	99	91
4	**2**	R = COOMe (*n* = 2)	4-Cl–$C_6H_4NH_2$	2	DMF	rt	**3d**	24	78	87
5	**2**	R = COOMe (*n* = 2)	3-MeO–$C_6H_4NH_2$	2	CH_3CN	0	**3e**	74	94	91
6	**2**	R = COOMe (*n* = 2)	3-Br–$C_6H_4NH_2$	2	DMF	rt	**3f**	21	79	87
7	**2**	R = COOMe (*n* = 2)	2-Cl–$C_6H_4NH_2$	2	CH_3CN	rt	**3g**	9	86	90
8	**2**	R = COOMe (*n* = 2)	2-Br–$C_6H_4NH_2$	2	CH_3CN	rt	**3h**	20	85	94
9	**2**	R = COOMe (*n* = 2)	Indoline	2	DMF	0	**3i**	15	99	96
10	**2**	R = COOMe (*n* = 2)	4-MeO–$C_6H_4NHCH_3$	2	DMF	0	**3j**	6	96	94
11	**6**	R = COOMe (*n* = 1)	4-MeO–$C_6H_4NH_2$	2	CH_3CN	−30	**7a**	72	95	78
12	**6**	R = COOMe (*n* = 1)	Indoline	2	CH_3CN	−30	**7b**	24	96	84
13	**8**	R = CN (*n* = 2)	4-MeO–$C_6H_4NH_2$	2	CH_3CN	0	**9**	46	99	91
14	**10**	R = CONMe(OMe) (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	CH_3CN	0	**11**	72	99	89
15	**4**	R = Ph (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	DMF	rt	**5a**	17	99	97 (*S*)[c]
16[d]	**4**	R = Ph (*n* = 2)	4-Cl–$C_6H_4NH_2$	5	DMF	rt	**5b**	24	73 (27)[e]	98
17[d]	**4**	R = Ph (*n* = 2)	Indoline	5	DMF	rt	**5c**	3	94	99
18	**12**	R = Ph (*n* = 1)	4-MeO–$C_6H_4NH_2$	2	DMF	0	**13**	12	97	96
19	**14**	R = 4-MeO-C_6H_4 (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	DMF	rt	**15**	48	56 (43)[e]	96
20	**16**	R = 4-F–C_6H_4 (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	DMF	rt	**17**	40	99	97
21	**18**	R = 2-naphthyl (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	DMF	rt	**19**	19	93	99
22	**20**	R = CH_2OTBS (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	CH_3CN	rt	**21**	48	79	78 (*S*)[f]
23	**22**	R = H (*n* = 2)	4-MeO–$C_6H_4NH_2$	5	CH_3CN	rt	**23**	48	91	44

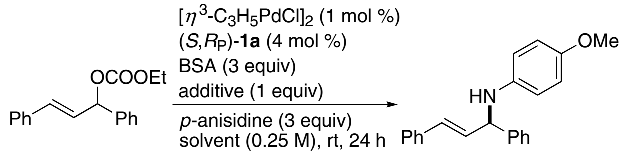
[a] Isolated yield.
[b] Determined by HPLC analysis.
[c] For the determination of the absolute configuration, see Scheme 4.
[d] Ten equivalents of amine were used as the nucleophile.
[e] Recovery of the starting material.
[f] The absolute configuration of **21** was determined by comparing the measured specific rotation of the authentic sample prepared from (*S*)-**3a**.

secondary aromatic amines were tolerant to this reaction, giving the corresponding products **3a**–**j** in good yield with 87–96% ee (entries 1–10).[12] Substrate **6**, a cyclopentenol-type substrate with a methyl ester, was also applicable to this reaction, affording the corresponding products with good enantioselectivities (entries 11 and 12). Similarly, a nitrile-type substrate **8**, as well as a Weinreb amide-type substrate **10**, could be utilized for this reaction, providing the corresponding products **9** and **11** in excellent yield with 91% ee and 89% ee, respectively (entries 13 and 14). The asymmetric allylic amination of 2-aryl-substituted cycloalkenyl alcohol derivatives was also examined using DMF as the solvent. Asymmetric allylic amination of **4** with primary and secondary aromatic amines proceeded using 5 mol % of the catalyst to afford the corresponding products in excellent enantioselectivity (entries 15–17). Similarly, 2-phenyl-substituted cyclopentenol derivative **12** was applicable to this reaction system, giving the product in 96% ee using 2 mol % of the catalyst (entry 18). This reaction system was also effective for cyclic allylic carbonates bearing a *p*-methoxyphenyl, *p*-fluorophenyl, or 2-naphthyl group, resulting in the formation of chiral amines with up to 99% ee (entries 19–21). There was a significant decrease in the reactivity, however, when **14**, a substrate with an electron-donating group on the aromatic ring, was used as the electrophile (entry 19). Moreover, we examined the asymmetric allylic amination of a 2-alkyl-substituted cyclohexenol derivative **20** using *p*-anisidine, and the corresponding product was produced in 79% yield with 78% ee (entry 22). A less satisfactory result was obtained when a simple cyclohexenyl carbonate was used as an electrophile (entry 23).

2.2. Asymmetric allylic amination of linear substrates using the Pd–DIAPHOX catalyst system

Thus, the present catalytic asymmetric reaction had a broad generality for both cyclic electrophiles and aromatic amine nucleophiles, affording *N*-aryl α-chiral allylic amines in up to 99% ee. The satisfactory results in the reaction system using cyclic substrates led us to turn our attention to the asymmetric allylic amination of linear substrates. The reaction conditions were optimized for the asymmetric allylic amination of 1,3-diphenylallyl carbonate **24** using *p*-anisidine (Table 3). When the reaction was performed using 2 mol % of the catalyst in DMF, the desired product was obtained in 74% ee, even though the yield was 30%. We hypothesized that the reactivity of the aromatic amine nucleophiles could be increased by the addition of amine bases through a hydrogen-bonding interaction. Detailed examinations revealed that there was a remarkable increase in the reactivity when 1 equiv of TMEDA or DMP was added, providing (*R*)-**25** in 99% yield with 90% ee, and 96% yield with 94% ee, respectively. DABCO was also an effective additive to achieve high enantioselectivity (38% yield, 93% ee), although the reactivity was low. We then examined the effect of the solvent in detail using DMP or DABCO as the additive. The best result was obtained when the reaction was performed in Et_2O using DABCO as the additive (99% yield, 97% ee).[13] The optimized conditions were applicable to other nucleophiles such as *p*-chloroaniline and indoline, affording the corresponding products in 99% yield with 96% ee, and in 97% yield with 86% ee, respectively (Scheme 3). The asymmetric allylic amination of 1,3-dialkylsubstituted allyl carbonate **28** was also examined using *p*-anisidine as the nucleophile. Decarboxylative elimination occurred exclusively when the reaction was performed in the presence of DABCO.[14] The reaction proceeded very sluggishly in the absence of DABCO, giving the corresponding product in 84% yield in 38% ee. There was no improvement in enantioselectivity when other DIAPHOXs were used as the preligands.

