Journal Pre-proof

Carbamate-based *P*,*O*-ligands for asymmetric allylic alkylations

Ádám Márk Pálvölgyi, Michael Schnürch, Katharina Bica-Schröder

PII: S0040-4020(20)30388-4

DOI: https://doi.org/10.1016/j.tet.2020.131246

Reference: TET 131246

To appear in: *Tetrahedron*

Received Date: 29 March 2020

Revised Date: 22 April 2020

Accepted Date: 25 April 2020

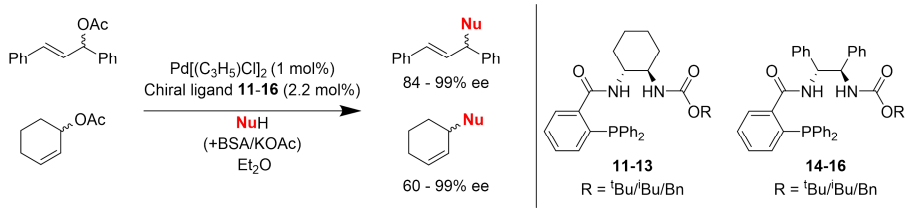
Please cite this article as: Pálvölgyi ÁáMá, Schnürch M, Bica-Schröder K, Carbamate-based *P*,*O*-ligands for asymmetric allylic alkylations, *Tetrahedron* (2020), doi: https://doi.org/10.1016/j.tet.2020.131246.

Graphical Abstract

Carbamate-based *P,O*-ligands for asymmetric allylic alkylations

Leave this area blank for abstract info.

Ádám Márk Pálvölgyi, Michael Schnürch and Katharina Bica-Schröder*
Institute of Applied Synthetic Chemistry, Vienna University of Technology, Getreidemarkt 9/163, A-1060, Vienna, Austria



Tetrahedron
journal homepage: www.elsevier.com

Carbamate-based *P,O*-ligands for asymmetric allylic alkylations

Ádám Márk Pálvölgyi[a], Michael Schnürch[a] and Katharina Bica-Schröder[a] *

[a]*Institute of Applied Synthetic Chemistry, Vienna University of Technology, Getreidemarkt 9/163, A-1060, Vienna, Austria*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Chiral *P,O*-ligands
Tsuji-Trost reaction
Asymmetric synthesis
Palladium-catalyzed allylation

ABSTRACT

Herein we report the design and successful catalytic application of modified *Trost*-ligands in asymmetric allylic alkylation (AAA) reactions. A small set of carbamate-monophosphine *P,O*-ligands has been prepared in a straightforward two-step synthetic procedure. After optimization of the reaction conditions, high catalytic activities and excellent enantioselectivity up to >99% have been attained.

* Corresponding author. e-mail: katharina.schroeder@tuwien.ac.at

1. Introduction

Highly functionalized and optically active allylic intermediates are invaluable building blocks for the total synthesis of numerous biologically active compounds.[1,2,3,4] In this field, palladium-catalyzed asymmetric allylic alkylation (AAA) provides a useful synthetic tool and thanks to its indisputable advantages, such as mild reaction conditions and operational simplicity, it is still one of the most relevant strategies for the synthesis of substituted allylic compounds.[5] The class of C_2-symmetric diamine-based chiral diphosphines, such as **1** and **2** have been already proven to be really efficient ligands for asymmetric allylic alkylation, resulting in high catalytic activities and excellent stereocontrol.[6]

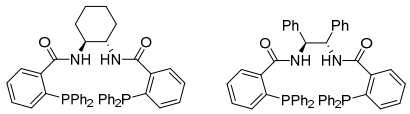


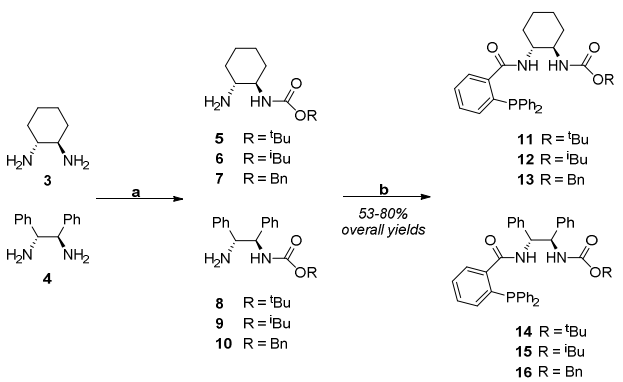
Figure 1. Typical *Trost*-type bidentate *P,P*-ligands for AAA reactions.

Despite the wide variety of other available chiral ligands including (bis)oxazolines,[7,8] amino acid-derived ligands,[9,10] or diphosphines featuring axial and planar chirality,[11,12,13,14] the *Trost*-type chiral diamine-based *P,P*-ligands still remain one of the most important tools in the field of asymmetric allylic alkylation. While such ligands have been already quite well studied, the chiral diamine-based monophosphine-analogues did not gain too much of attention. In 1994, *Trost* reported the first application of chiral diamine-based analogues bearing only one phosphine unit for asymmetric allylations, however low reactivities (20-50% yield) and poor enantioselectivity (< 20% ee) were observed.[15] Since then, only a few examples in the area of chiral diamine-based monophoshine ligands have been reported, but the enantio-selectivity could not be improved significantly in any case. In 2000, *Kim et al.* reported the synthesis of novel *P,N*-mono-phosphine ligands based on an (*R,R*)-1,2-diaminocyclohexane (*R,R*-DACH) core and in the absence of the second phosphine unit, they observed strong *P,N*- and *P,O*-chelation.[16] In contrast with the previous results, they could reach significantly higher enantio-selectivity (up to 75% ee), indicating that there is still potential in such diamine-based *P,N* and *P,O*-ligands for asymmetric allylic allylations.

Inspired by these results and based on our previous success with carbamate-based ligands in asymmetric transfer hydrogenations,[17] herein we report the synthesis and application of chiral diamine-based, carbamate-derived monophosphine ligands for asymmetric allylic allylations.

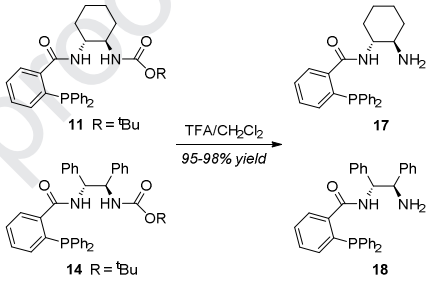
2. Results and Discussion

Starting from the cheap and easily accessible chiral pool of diamines **3-4**, a small library of carbamate-monophosphine ligands (**11-16**) has been prepared according to a straightforward two-step procedure (Scheme 1). At first, the chiral diamines have been reacted with the corresponding anhydride or chloroformate by using a temporary masking on one of the amino groups by means of HCl salt, resulting in the corresponding mono carbamate-protected intermediates as major products. These intermediates (**5-10**) have then been coupled with 2-(diphenylphosphino)-benzoic acid *via* simple DCC/DMAP coupling procedure, affording the chiral ligand **11-16** in good overall yields (Scheme 1).



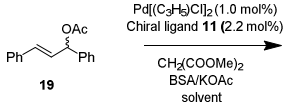
Scheme 1. Design of carbamate-based *P,O*-ligands. Reagents and conditions: (a) HCl, anhydride or chloroformate, anhydrous MeOH or EtOH, 0-25˚C (b) 2-PPh_2-PhCOOH, DCC/DMAP, anhydrous CH_2Cl_2, 0-25˚C.

In order to investigate whether the carbamate carbonyl group plays an important role in the complexation, the unprotected analogues of ligand **11** and **14** have also been synthesized (Scheme 2).



Scheme 2. Deprotection of carbamate ligands **11** and **14**

After the successful synthesis and characterization of the ligands, we investigated the asymmetric allylic alkylation of racemic (*E*)-1,3-diphenylallyl acetate (**19**) with dimethyl malonate as a benchmark reaction (Table 1). The initial screening aiming to find the most suitable solvent and base has been carried out by using 1.0 mol% of Pd-precursor and 2.2 mol% chiral ligand (**11**) at room temperature for 24 hours. As it can be seen from Table 1, ether-type solvents like THF and MTBE afforded the desired product **20a** with higher enantioselectivity than dichloromethane, without significantly effecting the catalytic activity (Table 1, entries 1 vs. 4-5.). To our delight, the product **20a** could be obtained in 93% isolated yield and excellent enantioselectivity (> 99% ee) by using diethyl ether as solvent in the presence of the chiral ligand **11** at room temperature (Table 1, entry 6.). Moreover, the reaction time could be also reduced to 6 hours without any loss in catalytic activity (Table 1, entries 6 vs. 7.).