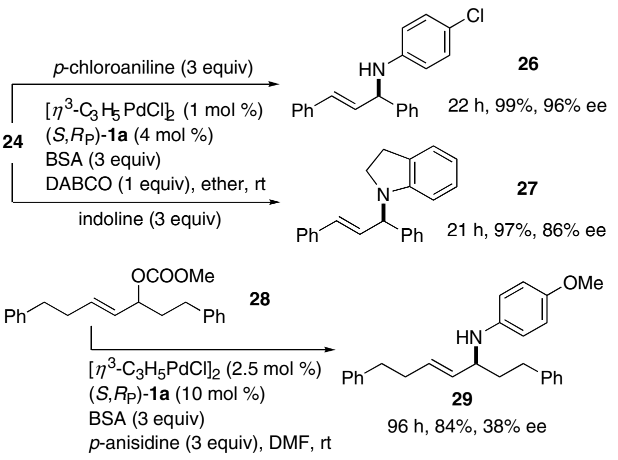
Table 3
Optimization of the reaction conditions



24 (*R*)-**25**[a]

Entry	Solvent	Additive	Yield[b] (%)	ee[c] (% ee)
1	CH_3CN	–	Trace	–
2	DMF	–	30	74
3	DMF	DBU	Trace	–
4	DMF	TMP[d]	21	85
5	DMF	Triethylamine	30	87
6	DMF	PMP[d]	Trace	–
7	DMF	TMEDA	99	90
8	DMF	DMP[d]	96	94
9	DMF	DABCO	38	93
10	DMF	Quinuclidine	7	89
11	Et_2O	–	Trace	–
12	Et_2O	DMP	88	95
13	Et_2O	DABCO	99	97

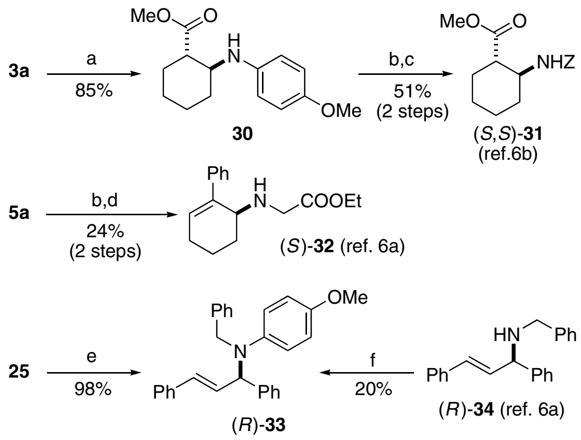
[a] For the determination of the absolute configuration, see Scheme 4.
[b] Isolated yield.
[c] Determined by HPLC analysis.
[d] TMP: 2,2,6,6-tetramethylpiperidine. PMP: 1,2,2,6,6-pentamethylpiperidine. DMP: *N*,*N*-dimethylpiperazine.



Scheme 3.

2.3. Determination of the absolute configuration of 3a, 5a, and 25

The absolute configuration of **3a**, **5a**, and **25** was determined by transforming them into known chiral compounds (Scheme 4). Hydrogenation of the conjugated olefin of **3a** (90% ee, Table 1, entry 1) was performed using $Pd(OH)_2$–C, to afford the cyclic *anti*-β-amino acid derivative **30** in 85% yield. In this hydrogenation, the reaction proceeded with complete diastereoselection, giving the *anti* product exclusively. Oxidative cleavage of the *p*-methoxyphenyl group of **30** using periodic acid,[15] followed by the protection of the resulting free amine with a carbobenzyloxy (*Z*) group, provided the known compound **31**.[6b] Comparison of the retention times of chiral HPLC analysis of **31** with the literature data revealed that the absolute stereochemistry of **3a** was (*S*).[16] Similarly, oxidative cleavage of the *p*-methoxyphenyl group of **5a** (97% ee, Scheme 2), followed by N-alkylation using ethyl bromoacetate, gave the known compound **32**,[6a] and the absolute configuration was determined to be (*S*).[16] The absolute configuration of **25** (97% ee, Table 3, entry 13) was determined using chiral HPLC analysis[16] after



Scheme 4. Determination of the absolute configuration of **3a**, **5a**, and **25**. Reagents and conditions: (a) $Pd(OH)_2$–C, H_2, AcOEt, rt; (b) $HIO_4{\cdot}2H_2O$, H_2SO_4, CH_3CN–H_2O, rt; (c) benzyl chloroformate (ZCl), pyridine, CH_2Cl_2, rt; (d) ethyl bromoacetate, NEt_3, THF, rt; (e) benzyl bromide, K_2CO_3, DMF, rt; (f) $Pd(dba)_2$ (5 mol %), t-Bu_3P (4 mol %), Cs_2CO_3, *p*-bromoanisole, toluene, 90 °C.

converting into *N*-benzyl adducts **33**, which could be prepared from the known chiral amine (*R*)-**34**[6a] using Pd-catalyzed amination of *p*-bromoanisole.[17]

3. Conclusion

In conclusion, we have succeeded in the general and highly enantioselective allylic amination with aromatic amine nucleophiles using Pd–DIAPHOX catalyst systems. Using 2–5 mol % of the catalyst, *N*-aryl α-chiral allylic amines were obtained in up to 99% ee for cyclic substrates and in up to 97% ee for acyclic substrates. Cyclic reaction adducts with a high enantiomeric purity will be useful for the asymmetric synthesis of nitrogen-containing natural products. Further studies are currently underway.

4. Experimental

4.1. General

Infrared (IR) spectra were recorded on a JASCO FT/IR 230 Fourier transform infrared spectrophotometer, equipped with ATR (Smiths Detection, DuraSample IR II). NMR spectra were recorded on a JEOL ecp 400 spectrometer, operating at 400 MHz for ^1H NMR, and 100 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$, were reported downfield from TMS (=0 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent signal [$CHCl_3$ (77.0 ppm)] as an internal reference. Optical rotations were measured on a JASCO P-1020 polarimeter. EI mass spectra were measured on JEOL GCmate. The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-980; detector, UV-970, measured at 254 nm; column, DAICEL CHIRALPAK AS-H, DAICEL CHIRALPAK AD-H, DAICEL CHIRALPAK AD, DAICEL CHIRALCEL OD-H, DAICEL CHIRALCEL OJ-H; mobile phase, hexane/2-propanol. Reactions were carried out in dry solvent under argon atmosphere. Other reagents were purified by the usual methods.

4.2. Experimental procedure of the Pd-catalyzed asymmetric allylic amination and compound characterization

Reaction products were prepared according to the general procedure. Alkenyl carbonates were prepared from the corresponding allylic alcohols using a usual procedure [methyl (or ethyl) chloroformate, pyridine, $CHCl_3$, rt]. For the spectroscopic data of these compounds, see Ref. 6.

4.2.1. General procedure for the asymmetric allylic amination of cyclic substrates: (6*S*)-6-(4-ethoxyphenylamino)cyclohex-1-enecarboxylic acid methyl ester (*S*)-3a

To a stirred solution of **2** (47.9 mg, 0.22 mmol), $[\eta^3\text{-}C_3H_5PdCl]_2$ (0.82 mg, 0.0022 mmol), and (S,R_P)-Ph-DIAPHOX **1a** (3.5 mg, 0.0089 mmol) in CH_3CN (1.1 mL) at room temperature was added BSA (165 μL, 0.67 mmol), and the reaction mixture was stirred for 10 min at the same temperature. After the reaction was cooled down to −30 °C, *p*-anisidine (82.7 mg, 0.67 mmol) was added, and the resulting mixture was stirred for 47 h. After the reaction was concentrated under reduced pressure, the crude residue was purified by flash column chromatography (hexane/AcOEt = 8:1) to give **3a** (57.8 mg, 99% yield, 94% ee) as a pale brown solid. Mp 80–81 °C; IR (ATR): ν 3386, 2943, 1708, 1645, 1508, 1434, 1229, 1059, 817, 748 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40–1.49 (m, 1H), 1.59–1.66 (m, 2H), 2.02–2.18 (m, 2H), 2.27–2.34 (m, 1H), 2.89 (broad peak (N*H*), 1H), 3.72 (s, 3H), 3.74 (s, 3H), 4.35–4.39 (m, 1H), 6.64–6.68 (m, 2H), 6.76–6.80 (m, 2H), 7.11 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.7, 26.5, 46.8, 51.7, 55.7, 114.8 (×2), 115.3 (×2), 131.5, 141.3, 142.5, 152.2, 167.3; EI-LRMS *m/z* 261 (M^+); EI-HRMS calcd for $C_{15}H_{19}NO_3$ (M^+): 261.1365. Found: 261.1368; $[\alpha]_D^{20} = -98.2$ (*c* 0.62, $CHCl_3$, 94% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 24.7 min [(*R*)-isomer] and 26.8 min [(*S*)-isomer], detection at 254 nm).

4.2.2. 6-Phenylaminocyclohex-1-enecarboxylic acid methyl ester 3b

White solid; Mp 98–99 °C; IR (ATR): ν 3382, 2946, 1698, 1597, 1435, 1244, 1060, 744 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.44–1.65 (m, 4H), 2.07–2.35 (m, 2H), 3.63 (broad peak (N*H*), 1H), 3.71 (s, 3H), 4.46–4.52 (m, 1H), 6.66–6.72 (m, 3H), 7.13 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H) 7.15–7.19 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.7, 26.6, 45.5, 51.8, 113.4 (×2), 117.3, 129.2 (×2), 131.3, 142.9, 147.0, 167.3; EI-LRMS *m/z* 231 (M^+); EI-HRMS calcd for $C_{14}H_{17}NO_2$ (M^+): 231.1259. Found: 231.1256; $[\alpha]_D^{25} = -80.4$ (*c* 1.28, $CHCl_3$, 93% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL/min, t_R 16.8 min [minor isomer] and 20.5 min [major isomer], detection at 254 nm).

4.2.3. 6-(4-*tert*-Butylphenylamino)cyclohex-1-enecarboxylic acid methyl ester 3c

White solid; Mp 84–85 °C; IR (ATR): ν 3382, 2944, 1704, 1613, 1517, 1306, 1242, 1059, 807, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.28 (s, 9H), 1.43–1.66 (m, 4H), 2.05–2.34 (m, 2H), 3.55 (broad peak (N*H*), 1H), 3.71 (s, 3H), 4.45–4.47 (m, 1H), 6.61–6.63 (m, 2H), 7.11 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H), 7.18–7.25 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.7, 26.6, 31.5 (×3), 33.8, 45.6, 51.8, 113.1 (×2), 126.0 (×2), 131.5, 140.0, 142.7, 144.6, 167.4; EI-LRMS *m/z* 287 (M^+); EI-HRMS calcd for $C_{18}H_{25}NO_2$ (M^+): 287.1885. Found: 287.1884; $[\alpha]_D^{25} = -60.2$ (*c* 1.23, $CHCl_3$, 91% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 99:1, flow rate: 0.5 mL/min, t_R 21.8 min [minor isomer] and 26.8 min [major isomer], detection at 254 nm).

4.2.4. 6-(4-Chlorophenylamino)cyclohex-1-enecarboxylic acid methyl ester 3d

White solid; Mp 113–114 °C; IR (ATR): ν 3378, 2949, 1700, 1595, 1509, 1438, 1268, 1065, 810 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.43–1.70 (m, 3H), 2.00–2.04 (m, 1H), 2.11–2.20 (m, 1H), 2.29–2.35 (m, 1H), 3.65 (broad peak (N*H*), 1H), 3.70 (s, 3H), 4.39–4.43

(m, 1H), 6.56–6.60 (m, 2H), 7.08–7.12 (m, 2H), 7.14 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.6, 26.7, 45.8, 51.8, 114.4 (×2), 121.8, 129.0 (×2), 130.9, 143.1, 145.6, 167.1; EI-LRMS *m/z* 265 (M^+); EI-HRMS calcd for $C_{14}H_{16}ClNO_2$ (M^+): 265.0870. Found: 265.0870; $[\alpha]_D^{24} = -88.0$ (*c* 1.41, $CHCl_3$, 87% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL/min, t_R 20.1 min [minor isomer] and 25.6 min [major isomer], detection at 254 nm).

4.2.5. 6-(3-Methoxyphenylamino)cyclohex-1-enecarboxylic acid methyl ester 3e

White solid; Mp 82–83 °C; IR (ATR): *ν* 3391, 2944, 1712, 1610, 1494, 1242, 1209, 1158, 1060, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.42–1.50 (m, 1H), 1.57–1.68 (m, 2H), 2.07–2.20 (m, 2H), 2.28–2.35 (m, 1H), 3.71 (s, 3H), 3.72 (broad peak (N*H*), 1H), 3.77 (s, 3H), 4.44–4.48 (m, 1H), 6.23 (dd, *J* = 2.4 Hz, 2.4 Hz, 1H), 6.25–6.28 (m, 2H), 7.07 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.13 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.7, 26.6, 45.4, 51.8, 55.0, 99.3, 102.4, 106.5, 129.9, 131.1, 143.0, 148.3, 160.8, 167.2; EI-LRMS *m/z* 261 (M^+); EI-HRMS calcd for $C_{15}H_{19}NO_3$ (M^+): 261.1365. Found: 261.1366; $[\alpha]_D^{25} = -72.0$ (*c* 1.43, $CHCl_3$, 91% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 20.4 min [major isomer] and 22.3 min [minor isomer], detection at 254 nm).

4.2.6. 6-(3-Bromophenylamino)cyclohex-1-enecarboxylic acid methyl ester 3f

Colorless oil; IR (ATR): *ν* 3394, 2947, 2088, 1716, 1507, 1262, 1060, 984, 771, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.46–1.67 (m, 3H), 2.02–2.19 (m, 2H), 2.31–2.36 (m, 1H), 3.68 (broad peak (N*H*), 1H), 3.72 (s, 3H), 4.40–4.45 (m, 1H), 6.55–6.57 (m, 1H), 6.79–6.81 (m, 2H), 6.99–7.03 (m, 1H), 7.15–7.16 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 16.2, 25.7, 26.7, 45.4, 51.8, 112.0, 115.8, 120.1, 123.3, 130.5, 130.8, 143.4, 148.3, 167.0; EI-LRMS *m/z* 309 (M^+); EI-HRMS calcd for $C_{14}H_{16}BrNO_2$ (M^+): 309.0364. Found: 309.0373; $[\alpha]_D^{23} = -54.6$ (*c* 0.48, $CHCl_3$, 87% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 13.5 min [minor isomer] and 14.9 min [major isomer], detection at 254 nm).