Similarly, high enantioselectivity was observed in toluene albeit the catalytic activity was significantly decreased compared to those reactions in other solvents (Table 1, entries 6-7 vs. 8).

Table 1. Parameter optimization for the AAA reaction of the allylic acetate **19**.

Entry[a]	Solvent	Conversion (%)[b]	Yield (%)[b]	ee (%)[c]
1	CH_2Cl_2	98	95	49 (*R*)
2[d]	CH_2Cl_2	75	70	48 (*R*)
3	EtOAc	85	55	70 (*R*)
4	THF	91	89	73 (*R*)
5	MTBE	96	93	75 (*R*)
6	Et_2O	95	94 (93)	>99 (*R*)
7[e]	Et_2O	95	94 (93)	>99 (*R*)
8	Toluene	60	57	>99 (*R*)

[a] Performed with 0.50 mmol rac-(*E*)-1,3-diphenylallyl acetate (**19**) using 0.011 mmol (2.2 mol%) chiral ligand **11**, 0.005 mmol (1.0 mol%) $[Pd(C_3H_5)Cl]_2$, 0.60 mmol (1.2 equiv.) dimethyl malonate, 1.0 mmol (2.0 equiv.) BSA and 2 mg (2 mol%) KOAc in 1 mL solvent at 25°C for 24 hours.

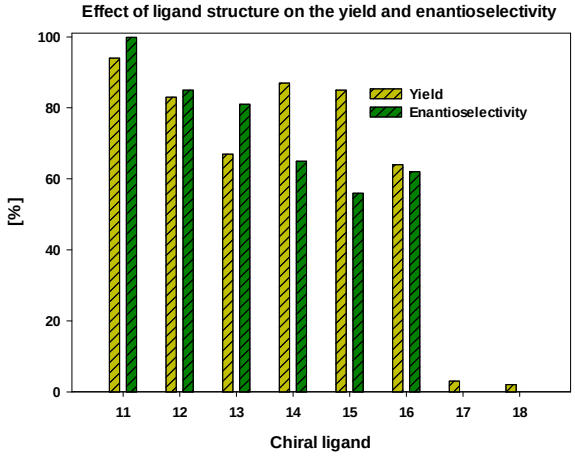
[b] Determined by GC analysis. Isolated yield in parenthesis.

[c] Determined by chiral HPLC analysis using Diacel Chiralcel IB column.

[d] Cs_2CO_3 instead of BSA/KOAc.

[e] Reaction time was 6 hours.

After determining the optimal reaction conditions, the catalytic efficiency of the chiral ligands was also evaluated

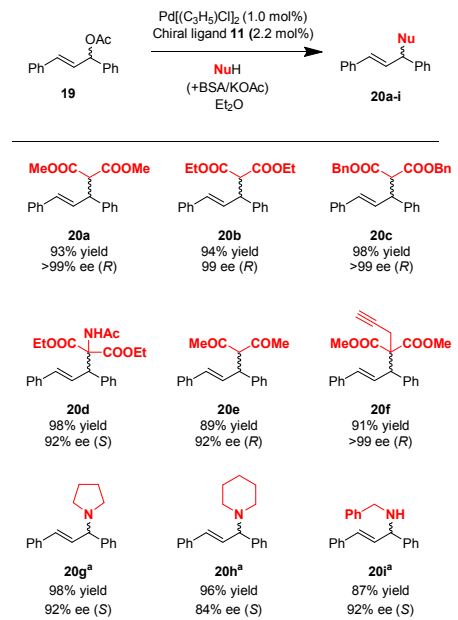


(Figure 2).

Figure 2. Catalyst screening for the AAA reaction of allylic acetate **19**. The reaction conditions and monitoring were identical to those used in Table 1, entry 7.

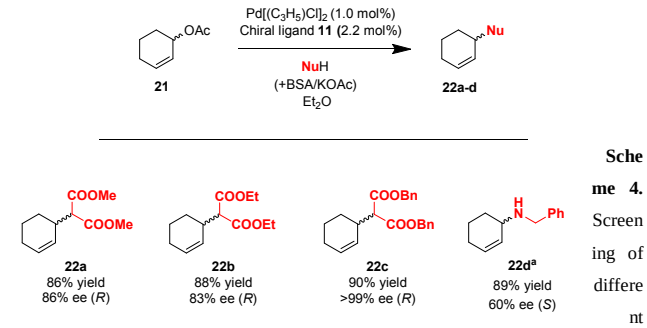
The catalyst screening revealed that the (*R*,*R*)-1,2-diamino-cyclohexane based ligands are in general superior over the (*R*,*R*)-1,2-diphenylethylenediamine analogues yielding the desired product **20a** with slightly higher yields and significantly higher enantiomeric excess (ligand **11**-**13** vs. **14**-**16**). Moreover, the presence of the bulky Boc-group was also found to be beneficial. Importantly, the compound **17** and **18** – the corresponding amino-monophosphine analogues of ligand **11** and **14** – gave basically no product under identical conditions, indicating that the presence of the carbamate unit is indeed crucial for the complex formation.

Encouraged by these results, a series of different nucleophiles have been successfully applied for the asymmetric allylic alkylation of the racemic (*E*)-1,3-diphenylallyl acetate (**19**) under the previously optimized reaction conditions. As it can be seen from Scheme 3, the corresponding products could be obtained with high isolated yields (87-98%) and excellent stereocontrol (84 - >99%). While the *C*-allylated products have been formed mainly in (*R*)-configuration, interestingly the reaction with diethyl-acetamido-malonate resulted in the formation of the (*S*)-**20d** as a major product, indicating that the *-NHAc* group might alter the chelation mode during the reaction. The high catalytic activity and selectivity were eventually retained by using *N*-nucleophiles as well, affording the amines **20g-i** in high yields and 84-92% ee. For all amine products, the (*S*)-enantiomer has been predominantly formed.

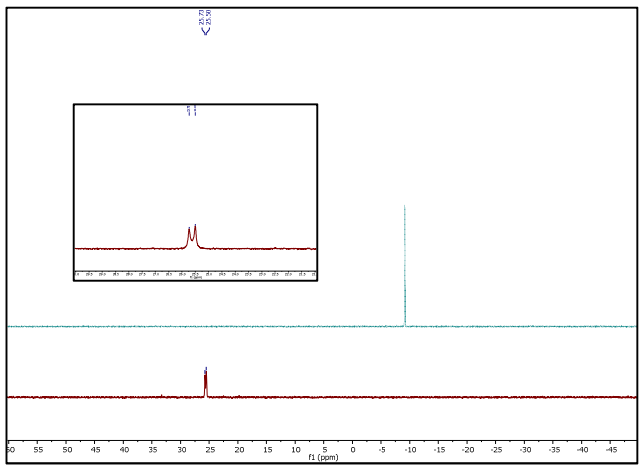


Scheme 3. Screening of different nucleophiles for the AAA reaction of allylic acetate **19** by using 0.50 mmol substrate, 0.011 mmol (2.2 mol%) chiral ligand **11**, 0.005 mmol (1.0 mol%) $[Pd(C_3H_5)Cl]_2$, 0.60 mmol (1.2 equiv.) nucleophile, 1.0 mmol (2.0 equiv.) BSA and 2 mg (2 mol%) KOAc in 1 mL Et_2O at 25°C for 6 hours. Yields refer to the pure products after preparative TLC/column chromatography. Enantiomeric excess values have been determined by chiral HPLC analysis. Absolute configuration was determined by comparison of the optical rotation with literature data. [a] Without BSA/KOAc.

Eventually, we further expanded our reaction scope with the asymmetric allylic alkylation of racemic 3-acetoxy-1-cyclohexene (**21**). By using diphenyl malonate as nucleophile, the product **22c** could be isolated in high yield and excellent enantiopurity (>99% ee), while the other products could be also obtained in good yields and moderate to good enantioselectivity (Scheme 4).



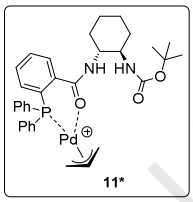
Scheme 4. Screening of different



nucleophiles for the AAA reaction of allylic acetate **21** by using 0.50 mmol substrate, 0.011 mmol (2.2 mol%) chiral ligand **11**, 0.005 mmol (1.0 mol%) $[Pd(C_3H_5)Cl]_2$, 0.60 mmol (1.2 equiv.) nucleophile, 1.0 mmol (2 equiv.) BSA and 2 mg (2 mol%) KOAc in 1 mL Et_2O at 25 °C for 24 hours. Yields refer to the pure products after column chromatography. Enantiomeric excess values have been determined by chiral HPLC analysis. Absolute configuration was determined by comparison of the optical rotation with literature data. [a] Without BSA/KOAc.

In order to get more insight into the chelation mode, $^{31}P\{^1H\}$ NMR analysis of the *in-situ* formed (π-allyl)Pd complex **11*** was carried out by using 1.0 equivalent of $[Pd(C_3H_5)Cl]_2$ and 2.0 equivalents of chiral ligand **11** (Pd/L* = 1). As shown in Figure 3, only one doublet of the complex at δ = 25.6 ppm with a coupling constant of $^2J(P,O)$ = 37.1 Hz was formed. This indicates, that basically only one type of chelation takes place and there is no competition between the different complexation modes which can be sometimes observed with the *P,P*-bidentate *Trost* ligands.[18] Based on the literature, the major complex should have a *P,O*-chelation motif in which the carboxamide oxygen acts as an *O*-ligand. While there is no direct proof for the carbamate unit participating in the chelation mode; based on the results, its presence is certainly crucial in order to reach high enantioselectivity.

Figure 3. $^{31}P\{^1H\}$ NMR spectra of the pure chiral ligand **11** (top, green), and the *in-situ* formed (π-allyl)Pd complex **11*** (bottom, red) showing only one major chelation mode.



3. Conclusion

Herein, we have reported the synthesis and application of carbamate-based *P,O*-ligands for palladium-catalyzed asymmetric allylic alkylation. After optimization of the catalyst structure and reaction conditions, the chiral ligand **11** bearing a bulky Boc-protecting group could be successfully applied for the AAA reaction of an aromatic and an aliphatic model substrate by using a series of different *C*- and *N*-nucleophiles. High isolated yields and excellent stereocontrol could be attained for all products of racemic (*E*)-1,3-diphenylallyl acetate (**19**), while moderate to excellent enantioselectivities were obtained in the AAA reaction of racemic 3-acetoxy-1-cylohexene (**21**).

4. Experimental section

4.1. General remarks

All reagents were purchased from commercial suppliers and used without further purification unless noted otherwise. Solvents intended for anhydrous reactions were pre-distilled and desiccated on Al_2O_3 columns (PURESOLV, Innovative Technology). Chromatography solvents were distilled prior to use. Column chromatography was performed on standard manual glass columns using silica gel from Merck (40-63 µm). TLC-analysis was carried out using precoated and aluminum-backed plates purchased from Merck (silica gel 60 F_{254}). UV active compounds were detected at 254 nm, while non-UV active compounds were detected by using potassium permanganate solution as staining agent. ^1H, ^{13}C and ^{31}P NMR spectra were recorded from $CDCl_3$ and MeOD solutions on a Bruker AC 200 (200 MHz) or Bruker Advance UltraShield 400 (400 MHz) spectrometer and chemical shifts (δ) are reported in ppm, using tetramethylsilane as internal standard. Coupling constants (*J*) are reported in Hertz (Hz). The following abbrevia-tions were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qvin. = qvintett, sex = sextet, m = multiplet, brs = broad singlet. Melting points above room tempe-rature were measured on an automated melting point system OPTI MELT of Stanford ResearchSystems and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Spectrum 65 FT IR spectrometer equipped with a specac MK II Golden Gate Single Reflection ATR unit. HR-MS analysis was carried out from methanol solutions (*c* = 10 ppm) by using an HTCPAL system auto sampler (CTC Analytics AG), an Agilent 1100/1200 HPLC with binary pumps, a degasser and a column thermostat (Agilent Technologies) and an Agilent 6230 AJS ESI-TOF mass spectrometer. Chiral HPLC analysis were carried out on a DIONEX UPLC, equipped with a PDA plus detector (190-360 nm) using Chiralcel Diacel IB, AS-H, OJ and OD columns (250 x 4.60 mm) as stationary phases. GC measurements have been performed on a Thermo Scientific Focus instrument, equipped with an FID detector using a BGB5 column. Optical rotation was measured on an Anton Paar MCP500 polarimeter at the specific conditions and the results have been compared to literature values. Concentrations are given in g / 100 ml.

*4.2. Synthesis of mono-protected carbamates (**5**-**10**)*

*4.2.1. tert-Butyl ((1R,2R)-2-aminocyclohexyl)carbamate (**5**)*

Prepared according to the modified literature procedure.[19] (1*R*,2*R*)-DACH (780 mg, 6.83 mmol, 1.0 equiv.) was dissolved in anhydrous MeOH (15 mL) and cooled *via* ice bath. 37% HCl (600 µL, 7.18 mmol, 1.05 equiv.) was diluted with 5 mL anhydrous MeOH, and it was added to the reaction mixture dropwise at 0 ˚C. The mixture was allowed to warm up, and it was stirred for 30 minutes. Then, di-*tert*-butyl dicarbonate (2.22 g, 10.25 mmol, 1.50 equiv.) in anhydrous MeOH (10 mL) was added dropwise at 0 ˚C. The mixture was stirred at room temperature for 4 hours. After evaporation of the MeOH, water was added, and the insoluble byproduct was filtered off. The aqueous layer was basified with 2 M NaOH, extracted with CH_2Cl_2 (4×), dried over Na_2SO_4 and concentrated *in vacuo*, affording compound **5** as a white solid, which was found to be pure without further purification (1.29 g, 88% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 4.43 (brs, 1H, N*H*COO), 3.13 (brs, 1H, C*H*-NHCOO), 2.32 (td, *J* = 10.2 Hz, 1H, C*H*-NH_2), 1.98 (t, *J* = 6.0 Hz, 2H, CH_2-CH), 1.70 (d, *J* = 6.02 Hz, 2H, CH_2-CH), 1.45–1.40 (m, 11H, C-(CH_3)$_3$, CH-NH_2), 1.28–1.07 (m, 4H, CH_2-CH_2); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 156.3 (NH*C*OO), 79.4 (*C*-(CH_3)$_3$), 57.9 (*C*H-NHCOO), 55.8 (*C*H-NH_2), 35.4 (*C*H_2-CH), 33.0 (*C*H_2-CH), 28.5 (C-(*C*H_3)$_3$), 25.3 (*C*H_2-CH_2), 25.2 (*C*H_2-CH_2).

*4.2.2. Isobutyl ((1R,2R)-2-aminocyclohexyl)carbamate (**6**)*

Prepared according to the procedure for the synthesis of compound **5** by using (1*R*,2*R*)-DACH (456 mg, 4.0 mmol, 1.0 equiv.), 37% HCl (351 µL, 4.2 mmol, 1.05 equiv.), isobutyl chloroformate (778 µL, 6.0 mmol, 1.50 equiv.) and anhydrous MeOH (10 + 5 + 10 mL) to afford product **6** as a light brown solid, which was found to be pure without further purification (705 mg, 82% yield). **M.p.:** 100-101 °C; **HRMS (ESI-TOF) m/z:** $[M+H]^+$ calculated for $C_{11}H_{23}N_2O_2$ 215.1760, found 215.1762; **α_D^{20}:** +10.5 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3358 (N-H ν), 2904 (C-H ν), 16852 (C=O ν), 1607 (C-C ν), 1511 (N-H δ), 1437 (CH_2 δ); 1242 (C-O ν); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 4.65 (brs, 1H, N*H*COO), 3.82 (d, *J* = 8.0 Hz, 2H, CH_2-CH(CH_3)$_2$), 3.15 (brs, 1H, C*H*-NHCOO), 2.33 (td, *J* = 10.2 Hz, 1H, C*H*-NH_2), 2.00–1.92 (m, 3H, CH_2-CH, CH_2-C*H*(CH_3)$_2$), 1.71–1.68 (m, 2H, CH_2-CH), 1.24–1.02 (m, 6H, CH_2-CH_2, CH-

NH_2), 0.85 (d, *J* = 4.0 Hz, 6H, CH_2-CH(CH_3)$_2$); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 157.0 (NH*C*OO), 71.0 (CH_2-*C*H(CH_3)$_2$), 57.9 (*C*H-NHCOO), 55.4 (*C*H-NH_2), 35.2 (CH_2-CH), 32.9 (CH_2-CH), 28.0 (CH_2-*C*H(CH_3)$_2$), 25.2 (CH_2-*C*H_2), 19.1 (CH_2-CH(*C*H_3)$_2$).