4.2.7. 6-(2-Chlorophenylamino)cyclohex-1-enecarboxylic acid methyl ester 3g

White solid; Mp 63–64 °C; IR (ATR): *ν* 3420, 2945, 1715, 1646, 1595, 1506, 1434, 1319, 1243, 1098, 1062, 1032, 739 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.45–1.54 (m, 1H), 1.62–1.70 (m, 2H), 1.99–2.05 (m, 1H), 2.12–2.22 (m, 1H), 2.33–2.39 (m, 1H), 3.71 (s, 3H), 4.27 (broad peak (N*H*), 1H), 4.50–4.58 (m, 1H), 6.60–6.64 (m, 1H), 6.86–6.88 (m, 1H), 7.13–7.17 (m, 1H), 7.19 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H), 7.22–7.26 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 16.1, 25.7, 26.8, 45.5, 51.8, 112.2, 117.2, 119.4, 127.7, 129.1, 130.7, 143.0, 143.4, 167.0; EI-LRMS *m/z* 265 (M^+); EI-HRMS calcd for $C_{14}H_{16}ClNO_2$ (M^+): 265.0870. Found: 265.0868; $[\alpha]_D^{23} = -93.7$ (*c* 2.14, $CHCl_3$, 90% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 200:1, flow rate: 0.5 mL/min, t_R 23.0 min [major isomer] and 25.7 min [minor isomer], detection at 254 nm).

4.2.8. 6-(2-Bromophenylamino)cyclohex-1-enecarboxylic acid methyl ester 3h

White solid; Mp 42–43 °C; IR (ATR): *ν* 3402, 2945, 1715, 1646, 1595, 1506, 1455, 1434, 1316, 1260, 1244, 1061, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.46–1.53 (m, 1H), 1.63–1.70 (m, 2H), 1.98–2.02 (m, 1H), 2.15–2.22 (m, 1H), 2.33–2.40 (m, 1H), 3.72 (s, 3H), 4.28 (broad peak (N*H*), 1H), 4.49–4.57 (m, 1H), 6.54–6.58 (m, 1H), 6.85–6.87 (m, 1H), 7.17–7.26 (m, 1H), 7.19 (dd, *J* = 2.8 Hz, 4.8 Hz, 1H), 7.40–7.41 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 16.2, 25.7, 26.8, 45.7, 51.8, 110.3, 112.4, 117.9, 128.4, 130.7, 132.4, 143.4, 144.0, 167.0; EI-LRMS *m/z* 309 (M^+); EI-HRMS calcd for $C_{14}H_{16}BrNO_2$ (M^+): 309.0364. Found: 309.0361; $[\alpha]_D^{24} = -115.6$ (*c* 1.61, $CHCl_3$, 94% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 200:1, flow rate: 0.5 mL/min, t_R 25.1 min [major isomer] and 28.7 min [minor isomer], detection at 254 nm).

4.2.9. 6-(2,3-Dihydroindol-1-yl)cyclohex-1-enecarboxylic acid methyl ester 3i

Violet oil; IR (ATR): *ν* 2945, 1715, 1646, 1605, 1488, 1434, 1394, 1242, 1065, 741 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.64–1.77 (m, 3H), 1.96–1.99 (m, 1H), 2.19–2.35 (m, 2H), 2.87–2.92 (m, 2H), 3.27–3.33 (m, 1H), 3.44–3.50 (m, 1H), 3.65 (s, 3H), 4.44–4.50 (m, 1H), 6.44 (d, *J* = 8.0 Hz, 1H), 6.52–6.57 (m, 1H), 7.00–7.05 (m, 2H), 7.12–7.25 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 18.8, 25.6, 25.9, 28.3, 48.6, 49.8, 51.7, 105.7, 116.0, 124.2, 127.2, 129.4, 130.8, 142.8, 150.8, 167.8; EI-LRMS *m/z* 257 (M^+); EI-HRMS calcd for $C_{16}H_{19}NO_2$ (M^+): 257.1416. Found: 257.1418; $[\alpha]_D^{25} = -105.2$ (*c* 1.94, $CHCl_3$, 96% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/2-propanol = 92:8, flow rate: 0.5 mL/min, t_R 20.4 min [major isomer] and 28.0 min [minor isomer], detection at 254 nm).

4.2.10. 6-[(4-Methoxyphenyl)-methylamino]-cyclohex-1-enecarboxylic acid methyl ester 3j

Yellow oil; IR (ATR): *ν* 2945, 1716, 1647, 1509, 1435, 1241, 1105, 1039, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.59–1.72 (m, 3H), 1.84–1.91 (m, 1H), 2.13–2.22 (m, 1H), 2.25–2.69 (m, 1H), 3.67 (s, 3H), 3.75 (s, 3H), 4.62–4.69 (m, 1H), 6.80–6.86 (m, 4H), 7.09 (dt, *J* = 1.6 Hz, 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 19.2, 25.6, 25.9, 33.8, 51.6, 53.9, 55.7, 114.5 (×2), 115.1 (×2), 132.2, 142.3, 144.3, 151.6, 167.9; EI-LRMS *m/z* 275 (M^+); EI-HRMS calcd for $C_{16}H_{21}NO_3$ (M^+): 275.1521. Found: 275.1519; $[\alpha]_D^{23} = -65.7$ (*c* 1.58, $CHCl_3$, 94% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 13.1 min [major isomer] and 14.7 min [minor isomer], detection at 254 nm).

4.2.11. (1*S*)-(4-Methoxyphenyl)-(2-phenylcyclohex-2-enyl)-amine 5a

Yellow oil; IR (ATR): *ν* 3403, 2935, 1716, 1540, 1508, 1457, 1236, 1039, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.60–1.74 (m, 3H), 2.12–2.32 (m, 3H), 3.48 (broad peak (N*H*), 1H), 3.74 (s, 3H), 4.35–4.43 (m, 1H), 6.31 (dd, *J* = 3.2 Hz, 4.4 Hz, 1H), 6.57–6.60 (m, 2H), 6.76–6.80 (m, 2H), 7.18–7.29 (m, 3H), 7.43–7.45 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 17.0, 26.0, 27.4, 48.9, 55.8, 114.1 (×2), 115.0 (×2), 125.5 (×2), 126.9, 128.4 (×2), 128.5, 137.3, 140.3, 141.4, 151.7; EI-LRMS *m/z* 279 (M^+); EI-HRMS calcd for $C_{19}H_{21}NO$ (M^+): 279.1623. Found: 279.1621; $[\alpha]_D^{23} = -165.4$ (*c* 0.14, $CHCl_3$, 97% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 10.6 min [minor isomer] and 16.5 min [major isomer], detection at 254 nm).

4.2.12. (4-Chlorophenyl)-(2-phenylcyclohex-2-enyl)amine 5b

White solid; Mp 88–89 °C; IR (ATR): *ν* 3414, 2930, 1596, 1495, 1399, 1308, 1247, 1091, 1003, 907, 814, 799, 756, 688 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.64–1.71 (m, 3H), 2.08–2.29 (m, 3H), 3.76 (broad peak (N*H*), 1H), 4.36–4.46 (m, 1H), 6.35 (dd, *J* = 3.2 Hz, 4.0 Hz, 1H), 6.50–6.54 (m, 2H), 7.08–7.12 (m, 2H), 7.18–7.29 (m, 3H), 7.39–7.41 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 17.0, 25.9, 27.3, 48.1, 113.8 (×2), 121.3, 125.3 (×2), 127.1, 128.4 (×2), 129.0, 129.1 (×2), 136.7, 139.9, 145.6; EI-LRMS *m/z* 283 (M^+); EI-HRMS calcd for $C_{18}H_{18}ClN$ (M^+): 283.1128. Found: 283.1131; $[\alpha]_D^{18} = -49.0$ (*c* 1.15, $CHCl_3$, 98% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 10.3 min [minor isomer] and 20.3 min [major isomer], detection at 254 nm).