*4.2.3. Benzyl ((1R,2R)-2-aminocyclohexyl)carbamate (**7**)*

Prepared according to the literature procedure.[20] (1*R*,2*R*)-DACH (456 mg, 4.0 mmol, 1.0 equiv.) was dissolved in 10 mL anhydrous EtOH, and the solution of benzyl-phenyl-carbonate (790 µL, 4.0 mmol, 1.0 equiv.) in anhydrous EtOH (10 mL) was added dropwise at room temperature. The reaction mixture was stirred for 24 hours and the EtOH was removed *in vacuo*. 10 M HCl (960 µL) was added, the formed precipitate was filtered off and it was successively washed with diethyl ether (2×) and H_2O (2×). Then, it was treated with a solution of NaOH (355 mg) in H_2O (2.40 mL). In a few minutes, the precipitate was filtered off, and it was washed with H_2O (3×10 mL), affording compound **7** as an off-white solid, which was found to be pure without further purifications (655 mg, 66% yield). **^{1}H NMR (200 MHz, $CDCl_3$)δ:** 7.26–7.18 (m, 5H, *H*-arom), 4.99 (brs, 3H, arom-CH_2, C*H*-NHCOO), 3.11–3.01 (m, 1H, N*H*COO), 2.28 (td, *J* = 10.2 Hz, 1H, C*H*-NH_2), 1.91–1.78 (m, 2H, CH_2-CH), 1.60–1.57 (m, 2H, CH_2-CH), 1.26–0.95 (m, 6H, CH_2-CH_2, CH-NH_2);**^{13}C NMR (100 MHz, $CDCl_3$)δ:** 156.7 (NH*C*OO), 136.6 (*C*-arom), 128.5 (*C*-arom), 128.1 (*C*-arom), 66.7 (arom-*C*H_2), 58.2 (*C*H-NHCOO), 55.4 (*C*H-NH_2), 35.3 (*C*H_2-CH), 32.8 (*C*H_2-CH), 25.1 (*C*H_2-CH_2), 25.0 (*C*H_2-CH_2).

*4.2.4. tert-Butyl ((1R,2R)-2-amino-1,2-diphenylethyl)carbamate (**8**)*

Prepared according to the procedure for the synthesis of compound **5** by using (1*R*,2*R*)-DPEN (1.93 g, 9.1 mmol, 1.0 equiv.), 37% HCl (900 µL, 10.8 mmol, 1.05 equiv.), di-*tert*-butyl dicarbonate (2.93 g, 13.5 mmol, 1.50 equiv.) and anhydrous MeOH (30 + 15 + 15 mL). After the work-up, the obtained crude product was dissolved in ethyl acetate and the solid residue was removed over a patch of silica. The solvent was removed under reduced pressure to yield **8** as a white solid (2.18 g, 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.28–7.14 (m, 10H, *H*-arom), 5.80 (d, *J* = 8.51 Hz, 1H, C*H*-NHCOO), 4.77 (brs, 1H, N*H*COO), 4.24 (s, 1H, C*H*-NH_2), 1.37 (s, 2H, CH-NH_2), 1.22 (s, 9H, C-(CH_3)$_3$); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 155.9 (NH*C*OO), 142.4 (*C*-arom), 141.2 (*C*-arom), 128.7 (*C*-arom), 128.5 (*C*-arom), 127.6 (*C*-arom), 127.4 (*C*-arom), 127.0 (*C*-arom), 126.6 (*C*-arom), 79.4 (*C*-(CH_3)$_3$), 60.0 (*C*H-NHCOO, *C*H-NH_2), 28.5 (C-(CH_3)$_3$).

*4.2.5. Isobutyl ((1R,2R)-2-amino-1,2-diphenylethyl)carbamate (**9**)*

Prepared according to the procedure for the synthesis of compound **5** by using (1*R*,2*R*)-DPEN (2.36 mmol, 500 mg), 37% HCl (207 µL 2.48 mmol, 1.05 equiv.) and isobutyl chloroformate (460 µL, 3.54 mmol, 1.50 equiv.) and anhydrous MeOH (10 + 5 + 5 mL). After the work-up, the obtained crude product was purified by column chromatography (15 g silica, light petrol: ethyl acetate 1:1 + 1 V/V % Et_3N), affording **9** as a white powder (479 mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.31–7.18 (m, 10H, *H*-arom), 5.91 (d, *J* = 7.84 Hz, 1H, C*H*-NHCOO), 4.80 (brs, 1H, N*H*COO), 4.29 (s, 1H, C*H*-NH_2), 3.64 (s, 2H, CH_2-CH(CH_3)$_2$), 1.74 (s, 1H, CH_2-C*H*(CH_3)$_2$), 1.46 (brs, 2H, CH-NH_2), 0.78 (s, 5H, CH_2-CH(CH_3)$_2$), 0.52 (s, 1H, CH_2-CH(CH_3)$_2$); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 156.7 (NH*C*OO), 142.3 (*C*-arom), 141.1 (*C*-arom), 128.8 (*C*-arom), 128.7 (*C*-arom), 127.8 (*C*-arom), 127.6 (*C*-arom), 127.0 (*C*-arom), 126.6 (*C*-arom), 71.2 (CH_2-CH(CH_3)$_2$), 60.4 (*C*H-NHCOO), 60.0 (*C*H-NH_2), 28.2 (CH_2-*C*H(CH_3)$_2$), 19.2 (CH_2-CH(*C*H_3)$_2$).

*4.2.6. Benzyl ((1R,2R)-2-amino-1,2-diphenylethyl)carbamate (**10**)*

Prepared according to the synthesis of compound **7** by using (1*R*,2*R*)-DPEN (2.36 mmol, 500 mg), 10 mL anhydrous EtOH, and benzyl-phenyl-carbonate (2.36 mmol, 540 mg, 1.0 equiv.), affording the product **10** as an off-white solid (570 mg, 70% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.29–7.20 (m, 15H, *H*-arom), 6.05 (d, *J* = 7.24 Hz, 1H, C*H*-NHCOO), 4.91 (s, 2H, CH_2-arom), 4.83 (brs, 1H, N*H*COO), 4.29 (s, 1H, C*H*-NH_2), 1.32 (brs, 2H, CH-NH_2); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 156.3 (NH*C*OO), 142.3
(*C*-arom), 141.0 (*C*-arom), 136.9 (*C*-arom), 128.8 (*C*-arom),128.7 (*C*-arom) 128.2 (*C*-arom), 127.8 (*C*-arom), 127.6 (*C*-arom), 126.9 (*C*-arom), 126.6 (*C*-arom), 66.8 (*C*H_2-arom), 60.6 (*C*H-NHCOO), 60.0 (*C*H-NH_2).

*4.3. General procedure for the ligand synthesis (**11-16**)*

Compound **11-16** have been prepared according to the literature procedure.[16] To the solution of 2-(diphenylphosphino)benzoic acid (1.05 equiv.) in anhydrous CH_2Cl_2 at 0°C, DCC (2.0 mmol, 1.05 equiv.) was added and the mixture was stirred at 0˚C for 15 minutes. To this, the solution of monoprotected carbamate **5-10** (1.0 equiv.) and DMAP (0.1 equiv.) in anhydrous CH_2Cl_2 was slowly added at 0 °C. The mixture was allowed to warm up to room temperature and it was stirred overnight. The reaction mixture was cooled at 5˚C for 1 hour, filtered and washed with cold CH_2Cl_2 to remove the majority of the dicyclohexyl urea. The filtrate was successively washed with 0.5 M HCl (3×), sat. $NaHCO_3$ (3×) and water (2×). After evaporation of the solvent, the crude products were purified by column chromatography.

*4.3.1. tert-Butyl ((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido) -cyclohexyl)carbamate (**11**)*

Prepared from compound **5** following the general procedure on a 1.9 mmol scale. Flash column chromatography (silica gel, light petrol:ethyl-acetate 4:1) afforded **11** as a white solid (870 mg, 91% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.51 (brs, 1H, N*H*CO), 7.25–7.20 (m, 12H, *H*-arom), 6.86 (brs, 1H, *H*-arom), 6.38 (brs, 1H, *H*-arom), 4.74 (d, *J* = 8.0 Hz, 1H, N*H*COO), 3.61–3.58 (m, 1H, C*H*-NHCO), 3.29–3.26 (m, 1H, C*H*-NHCOO), 1.93 (d, *J* = 8.0 Hz, 1H, CH_{2a}-CH), 1.82 (d, *J* = 8.0 Hz, 1H, CH_{2b}-CH), 1.63 (brs, 1H, CH_{2a}-CH), 1.55 (brs 1H, CH_{2b}-CH), 1.31 (s, 9H, C-(CH_3)$_3$), 1.20–1.12 (m, 3H, CH_2-CH_{2a}), 0.92–0.88 (m, 1H, CH_2- CH_{2b}); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −9.15; **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 169.2 (NH*C*O), 156.9 (NH*C*OO), 141.1 (*C*-arom), 140.9 (*C*-arom), 137.8 (*C*-arom), 134.5 (*C*-arom), 134.2 (*C*-arom), 130.3 (*C*-arom), 128.7 (*C*-arom), 127.6 (*C*-arom), 79.7 (*C*-(CH_3)$_3$), 55.1 (*C*H-NHCO), 54.3 (*C*H-NHCOO), 33.0 (*C*H_2-CH), 32.4 (*C*H_2-CH), 28.6 (C-(*C*H_3)$_3$), 25.2 (*C*H_2-CH_2), 24.7 (*C*H_2-CH_2).

*4.3.2. Isobutyl ((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido)-cyclohexyl)carbamate (**12**)*

Prepared from compound **6** following the general procedure on a 1.4 mmol scale. Flash column chromatography (silica gel, light petrol: ethyl-acetate 4:1) afforded **12** as a white solid (610 mg, 87% yield). **M.p.:** 90-92 °C; **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calculated for $C_{30}H_{36}N_2O_3P$ 503.2464, found 503.2463; $\boldsymbol{\alpha_D^{20}}$: +35.5 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3332 (N-H ν), 2930 (C-H ν), 1680 (C=O ν), 1635 (C=O ν), 1526 (N-H δ), 1452 (C=C ν), 1432 (CH_2 δ); 1240 (C-O ν), 1150 (C-N ν), 743 (C-H arom δ), 695 (C-H arom δ); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.48 (brs, 1H, N*H*CO), 7.25–7.20 (m, 12H, *H*-arom), 6.88 (brs, 1H, *H*-arom), 6.16 (brs, 1H, *H*-arom), 5.01 (d, *J* = 8.0 Hz, 1H, N*H*COO), 3.73–

3.63 (m, 3H, C*H*-NHCO, CH_2-CH(CH_3)$_2$), 3.34–3.32 (m, 1H, C*H*-NHCOO), 1.87–1.85 (m, 1H, CH_2-C*H*(CH_3)$_2$), 1.82–1.80 (m, 2H, CH_2-CH), 1.65–1.50 (m, 2H, CH_2-CH), 1.26–1.11 (m, 4H, CH_2-CH_2), 0.81 (d, *J* = 8.0 Hz, 6H, CH_2-CH(CH_3)$_2$); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −9.78; **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 169.2 (NH*C*O), 157.3 (NH*C*OO), 141.2 (*C*-arom), 140.9 (*C*-arom), 137.6 (*C*-arom), 137.3 (*C*-arom), 136.4 (*C*-arom), 136.2 (*C*-arom), 133.7 (*C*-arom), 130.2 (*C*-arom), 128.4 (*C*-arom), 127.3 (*C*-arom), 71.0 (*C*H_2-CH(CH_3)$_2$), 55.0 (*C*H-NHCO), 54.0 (*C*H-NHCOO), 32.7 (*C*H_2-CH), 32.0 (*C*H_2-CH), 27.9 (CH_2-*C*H(CH_3)$_2$), 24.7 (*C*H_2-CH_2), 24.5 (*C*H_2-CH_2), 19.0 (CH_2-CH(*C*H_3)$_2$).

*4.3.3. Benzyl ((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido)-cyclohexyl)carbamate (**13**)*

Prepared from compound **7** following the general procedure on a 1.27 mmol scale. Flash column chromatography (silica gel, light petrol: ethyl-acetate 4:1) afforded **13** as a white solid (540 mg, 83% yield). **M.p.:** 101-103 °C; **HRMS (ESI-TOF) m/z:** $[M+H]^+$ calculated for $C_{33}H_{34}N_2O_3P$ 537.2307, found 537.2310; $\boldsymbol{\alpha_D^{20}}$: +30.1 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3301 (N-H ν), 2923 (C-H ν), 1691 (C=O ν), 1637 (C=O ν), 1529 (N-H δ), 1450 (C=C ν), 1436 (CH_2 δ); 1250 (C-O ν), 1158 (C-N ν), 743 (C-H arom δ), 694 (C-H arom δ); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.45 (brs, 1H, N*H*CO), 7.31–7.21 (m, 17H, *H*-arom), 6.94–6.92 (m, 1H, *H*-arom), 6.27 (d, *J* = 8.0 Hz, 1H, *H*-arom), 5.33 (d, *J* = 8.0 Hz, 1H, N*H*COO), 5.05 (s, 2H, arom-CH_2) 3.79–3.68 (m, 1H, C*H*-NHCO), 3.38–3.36 (m, 1H, C*H*-NHCOO), 2.05 (m, 1H, CH_{2a}-CH), 1.88–1.86 (m, 1H, CH_{2b}-CH), 1.71–1.69 (m, 2H, CH_2-CH), 1.25–1.22 (m, 3H, CH_2-CH_{2a}), 0.96–0.89 (m, 1H, CH_2-CH_{2b}); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −9.34; **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 169.5 (NH*C*O), 157.1 (NH*C*OO), 141.5 (*C*-arom), 141.0 (*C*-arom), 137.9 (*C*-arom), 136.7 (*C*-arom), 134.4 (*C*-arom), 134.2 (*C*-arom), 133.9 (*C*-arom), 133.8 (*C*-arom), 130.3 (*C*-arom), 128.8 (*C*-arom), 128.1 (*C*-arom), 127.5 (*C*-arom), 66.7 (arom-*C*H_2), 55.6 (*C*H-NHCO), 54.0 (*C*H-NHCOO), 32.9 (*C*H_2-CH), 32.2 (*C*H_2-CH), 24.9 (*C*H_2-CH_2), 24.8 (*C*H_2-CH_2).

*4.3.4. tert-Butyl((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido)-1,2-diphenylethyl)carbamate (**14**)*

Prepared from compound **8** following the general procedure on a 1.0 mmol scale. Flash column chromatography (silica gel, light petrol: ethyl-acetate 4:1) afforded **14** as a white solid (540 mg, 83% yield). **M.p.:** 110-112 °C; **HRMS (ESI-TOF) m/z:** $[M+H]^+$ calculated for $C_{38}H_{38}N_2O_3P$ 601.2620, found 601.2615; $\boldsymbol{\alpha_D^{20}}$: +44.7 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3318 (N-H ν), 2933 (C-H ν), 1682 (C=O ν), 1639 (C=O ν), 1526 (N-H δ), 1450 (C=C ν), 1241 (C-O ν), 1170 (C-N ν), 742 (C-H arom δ), 695 (C-H arom δ); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.67 (brs, 1H, N*H*CO), 7.34–6.90 (m, 25H, *H*-arom), 5.75 (d, *J* = 8.0 Hz, 1H, C*H*-NHCO), 5.26 (t, *J* = 8.0 Hz, 1H, C*H*-NHCOO), 4.92 (t, *J* = 12.0 Hz, 1H, N*H*COO), 1.36 (s, 9H, C-(CH_3)$_3$); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −11.15; **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 169.2 (NH*C*O), 156.4 (NH*C*OO), 141.1 (*C*-arom) 139.4 (*C*-arom), 138.4 (*C*-arom), 134.3 (*C*-arom), 134.2 (*C*-arom), 133.8 (*C*-arom), 133.5 (*C*-arom), 130.3 (*C*-arom), 128.7 (*C*-arom), 128.5 (*C*-arom), 128.4 (*C*-arom), 128.1 (*C*-arom), 127.6 (*C*-arom), 127.5 (*C*-arom), 79.8 (*C*-(CH_3)$_3$), 60.8 (*C*H-NHCO), 59.6 (*C*H-NHCOO), 28.4 (C-(*C*H_3)$_3$).