4.2.13. 1-(2,3-Dihydro-indol-1-yl)2-phenylcyclohex-2-ene 5c

Yellow oil; IR (ATR): ν 3023, 2930, 2856, 1605, 1489, 1459, 1392, 1264, 740, 695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.70–1.97 (m, 4H), 2.25–2.28 (m, 2H), 2.63–2.69 (m, 1H), 2.76–2.79 (m, 1H), 3.06–3.12 (m, 1H), 3.37–3.44 (m, 1H), 4.63–4.66 (m, 1H), 6.31 (dt, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.46–6.54 (m, 2H), 6.94–6.96 (m, 1H), 7.03–7.07 (m, 1H), 7.15–7.25 (m, 3H), 7.33–7.36 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 20.3, 24.7, 26.0, 28.1, 48.3, 50.5, 105.4, 115.8, 124.2, 125.6 (×2), 126.6, 127.2, 128.0 (×2), 129.8, 129.8, 137.4, 140.8, 150.8; EI-LRMS *m/z* 275 (M^+); EI-HRMS calcd for $C_{20}H_{21}N$ (M^+): 275.1674. Found: 275.1675; $[\alpha]_D^{19} = -152.0$ (*c* 0.31, $CHCl_3$, 99% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 92:8, flow rate: 0.5 mL/min, t_R 9.2 min [minor isomer] and 10.7 min [major isomer], detection at 254 nm).

4.2.14. 5-(4-Methoxyphenylamino)cyclopent-1-enecarboxylic acid methyl ester 7a

Yellow oil; IR (ATR): ν 3385, 2950, 2833, 1715, 1635, 1510, 1437, 1362, 1290, 1233, 1097, 1036, 821, 748 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.94–2.01 (m, 1H), 2.27–2.36 (m, 1 H), 2.44–2.53 (m, 1H), 2.61–2.70 (m, 1H), 3.72 (broad peak (N*H*), 1H), 3.74 (s, 3H), 3.75 (s, 3H), 4.59–4.63 (m, 1H), 6.63–6.67 (m, 2H), 6.77–6.81 (m, 2H), 6.99–7.01 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 31.2, 31.5, 51.6, 55.7, 59.6, 114.7 (×2), 115.5 (×2), 136.8, 141.8, 147.5, 152.5, 165.1; EI-LRMS *m/z* 247 (M^+); EI-HRMS calcd for $C_{14}H_{17}NO_3$ (M^+): 247.1208. Found: 247.1201; $[\alpha]_D^{20} = +50.6$ (*c* 1.35, $CHCl_3$, 78% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 21.6 min [major isomer] and 26.3 min [minor isomer], detection at 254 nm).

4.2.15. 6-(2,3-Dihydro-indol-1-yl)cyclopent-1-enecarboxylic acid methyl ester 7b

Yellow oil; IR (ATR): ν 2949, 2841, 1717, 1606, 1541, 1507, 1489, 1473, 1288, 1265, 1100, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.91–1.98 (m, 1H), 2.19–2.28 (m, 1H), 2.47–2.64 (m, 2H), 2.89–2.93 (m, 2H), 3.18–3.29 (m, 2H), 3.69 (s, 3H), 5.00–5.07 (m, 1H), 6.52–6.61 (m, 2H), 7.00–7.06 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 26.6, 28.1, 32.1, 47.7, 51.5, 60.1, 107.0, 116.8, 124.3, 127.1, 130.0, 135.8, 146.8, 151.0, 165.1; EI-LRMS *m/z* 243 (M^+); EI-HRMS calcd for $C_{15}H_{17}NO_2$ (M^+): 243.1259. Found: 243.1255; $[\alpha]_D^{20} = -42.0$ (*c* 0.59, $CHCl_3$, 84% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 97:3, flow rate: 0.5 mL/min, t_R 14.1 min [minor isomer] and 15.2 min [major isomer], detection at 254 nm).

4.2.16. 6-(4-Methoxy-phenylamino)cyclohex-1-enecarbonitrile 9

Yellow oil; IR (ATR): ν 3368, 2946, 2217, 1510, 1464, 1232, 1039, 822, 763 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.60–1.86 (m, 4H), 2.16–2.33 (m, 2H), 3.47 (broad peak (N*H*), 1H), 3.76 (s, 3H), 4.03–4.08 (m, 1H), 6.68–6.70 (m, 2H), 6.77–6.80 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 17.2, 25.9, 27.5, 49.7, 55.7, 114.9 (×2), 115.4 (×2), 115.6, 118.7, 140.3, 147.8, 152.7; EI-LRMS *m/z* 228 (M^+); EI-HRMS calcd for $C_{14}H_{16}N_2O$ (M^+): 228.1263. Found: 228.1254; $[\alpha]_D^{23} = -65.1$ (*c* 0.32, $CHCl_3$, 91% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 27.0 min [minor isomer] and 28.9 min [major isomer], detection at 254 nm).

4.2.17. 6-(4-Methoxyphenylamino)-cyclohex-1-enecarboxylic acid methoxy-methyl-amide 11

Colorless oil; IR (ATR): ν 3343, 2933, 2830, 1625, 1508, 1463, 1440, 1379, 1289, 1230, 1179, 1115, 1036, 985, 820, 728 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.64–2.08 (m, 4H), 2.12–2.23 (m, 2H), 3.15 (s, 3H), 3.64 (s, 3H), 3.73 (s, 3H), 4.35–4.41 (m, 1H), 6.15–6.17 (m, 1H), 6.60–6.63 (m, 2H), 6.73–6.76 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 18.2, 24.9, 28.3, 33.2, 49.3, 55.7, 61.1, 114.7 (×2), 115.1 (×2), 131.5, 136.2, 141.2, 152.0, 171.3; EI-LRMS *m/z* 290 (M^+); EI-HRMS calcd for $C_{16}H_{22}N_2O_3$ (M^+): 290.1630. Found: 290.1635; $[\alpha]_D^{21} = -19.4$ (*c* 0.34, $CHCl_3$, 89% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 19.7 min [minor isomer] and 22.1 min [major isomer], detection at 254 nm).

4.2.18. (4-Methoxyphenyl)-(2-phenylcyclopent-2-enyl)amine 13

Yellow oil; IR (ATR): ν 3588, 2929, 1509, 1242, 1048, 832, 763, 693 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.99–2.05 (m, 1H), 2.29–2.38 (m, 1H), 2.47–2.54 (m, 1H), 3.52 (broad peak (N*H*), 1H), 3.76 (s, 3H), 4.77–4.85 (m, 1H), 6.38 (dd, *J* = 2.4 Hz, 3.2 Hz, 1H), 6.58–6.62 (m, 2 H), 6.79–6.82 (m, 2H), 7.21–7.32 (m, 3H), 7.49–7.51 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 31.0, 31.5, 55.9, 59.9, 114.3 (×2), 115.0 (×2), 126.2 (×2), 127.3, 128.5 (×2), 129.8, 134.7, 142.0, 143.0, 151.9; EI-LRMS *m/z* 265 (M^+); EI-HRMS calcd for $C_{18}H_{19}NO$ (M^+): 265.1467. Found: 265.1465; $[\alpha]_D^{23} = +43.7$ (*c* 0.14, $CHCl_3$, 96% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 93:7, flow rate: 0.5 mL/min, t_R 11.4 min [minor isomer] and 13.7 min [major isomer], detection at 254 nm).

4.2.19. (4-Methoxyphenyl)-[2-(4-methoxyphenyl)cyclohex-2-enyl]amine 15

Yellow oil; IR (ATR): ν 3410, 2932, 2830, 1611, 1509, 1456, 1283, 1239, 1180, 1036, 817, 737 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.59–1.72 (m, 3H), 2.11–2.30 (m, 3H), 3.50 (broad peak (N*H*), 1H), 3.75 (s, 3H), 3.77 (s, 3H), 4.32–4.36 (m, 1H), 6.22 (dd, *J* = 3.2 Hz, 4.4 Hz, 1H), 6.56–6.62 (m, 2H), 6.76–6.83 (m, 4H), 7.35–7.39 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 17.0, 25.9, 27.5, 48.9, 55.2, 55.8, 113.7 (×2), 114.0 (×2), 115.0 (×2), 126.5 (×2), 126.8, 132.8, 136.5, 141.5, 151.7, 158.6; EI-LRMS *m/z* 309 (M^+); EI-HRMS calcd for $C_{20}H_{23}NO_2$ (M^+): 309.1729. Found: 309.1715; $[\alpha]_D^{20} = -88.9$ (*c* 0.68, $CHCl_3$, 96% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 14.0 min [minor isomer] and 17.4 min [major isomer], detection at 254 nm).

4.2.20. [2-(4-Fluoro-phenyl)-cyclohex-2-enyl]-(4-methoxy-phenyl)amine 17

Violet oil; IR (ATR): ν 3396, 2932, 1599, 1505, 1403, 1224, 1160, 1114, 1036, 812, 778, 737 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.60–1.72 (m, 3H), 2.10–2.31 (m, 3H), 3.47 (broad peak (N*H*), 1H), 3.74 (s, 3H), 4.31–4.35 (m, 1H), 6.24 (dd, *J* = 3.2 Hz, 4.4 Hz, 1H), 6.56–6.59 (m, 2H), 6.76–6.80 (m, 2H), 6.92–6.98 (m, 2H), 7.38–7.42 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 16.8, 25.9, 27.3, 49.0, 55.7, 114.1 (×2), 114.9 (×2), 115.0 (d, *J* = 20.6 Hz) (×2), 127.0 (d, *J* = 7.4 Hz) (×2), 128.3, 136.4, 136.5 (d, *J* = 3.3 Hz), 141.2, 151.8, 161.9 (d, *J* = 244 Hz); EI-LRMS *m/z* 297 (M^+); EI-HRMS calcd for $C_{19}H_{20}FNO$ (M^+): 297.1529. Found: 297.1528; $[\alpha]_D^{22} = -106.5$ (*c* 0.50, $CHCl_3$, 97% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 10.9 min [minor isomer] and 11.8 min [major isomer], detection at 254 nm).

4.2.21. (4-Methoxyphenyl)-(2-naphthalen-2-yl-cyclohex-2-enyl)amine 19

Yellow oil; IR (ATR): ν 3403, 3053, 2931, 2828, 1763, 1508, 1231, 1178, 1114, 1037, 815, 748 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.68–1.79 (m, 3H), 2.17–2.39 (m, 3H), 3.57 (broad peak (N*H*), 1H), 3.76 (s, 3H), 4.51–4.56 (m, 1H), 6.46 (dd, *J* = 3.2 Hz, 4.8 Hz, 1H), 6.59–6.63 (m, 2H), 6.78–6.80 (m, 2H), 7.38–7.42 (m, 2H), 7.59–7.62 (m, 1H), 7.71–7.78 (m, 3H), 7.82–7.88 (m, 1H); ^{13}C NMR (CDCl$_3$): δ 17.0, 26.1, 27.5, 49.0, 55.7, 114.1 (×2), 114.9 (×2), 124.0, 124.1, 125.5, 125.9, 127.3, 127.7, 128.1, 129.1, 132.5, 133.4, 137.2, 137.6, 141.4, 151.7; EI-LRMS *m/z* 329 (M$^+$); EI-HRMS calcd for C$_{23}$H$_{23}$NO (M$^+$): 329.1780. Found: 329.1783; $[\alpha]_D^{19} = -169.9$ (*c* 3.10, CHCl$_3$, 98% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 13.0 min [minor isomer] and 17.6 min [major isomer], detection at 254 nm).

4.2.22. (1*S*)-[2-(*tert*-Butyl-dimethylsilanyloxymethyl)cyclohex-2-enyl]-(4-methoxy-phenyl)-amine 21

Yellow oil; IR (ATR): ν 3394, 2928, 2855, 1509, 1462, 1230, 1164, 1043, 1004, 835, 815, 775 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 0.04 (s, 6H), 0.90 (s, 9H), 1.53–1.61 (m, 3H), 1.89–2.08 (m, 3H), 3.55 (broad peak (N*H*), 1H), 3.74 (s, 3H), 3.86–3.91 (m, 1H), 4.13 (dd, *J* = 1.6 Hz, 12.8 Hz, 1H), 4.19 (dd, *J* = 1.6 Hz, 12.8 Hz, 1H), 5.84–5.89 (m, 1H), 6.56–6.60 (m, 2H), 6.75–6.78 (m, 2H); ^{13}C NMR (CDCl$_3$): δ −5.3 (×2), 17.8, 18.4, 25.0, 26.0 (×3), 27.5, 48.3, 55.9, 65.4, 114.4 (×2), 114.9 (×2), 125.9, 137.8, 141.9, 151.7; EI-LRMS *m/z* 347 (M$^+$); EI-HRMS calcd for C$_{20}$H$_{33}$NO$_2$Si (M$^+$): 347.2281. Found: 347.2274; $[\alpha]_D^{23} = -14.7$ (*c* 0.75, CHCl$_3$, 78% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 200:1, flow rate: 0.5 mL/min, t_R 10.8 min [minor isomer] and 12.7 min [major isomer], detection at 254 nm).

4.2.23. Cyclohex-2-enyl-(4-methoxyphenyl)amine 23

Colorless oil; IR (ATR): ν 3394, 3022, 2929, 2830, 1509, 1463, 1230, 1179, 1038, 817 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.56–1.73 (m, 3H), 1.87–2.05 (m, 3H), 2.84 (broad peak (N*H*), 1H), 3.74 (s, 3H), 3.87–3.94 (m, 1H), 5.73–5.77 (m, 1H), 5.80–5.85 (m, 1H), 6.58–6.62 (m, 2H), 6.76–6.80 (m, 2H); ^{13}C NMR (CDCl$_3$): δ 19.7, 25.2, 29.0, 49.0, 55.8, 114.8 (×2), 114.9 (×2), 128.8, 129.8, 141.3, 152.0; EI-LRMS *m/z* 203 (M$^+$); EI-HRMS calcd for C$_{13}$H$_{17}$NO (M$^+$): 203.1310. Found: 203.1302; $[\alpha]_D^{23} = -30.4$ (*c* 0.91, CHCl$_3$, 44% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL/min, t_R 15.8 min [minor isomer] and 17.2 min [major isomer], detection at 254 nm).