*4.3.5. Isobutyl ((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido)-1,2-diphenylethyl)carbamate (**15**)*

Prepared from compound **9** following the general procedure on a 1.0 mmol scale. Flash column chromatography (silica gel, light petrol: ethyl-acetate 4:1) afforded **15** as a white solid (505 mg, 78% yield). **M.p.:** 106-108 °C **HRMS (ESI-TOF) m/z:** $[M+H]^+$ calculated for $C_{38}H_{38}N_2O_3P$ 601.2620, found 601.2619 $\boldsymbol{\alpha_D^{20}}$: +43.4 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3321 (N-H ν), 2930 (C-H ν), 1680 (C=O ν), 1641 (C=O ν), 1530 (N-H δ), 1451 (C=C ν), 1243 (C-O ν), 1173 (C-N ν), 740 (C-H arom δ), 696 (C-H arom δ); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.74 (brs, 1H, N*H*CO), 7.49–7.33 (m, 20H, *H*-arom), 7.12–7.08 (m, 1H, *H*-arom), 7.08–6.89 (m, 3H, *H*-arom), 6.25 (d, *J* = 8.0 Hz, 1H, C*H*-NHCO), 5.45 (t, *J* = 8.0 Hz, 1H, C*H*-NHCOO), 5.09 (t, *J* = 12.0 Hz, 1H, N*H*COO), 3.91 (d, *J* = 6.0 Hz, 2H, CH_2-CH(CH_3)$_2$), 1.93 (brs, 1H, CH_2-C*H*(CH_3)$_2$), 1.38–1.34 (m, 1H, CH_2-CH(CH_3)$_2$), 0.99–0.96 (m, 5H, CH_2-CH(CH_3)$_2$); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −11.22; **^{13}C NMR (100 MHz, $CDCl_3$) δ:** 169.9 (NH*C*O), 157.3 (NH*C*OO), 141.4 (*C*-arom) 139.7 (*C*-arom), 138.2 (*C*-arom), 134.5 (*C*-arom), 134.1 (*C*-arom), 134.0 (*C*-arom), 133.8 (*C*-arom), 130.6 (*C*-arom), 128.9 (*C*-arom), 128.5 (*C*-arom), 127.8 (*C*-arom), 127.6 (*C*-arom) 71.5 (*C*H_2-CH(CH_3)$_2$), 61.7 (*C*H-NHCO), 59.4 (*C*H-NHCOO), 28.2 (CH_2-*C*H(CH_3)$_2$), 19.3 (CH_2-CH(*C*H_3)$_2$).

*4.3.6. Benzyl ((1R,2R)-2-(2-(diphenylphosphaneyl)benzamido)-1,2-diphenylethyl)carbamate (**16**)*

Prepared from compound **10** following the general procedure on a 1.0 mmol scale. Flash column chromatography (silica gel, light petrol: ethyl-acetate 4:1) afforded **16** as a white solid (505 mg, 75% yield). **M.p.:** 100-104 °C; **HRMS (ESI-TOF) m/z:** $[M+H]^+$ calculated for $C_{41}H_{36}N_2O_3P$ 635.2464, found 635.2466; $\boldsymbol{\alpha_D^{20}}$: +47.8 (*c* 1.0, $CHCl_3$); **IR (ν_{max}/cm^{-1}):** 3311 (N-H ν), 3010 (C-H ν), 1695 (C=O ν), 1630 (C-C ν), 1525 (N-H δ), 1450 (C=C ν), 1170 (C-N ν), 742 (C-H arom δ), 696 (C-H arom δ); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.44 (brs, 1H, N*H*CO), 7.21–7.03 (m, 26H, *H*-arom), 6.86 (brs, 1H, *H*-arom), 6.71 (d, *J* = 8.0 Hz, 2H, *H*-arom), 6.28 (d, *J* = 8.0 Hz, 1H, C*H*-NHCO), 5.24 (t, *J* = 8.0 Hz, 1H, C*H*-NHCOO), 4.99–4.85 (m, 3H, N*H*COO, CH_2-arom); **^{31}P NMR (167 MHz, $CDCl_3$)δ:** −11.16; **^{13}C NMR (100 MHz, $CDCl_3$) δ:** 169.8 (NH*C*O), 156.7 (NH*C*OO), 141.4 (*C*-arom) 139.4 (*C*-arom), 137.3 (*C*-arom), 136.8 (*C*-arom), 136.5 (*C*-arom), 134.3 (*C*-arom), 134.0 (*C*-arom), 133.8 (*C*-arom), 133.5 (*C*-arom), 130.4 (*C*-arom), 128.8 (*C*-arom), 128.6 (*C*-arom), 128.5 (*C*-arom), 128.3 (*C*-arom), 127.9 (*C*-arom), 127.8 (*C*-arom), 127.6 (*C*-arom), 127.5 (*C*-arom), 66.7 (*C*H_2-arom), 61.8 (*C*H-NHCO), 59.2 (*C*H-NHCOO).

*4.4. General procedure for ligand deprotection (**17**-**18**)*

Prepared according to the literature procedure.[16] To a solution of **17** or **18** (0.5 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (1.5 mL), trifluoroacetic acid (765 µL, 10.0 mmol, 20.0 equiv.) was added, and the reaction mixture was stirred at room temperature for 4 hours. Then, the mixture was poured onto saturated $NaHCO_3$ solution, and it was extracted with CH_2Cl_2 (4×). The crude product was purified by flash column chromatography. All data were in accordance with the literature.[16,21]

*4.4.1 N-((1R,2R)-2-aminocyclohexyl)-2-(diphenylphosphaneyl)-benzamide (**17**)*

The crude product was purified by column chromatography (silica gel, CH_2Cl_2: MeOH 30:1) affording **17** as a white solid (197 mg, 98% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.32 (brs, 1H, N*H*CO), 7.28–7.21 (m, 13H, *H*-arom), 6.92 (m, 1H, *H*-arom) 5.76 (d, *J* = 8.0 Hz, 1H, C*H*-NHCO), 3.59 (m, 1H, C*H*-NH_2), 2.19–2.14 (m, 1H, CH_{2a}-CH), 1.90–1.86 (m, 2H, CH_2-CH), 1.69–1.63 (m, 3H, CH_{2b}-CH, CH-NH_2), 1.26–1.21 (m, 3H, CH_{2a}-CH_2), 0.89–0.86 (m, 1H, CH_{2b}-CH_2).

*4.4.2 N-((1R,2R)-2-amino-1,2-diphenylethyl)-2-(diphenyl-phosphaneyl)benzamide (**18**)*

The crude product was purified by column chromatography (silica gel, CH_2Cl_2: MeOH 30:1) affording **18** as a white solid (240 mg, 96% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.45 (brs, 1H, N*H*CO), 7.31–7.18 (m, 21H, *H*-arom), 7.05 (d, *J* = 8.0 Hz, 2H, *H*-arom), 6.96 (brs, 1H, *H*-arom), 5.25 (dd, *J* = 8.0 Hz, 4.0 Hz, 1H, C*H*-NHCO), 4.28 (d, *J* = 4.0 Hz, 1H, C*H*-NH_2), 1.69 (brs, 2H, CH-NH_2).