4.2.24. General procedure for the asymmetric allylic amination of linear substrates: (1*R*)-(1,3-diphenylallyl)-(4-methoxy-phenyl)amine 25

To a stirred solution of **24** (67.3 mg, 0.24 mmol), [η^3-C$_3$H$_5$PdCl]$_2$ (0.87 mg, 0.0024 mmol), (*S*,*R*$_P$)-Ph-DIAPHOX **1a** (3.7 mg, 0.0096 mmol), and DABCO (26.7 mg 0.24 mmol) in Et$_2$O (0.95 mL) at room temperature was added BSA (175 µL, 0.72 mmol), and the mixture was stirred at the same temperature. After 10 min, *p*-anisidine (88.6 mg, 0.72 mmol) was added, and the resulting mixture was stirred for 24 h. After the reaction was concentrated under reduced pressure, the crude residue was purified by flash column chromatography (hexane/AcOEt = 30:1) to give **25** (75.2 mg, 99% yield, 97% ee) as a pale yellow solid. Mp 99–100 °C; IR (ATR): ν 3385, 1509, 1239, 1178, 1035, 968, 819, 744, 698 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 3.72 (s, 3H), 3.89 (broad peak (N*H*), 1H), 5.00 (d, *J* = 6.4 Hz, 1H), 6.39 (dd, *J* = 6.4 Hz, 15.6 Hz, 1H), 6.59–6.62 (m, 2H), 6.62 (d, *J* = 15.6 Hz, 1H), 6.72–6.76 (m, 2H), 7.20–7.44 (m, 10H); ^{13}C NMR (CDCl$_3$): δ 55.7, 61.5, 114.7 (×2), 114.9 (×2), 126.5 (×2), 127.2 (×2), 127.4, 127.6, 128.5 (×2), 128.8 (×2), 130.9, 131.1, 136.7, 141.5, 142.3, 152.2; EI-LRMS *m/z* 315 (M$^+$); EI-HRMS calcd for C$_{22}$H$_{21}$NO (M$^+$): 315.1623. Found: 315.1635; $[\alpha]_D^{22} = -56.2$ (*c* 0.80, CHCl$_3$, 97% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 48.0 min [major isomer] and 63.9 min [minor isomer], detection at 254 nm).

4.2.25. (4-Chloro-phenyl)-(1,3-diphenylallyl)amine 26

Yellow oil; IR (ATR): ν 3385, 1596, 1494, 1313, 814, 746, 699 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 4.13 (broad peak (N*H*), 1H), 5.00 (d, *J* = 6.4 Hz, 1H), 6.35 (dd, *J* = 6.4 Hz, 16.0 Hz, 1H), 6.51–6.55 (m, 2H), 6.59 (d, *J* = 16.0 Hz, 1H), 7.05–7.09 (m, 2H), 7.20–7.41 (m, 10H); ^{13}C NMR (CDCl$_3$): δ 60.7, 114.7 (×2), 122.3, 126.5 (×2), 127.1 (×2), 127.7, 127.8, 128.6 (×2), 128.9 (×2), 129.0 (×2), 130.2, 131.3, 136.5, 141.6, 145.7; EI-LRMS *m/z* 319 (M$^+$); EI-HRMS calcd for C$_{21}$H$_{18}$ClN (M$^+$): 319.1128. Found: 319.1132; $[\alpha]_D^{23} = -19.3$ (*c* 1.60, CHCl$_3$, 96% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 29.9 min [minor isomer] and 42.8 min [major isomer], detection at 254 nm).

4.2.26. 1-(1,3-Diphenylallyl)-2,3-dihydro-1*H*-indole 27

Yellow oil; IR (ATR): ν 3023, 1603, 1483, 1387, 1246, 1156, 1072, 1025, 966, 916, 869, 740, 695 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 2.95 (t, *J* = 8.0 Hz, 2H), 3.37–3.42 (m, 2H), 5.10 (d, *J* = 7.6 Hz, 1H), 6.34–6.36 (m, 1H), 6.47 (dd, *J* = 7.6 Hz, 16.0 Hz, 1H), 6.60–6.64 (m, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.92–6.95 (m, 1H), 7.05–7.06 (m, 1H), 7.20–7.46 (m, 10H); ^{13}C NMR (CDCl$_3$): δ 28.3, 50.6, 64.0, 108.4, 117.5, 124.4, 126.5 (×2), 127.0, 127.2, 127.6, 127.7 (×2), 127.8, 128.5 (×2), 128.5 (×2), 130.4, 132.7, 136.6, 140.7, 151.3; EI-LRMS *m/z* 311 (M$^+$); EI-HRMS calcd for C$_{23}$H$_{21}$N (M$^+$): 311.1674. Found: 311.1664; $[\alpha]_D^{25} = -10.8$ (*c* 3.32, CHCl$_3$, 86% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 200:1, flow rate: 0.3 mL/min, t_R 31.6 min [minor isomer] and 35.0 min [major isomer], detection at 254 nm).

4.2.27. (4-Methoxy-phenyl)-(1-phenethyl-5-phenylpent-2-enyl)amine 29

Yellow oil; IR (ATR): ν 3025, 2925, 2853, 1509, 1455, 1237, 1178, 1035, 970, 818, 747, 699 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 1.75–1.93 (m, 2H), 2.32–2.37 (m, 2H), 2.60–2.68 (m, 4H), 3.65–3.70 (m, 1H), 3.74 (s, 3H), 3.75 (broad peak (N*H*), 1H), 5.33 (dd, *J* = 6.8 Hz, 15.2 Hz, 1H), 5.63 (dt, *J* = 15.2 Hz, 6.8 Hz, 1H), 6.48–6.52 (m, 2H), 6.72–6.76 (m, 2H), 7.12–7.29 (m, 10H); ^{13}C NMR (CDCl$_3$): δ 32.2, 34.0, 35.8, 37.6, 55.7, 55.8, 114.7 (×2), 114.8 (×2), 125.7, 125.8, 128.2 (×2), 128.3 (×2), 128.4 (×2), 128.5 (×2), 130.9, 132.6, 141.7, 141.9, 151.9; EI-LRMS *m/z* 371 (M$^+$); EI-HRMS calcd for C$_{27}$H$_{29}$NO (M$^+$): 371.2249. Found: 371.2258; $[\alpha]_D^{25} = -0.3$ (*c* 0.32, CHCl$_3$, 40% ee). The enantiomeric excess was determined by chiral HPLC analysis (DAICEL CHIRALPAK AS-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 11.9 min [major isomer] and 16.0 min [minor isomer], detection at 254 nm).

4.3. Determination of the absolute configuration of 3a, 5a, and 25

4.3.1. (1*S*,2*S*)-2-(4-Methoxy-phenylamino)cyclohexane-carboxylic acid methyl ester 30

A suspension of **3a** (61.8 mg, 0.24 mmol) and 20 wt % Pd(OH)$_2$–C (6.2 mg) in AcOEt (2.4 mL) was stirred under H$_2$ atmosphere at room temperature. After 4 h, the reaction mixture was filtered through a short pad of Celite, and the resulting solution was evaporated under reduced pressure. The obtained residue was purified by flash column chromatography (SiO$_2$, hexane/AcOEt = 5:1) to give **30** (52.9 mg, 85% yield) as a white solid. IR: ν 3352, 2933, 2856, 1730, 1509, 1448, 1370, 1240, 1168, 1121, 1038, 822 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.00–1.04 (m, 1H), 1.21–1.39 (m, 2H), 1.57–1.67 (m, 1H), 1.73–1.77 (m, 2H), 1.92–1.98 (m, 1H), 2.14–2.19 (m, 1H), 2.24–2.30 (m, 1H), 2.90 (broad peak (N*H*), 1H), 3.44 (dt, *J* = 4.4 Hz, 10.4 Hz, 1H), 3.60 (s, 3H), 3.73 (s, 3H), 6.59–6.62 (m, 2H), 6.72–6.76 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 24.6, 24.7, 29.0, 32.9, 50.9, 51.6, 55.5, 55.7, 114.6 (×2), 115.6 (×2), 141.2, 152.2, 175.4; EI-LRMS *m/z* 263 (M^+); $[\alpha]_D^{25} = +5.8$ (*c* 2.30, $CHCl_3$).