4.5. Synthesis of the allylic acetates

*4.5.1. (±)-(E)-1,3-Diphenylallyl acetate (**19**)*

Prepared according to the literature procedure.[22] (±)-(*E*)-1,3-Diphenylallyl alcohol (28.6 mmol, 6.0 g, 1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (70 mL) and Et_3N (34.8 mmol, 4.83 mL, 1.22 equiv.) was added. The mixture was cooled to 0 °C *via* ice bath, and a solution of acetyl chloride (34.3 mmol, 2.46 mL, 1.20 equiv.) in anhydrous CH_2Cl_2 was ***slowly*** added. Then, the solution was allowed to warm up to room temperature and it was stirred for 4 hours. The reaction mixture was washed with 2 M NaOH (3×), water (2×) and brine (2×) successively, dried over Na_2SO_4, filtered and evaporated. The crude product was purified by *Kugelrohr* distillation (0.35 mBar, 150-170 °C) to obtain the product **19** as a light-yellow oil (6.84 g, 95% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.37–7.21 (m, 10H, *H*-arom), 6.56 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.37 (d, *J* = 8.0 Hz, 1H, arom-CH=C*H*), 6.27 (dd, *J* = 16.0 Hz, 4.0 Hz, 1H, arom-C*H*), 2.09 (s, 3H, CH_3-CO); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 170.3 (CH_3-*C*O), 139.5 (*C*-arom), 136.4 (arom-*C*H), 132.8 (arom-*C*H=CH), 128.9 (*C*-arom), 128.8 (*C*-arom), 128.4 (*C*-arom), 128.3 (*C*-arom), 127.7 (*C*-arom), 127.3 (arom-CH=*C*H), 126.9 (*C*-arom), 76.4 (arom-*C*H), 21.6 (*C*H_3-CO).

*4.5.2. (±)-3-Acetoxy-1-cyclohexene (**21**)*

Prepared according to literature procedure.[23] Freshly distilled 3-bromo-1-cyclohexene (30.3 mmol, 3.5 mL, 1.0 equiv.) was dissolved in acetone (60 mL). Glacial acetic acid (0.3 mol, 17.5 mL, 10.0 equiv.) was added, followed by the dropwise addition of Et_3N (0.31 mol, 43 mL, 10.2 equiv.) at 0 °C. The mixture was allowed to warm up and it was subsequently stirred at room temperature overnight. The solvent was removed *in vacuo* and the residue was dissolved in diethyl-ether. The organic layer was washed with 0.5 M HCl (3×), saturated $NaHCO_3$-solution (3×), brine (1×) and water (1×) successively, dried over Na_2SO_4 and concentrated *in vacuo*. Vacuum distillation (20 mBar, 85 °C) afforded product **21** as a colourless liquid (3.56 g, 84% yield). **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 5.96–5.93 (m, 1H, CH-C*H*=CH), 5.71–5.67 (m, 1H, CH-CH=C*H*), 5.26–5.23 (m, 1H, C*H*-CH=CH), 2.12–2.09 (m, 1H, CH_2-CH_{2a}-CH), 2.04 (s, 3H, CH_3-CO), 2.01–1.98 (m, 1H, CH_2-CH_{2b}-CH), 1.89–1.83 (m, 1H, CH_{2a}-CH_2-CH), 1.77–1.68 (m, 1H, CH_2-CH=CH), 1.66–1.60 (m, 1H, CH_{2b}-CH_2-CH); **^{13}C NMR (100 MHz, $CDCl_3$)δ:** 170.9 (CH_3-*C*O), 132.8 (CH-*C*H=CH), 125.8 (CH-CH=*C*H), 68.2 (*C*H-CH=CH), 28.4 (CH-*C*H_2-CH_2), 25.0 (*C*H_2-CH=CH), 21.5 (*C*H_3-CO), 19.0 (CH-CH_2-*C*H_2).

4.6. General procedure for the asymmetric allylic alkylation

A mixture of $[Pd(C_2H_5)Cl)]_2$ (1.83 mg, 0.005 mmol, 1.0 mol%) and the chiral ligand (0.011 mmol, 2.2 mol%) in 0.5 mL solvent was stirred for 30 minutes under argon atmosphere to form the active catalyst species. The allylic acetate (0.5 mmol, 1.0 equiv.) was dissolved in 0.5 mL solvent, and it was added to the reaction mixture. After an additional 10 minutes of stirring, the corresponding malonate or amine (0.60 mmol, 1.2 equiv.), and optionally BSA (250 µL, 1.0 mmol, 2.0 equiv.) and KOAc (2 mg, 2.0 mol%) were added. The mixture was stirred at room temperature. After completion, 5 mL diethyl ether was added. In case of *C*-allylation reactions the organic layer was washed with saturated NH_4Cl solution and water, dried over Na_2SO_4 and concentrated under reduced pressure. For the *N*-allylations, the reaction mixtures were simply concentrated *in vacuo*. The crude products were purified by column chromatography or preparative TLC.

*4.6.1. Dimethyl-(R,E)-2-(1,3-diphenylallyl)malonate (**20a**)[24]*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a colorless liquid (151 mg, 93% yield; >99% ee). $\boldsymbol{\alpha_D^{20}}$: +12.4 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.29–7.17 (m, 10H, *H*-arom), 6.45 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.30 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H, arom-CH=C*H*), 4.24 (dd, *J* = 12.0 Hz, 8.0 Hz, 1H, arom-C*H*), 3.91 (d, *J* = 12.0 Hz, 1H, C*H*($COOCH_3$)), 3.66 (s, 3H, $COOCH_3$), 3.47 (s, 3H, $COOCH_3$); **Chiral HPLC analysis:** (chiralcel IB column, ^{n}hexane : EtOH 99:1 V/V, 1.0 mL/min, 25 °C, UV 254 nm) t_R = 7.71 min (*R*).

*4.6.2. Diethyl-(R,E)-2-(1,3-diphenylallyl)malonate (**20b**)[24]*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a colorless oil (166 mg, 94% yield; 99% ee). $\boldsymbol{\alpha_D^{20}}$: +17.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.23–7.16 (m, 10H, *H*-arom), 6.44 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.28 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H, arom-CH=C*H*), 4.28–4.08 (m, 3H, arom-C*H*, $COOCH_2CH_3$), 3.91–3.85 (m, 3H, $COOCH_2CH_3$, C*H*($COOCH_2CH_3$)), 1.20 (t, *J* = 8.0 Hz, 3H, $COOCH_2CH_3$), 0.97 (t, *J* = 8.0 Hz, 3H, $COOCH_2CH_3$); **Chiral HPLC analysis:** (chiralcel IA column, ^{n}hexane : 2-propanol 90:10 V/V, 0.5 mL/min, 25 °C, UV 254 nm) t_R = 11.3 min (*R*), t_R = 13.5 min (*S*).

*4.6.3. Dibenzyl-(R,E)-2-(1,3-diphenylallyl)malonate (**20c**)[24]*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a colorless oil (233 mg, 98% yield; >99% ee). $\boldsymbol{\alpha_D^{20}}$: +7.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.27–7.22 (m, 18H, *H*-arom), 7.05 (d, *J* = 8.0 Hz, 2H, *H*-arom), 6.42 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.31 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H, arom-CH=C*H*), 5.11 (dd, *J* = 16.0 Hz, 12.0 Hz, CH_2-arom), 4.94 (dd, *J* = 16.0 Hz, 12.0 Hz, CH_2-arom), 4.30 (dd, *J* = 12.0 Hz, 8.0 Hz, 1H, arom-C*H*), 4.05 (d, *J* = 12.0 Hz, 1H, C*H*($COOCH_2Ph$); **Chiral HPLC analysis:** (chiralcel IA column, ^{n}hexane : 2-propanol 90:10 V/V, 0.5 mL/min, 25 °C, UV 254 nm) t_R = 21.0 min (*R*).

*4.6.4. Diethyl-(S,E)-2-acetamido-2-(1,3-diphenylallyl)malonate (**20d**)[25]*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a white solid (200 mg, 98% yield; 92% ee). $\boldsymbol{\alpha_D^{20}}$: +44.0 (*c* 1.0, EtOH); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.29–7.21 (m, 9H, *H*-arom), 7.16–7.12 (m, 1H, *H*-arom), 6.74 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H, arom-CH=C*H*), 6.56 (brs, 1H, N*H*), 6.27 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 4.75 (d, *J* = 12.0 Hz, 1H, arom-C*H*), 4.29–4.20 (m, 2H, $COOCH_2CH_3$), 4.13–3.99 (m, 2H, $COOCH_2CH_3$), 1.94 (s, 3H, CH_3-CO), 1.23 (t, *J* = 8.0 Hz, 1H, $COOCH_2CH_3$), 1.14 (t, *J* = 8.0 Hz, 3H, $COOCH_2CH_3$); **Chiral HPLC analysis:** (chiralcel IA column, ^{n}hexane : 2-propanol 90:10 V/V, 0.5 mL/min, 25 °C, UV 254 nm) t_R = 12.9 min (*S*), t_R = 15.1 min (*R*).