4.3.2. (1*S*,2*S*)-2-Benzyloxycarbonylaminocyclohexanecarboxylic acid methyl ester 31[6b]

To a stirred solution of **30** (100.1 mg, 0.38 mmol) in CH_3CN/H_2O (7.6 mL, 1:1, v/v) were added $HIO_4{\cdot}2H_2O$ (140 mg, 0.57 mmol) and 1 M aqueous H_2SO_4 (0.38 mL). The mixture was stirred for 18 h at room temperature, and then washed with CH_2Cl_2 (×3). After separation of the organic phase, the aqueous phase was brought to pH 11 by the addition of 1 M aqueous NaOH, and extracted with AcOEt (×3). The combined organic layers were evaporated under reduced pressure, and the obtained crude residue was used directly for the next reaction. To a stirred solution of crude sample and pyridine (40 μL, 0.54 mmol) in CH_2Cl_2 (1.1 mL) at 0 °C was added benzyl chloroformate (60 μL, 0.40 mmol) and the reaction mixture was stirred for 4 h at room temperature. The reaction mixture was diluted with AcOEt and washed with 1 M aqueous HCl and brine, and then dried over Na_2SO_4. After concentration in vacuo, the obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt = 5:1) to give (*S*,*S*)-**31** (56.3 mg, 2 steps 51% yield) as a white solid. Conditions of chiral HPLC analysis: DAICEL CHIRALPAK AD-H, hexane/2-propanol = 9:1, flow rate: 0.5 mL/min, t_R 33.2 min [(*S*,*S*)-isomer] and 35.2 min [(*R*,*R*)-isomer], detection at 254 nm).

4.3.3. (1*S*)-(2-Phenylcyclohex-2-enylamino)acetic acid ethyl ester 32[6a]

To a stirred solution of **5a** (74.3 mg, 0.26 mmol) in CH_3CN/H_2O (7.4 mL, 1:1, v/v) were added $HIO_4{\cdot}2H_2O$ (96.6 mg, 0.40 mmol) and 1 M aqueous H_2SO_4 (0.26 mL). The mixture was stirred for 18 h at room temperature, and then washed with CH_2Cl_2 (×3). After separation of the organic phase, the aqueous phase was brought to pH 11 by the addition of 1 M aqueous NaOH, and was extracted with AcOEt (×3). The combined organic layers were evaporated under reduced pressure, and the obtained crude residue was used directly for the next reaction. To a stirred solution of crude sample and triethylamine (20 μL, 0.12 mmol) in THF (0.5 mL) at room temperature was added ethyl bromoacetate (10 μL, 0.10 mmol), and the reaction mixture was stirred for 3 h at the same temperature. After concentration of the reaction mixture in vacuo, the residue was purified by flash column chromatography (SiO_2, hexane/AcOEt = 10:1 to 7:1) to give (*S*)-**32** (16.7 mg, 2 steps 24% yield) as yellow oil. Conditions of chiral HPLC analysis: DAICEL CHIRALPAK AD, hexane/2-propanol = 98:2, flow rate: 0.4 mL/min, t_R 19.0 min [(*S*)-isomer] and 22.8 min [(*R*)-isomer], detection at 254 nm).

4.3.4. (1*R*)-Benzyl-(1,3-diphenylallyl)-(4-methoxyphenyl)amine 33

To a stirred solution of **25** (31.0 mg, 0.10 mmol) in DMF (0.5 mL) at room temperature were added K_2CO_3 (20.4 mg, 0.15 mmol) and benzyl bromide (20 μL, 0.15 mmol). After being stirred for 18 h, the reaction was diluted with Et_2O, washed with water and brine, and then dried over Na_2SO_4. After concentration in vacuo, the obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt = 20:1) to give (*R*)-**33** (37.7 mg, 95% yield) as a colorless oil. IR: ν 3413, 3026, 2830, 1599, 1507, 1450, 1421, 1285, 1215, 1158, 1043, 973, 805, 747, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.68 (s, 3H), 4.43 (d, *J* = 16.8 Hz, 1H), 4.52 (d, *J* = 16.8 Hz, 1H), 5.45 (d, *J* = 6.0 Hz, 1H), 6.45–6.48 (m, 2H), 6.69–6.72 (m, 2H), 6.75–6.78 (m, 2H), 7.14–7.39 (m, 15H); ^{13}C NMR ($CDCl_3$): δ 53.2, 55.5, 66.9, 114.2 (×2), 118.5 (×2), 126.4, 126.4 (×2), 127.1, 127.2 (×2), 127.5, 127.9 (×2), 128.2 (×2), 128.4 (×2), 128.5 (×2), 128.9, 132.7, 136.8, 139.9, 141.0, 143.1, 152.7; EI-LRMS *m/z* 405 (M^+); $[\alpha]_D^{26} = +1.68$ (*c* 0.25, $CHCl_3$). Conditions of chiral HPLC analysis: DAICEL CHIRALPAK AD-H, hexane/2-propanol = 93:7, flow rate: 0.5 mL/min, t_R 9.9 min [(*S*)-isomer] and 10.2 min [(*R*)-isomer], detection at 254 nm).

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10. The ratio of *p*-anisidine and BSA affected the yield and enantioselectivity of the reactions when using **2** and **4**. Although both reactions proceeded using 0.5 or 1 equiv of BSA to the electrophile, there was a decrease in enantioselectivity compared with the case using 3 equiv of BSA to the electrophile (1 equiv to *p*-anisidine).
11. For mechanistic studies on the catalyst structure of the Pd–DIAPHOX catalyst system, see Ref. 7b.
12. When the asymmetric allylic amination of **2** was performed using *N*-tosyl-protected *p*-anisidine as a nucleophile [conditions: Pd catalyst (2 mol %), (S,R_P)-**1a** (4 mol %), BSA (3 equiv), nucleophile (3 equiv), CH_3CN, 0 °C], the product was obtained with lower enantioselectivity (2 h, 92% yield, 61% ee.).
13. When the asymmetric allylic amination of **24** with *p*-anisidine was performed using catalytic amount of DABCO, there was a decrease in reactivity without significant loss of enantioselectivity [conditions: Pd catalyst (2 mol %), (S,R_P)-**1a** (4 mol %), BSA (3 equiv), *p*-anisidine (3 equiv), Et_2O, rt]. DABCO = 100 mol %, 17 h, 99%, 97% ee. DABCO = 10 mol %, 24 h, 75%, 95% ee. DABCO = 5 mol %, 24 h, 29%, 92% ee. Although the role of DABCO is unknown at the present stage, these data indicate that DABCO would interact with *p*-anisidine, rather than the Pd catalyst, resulting in an increase in both reactivity and enantioselectivity.
14. Partial decarboxylative decomposition occurred when asymmetric allylic amination of **2** or **4** with *p*-anisidine was performed in the presence of DABCO.
15. Verkade, J. M. M.; van Hemert, L. J. C.; Quaedflieg, P. J. L. M.; Alsters, P. L.; van Delft, F. L.; Rutjes, F. P. J. T. *Tetrahedron Lett.* **2006**, *47*, 8109.
16. For the conditions of chiral HPLC analysis, see Section 4.
17. Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575.