*4.6.5. (R,E)-3-(1,3-Diphenylallyl)pentane-2,4-dione (**20e**)[26]*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a white solid (130 mg, 95% yield; 92% ee). $\boldsymbol{\alpha_D^{20}}$: −11.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR**

(400 MHz, $CDCl_3$)δ: 7.32–7.18 (m, 10H, *H*-arom), 6.41 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.19–6.15 (m, 1H, arom-CH=C*H*), 4.33–4.31 (m, 2H, arom-C*H*, C*H*($COCH_3$)), 2.23 (s, 3H, $COCH_3$), 1.91 (s, 3H, $COCH_3$); **Chiral HPLC analysis:** (chiralcel OJ column, ^{n}hexane : 2-propanol 98:2 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R (major) = 37.3 min (*R*), t_R (minor) = 47.5 min (*S*).

*4.6.6. Dimethyl (R,E)-2-(1,3-diphenylallyl)-2-(prop-2-yn-1-yl)malonate (**20f**)*

Purification by preparative TLC (light petrol : ethyl-acetate 10:1, UV visualization) afforded the pure product as a light-yellow oil (165 mg, 94% yield; 99% ee). $\boldsymbol{\alpha_D^{20}}$: +15.2 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.34–7.19 (m, 10H, *H*-arom), 6.76 (dd, *J* = 16.0 Hz. 8.0 Hz, 1H, arom-CH=C*H*), 6.43 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 4.42 (d, *J* = 12.0 Hz, 1H, arom-C*H*), 3.76 (s, 3H, $COOCH_3$), 3.69 (s, 3H, $COOCH_3$), 2.80 (d, *J* = 20.0 Hz, 1H, $CHCCH_{2a}$), 2.62 (d, *J* = 20.0 Hz, 1H, $CHCCH_{2b}$), 2.11–2.09 (m, 1H, C*H*CCH_2); **Chiral HPLC analysis:** (chiralcel IA column, ^{n}hexane : 2-propanol 99:1 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R = 20.1 min (*R*).

*4.6.7. (S,E)-1-(1,3-diphenylallyl)pyrrolidine (**20g**)*[27]

Purification by preparative TLC (light petrol : ethyl-acetate 7:1, UV visualization) afforded the pure product as a yellow oil (129 mg, 98% yield; 92% ee). $\boldsymbol{\alpha_D^{20}}$: +4.1 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.35–7.12 (m, 10H, *H*-arom), 6.49 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.34 (dd, *J* = 16.0 Hz, 8.0 Hz, arom-CH=C*H*), 3.69 (d, *J* = 8.0 Hz, 1H, arom-C*H*), 2.50–2.49 (m, 2H, N-CH_2), 2.37–2.35 (m, 2H, N-CH_2), 1.73–1.69 (m, 2H, N-CH_2-CH_2), 1.51 (brs, 2H, N-CH_2-CH_2); **Chiral HPLC analysis:** (chirlacel OD column, ^{n}hexane : 2-propanol 99.5:0.5 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R = 10.1 min (*R*), t_R = 10.9 min (*S*).

*4.6.8. (S,E)-1-(1,3-diphenylallyl)piperidine (**20h**)*[27]

Purification by preparative TLC (light petrol : ethyl-acetate 7:1, UV visualization) afforded the pure product as a yellow oil (133 mg, 98% yield; 84% ee). $\boldsymbol{\alpha_D^{20}}$: +5.2 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.33–7.12 (m, 10H, *H*-arom), 6.45 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.26 (dd, *J* = 16.0 Hz, 8.0 Hz, arom-CH=C*H*), 3.74 (d, *J* = 8.0 Hz, 1H, arom-C*H*), 2.43–2.38 (m, 2H, N-CH_2), 2.30–2.25 (m, 2H, N-CH_2), 1.51–1.47 (m, 4H, N-CH_2-CH_2), 1.39–1.35 (m, 2H, N-$(CH_2)_2$-CH_2); **Chiral HPLC analysis:** (chiralcel OD column, ^{n}hexane : 2-propanol 99.5:0.5 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R = 9.6 min (*R*), t_R = 10.5 min (*S*).

*4.6.9. (S,E)-N-benzyl-1,3-diphenylprop-2-en-1-amine (**20i**)*[27]

Purification by preparative TLC (light petrol : ethyl-acetate 7:1, UV visualization) afforded the pure product as a light-yellow oil (131 mg, 87% yield; 92% ee). $\boldsymbol{\alpha_D^{20}}$: +29.5 (*c* 1.5, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.36 (d, *J* = 8.0 Hz, 2H, *H*-arom), 7.29–7.10 (m, 13H, *H*-arom), 6.50 (d, *J* = 16.0 Hz, 1H, arom-C*H*=CH), 6.24 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H, arom-CH=C*H*), 4.32 (d, *J* = 8.0 Hz, 1H, arom-C*H*), 3.71 (dd, *J* = 16.0 Hz, 12.0 Hz, 2H, arom-CH_2), 1.63 (brs, 1H, N*H*); **Chiral HPLC analysis:** (chirlacel OD column, ^{n}hexane: 2-propanol 99.5:0.5 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R = 24.66 min (*R*), t_R = 27.4 min (*S*).

*4.6.10. Dimethyl 2-(cyclohex-2-en-1-yl)malonate (**22a**)*[28]

Purification by column chromatography (light petrol : diethyl-ether 10:1, visualization by potassium permanganate stain) afforded the pure product as a colorless oil (91 mg, 86% yield; 86% ee). $\boldsymbol{\alpha_D^{20}}$: +35.2 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 5.80–5.76 (m, 1H, CH-C*H*=CH), 5.51 (d, *J* = 12.0 Hz, 1H CH-CH=C*H*), 3.73 (s, 6H, 2 x $COOCH_3$), 3.29 (d, *J* = 8.0 Hz, 1H, C*H*-CH=CH), 2.93–2.87 (m, 1H, C*H*$(COOCH_3)_2$), 2.00–1.97 (m, 2H, CH_2-CH), 1.79–1.73 (m, 2H, CH_2-CH_2-CH), 1.60–1.54 (m, 1H, CH_{2a}-$(CH_2)_2$-CH), 1.40–1.33 (m, 1H, CH_{2b}-$(CH_2)_2$-CH); **Chiral HPLC analysis:** (chiralcel AS-H column, ^{n}hexane : 2-propanol 95:5 V/V, 1.0 mL/min, 25 ºC, UV 220 nm) t_R = 6.6 min (*R*), t_R = 7.7 min (*S*).

*4.6.11. Diethyl 2-(cyclohex-2-en-1-yl)malonate (**22b**)*[28]

Purification by column chromatography (light petrol : diethyl-ether 10:1, visualization by potassium permanganate stain) afforded the pure product as a colorless oil (106 mg, 88% yield; 83% ee). $\boldsymbol{\alpha_D^{20}}$: +23.2 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 5.73–5.65 (m, 1H, CH-C*H*=CH), 5.48 (d, *J* = 12.0 Hz, 1H, CH-CH=C*H*), 4.13 (q, 4H, 2 x $COOCH_2CH_3$), 3.17 (d, *J* = 8.0 Hz, 1H, C*H*-CH=CH),2.87–2.77 (m, 1H, C*H*$(COOCH_2CH_3)_2$), 1.95–1.91 (m, 2H, CH_2-CH), 1.75–1.35 (m, 4H, CH_2-CH_2-CH, CH_{2a}-$(CH_2)_2$-CH, CH_{2b}-$(CH_2)_2$-CH), 1.20 (t, *J* = 12.0 Hz, 2 x $COOCH_2CH_3$); **Chiral HPLC analysis:** (chiralcel OJ column, ^{n}hexane : 2-propanol 98:2 V/V, 0.5 mL/min, 25 ºC, UV 220 nm) t_R = 10.5 min (*R*), t_R = 10.9 min (*S*).

*4.6.12. Dibenzyl 2-(cyclohex-2-en-1-yl)malonate (**22c**)*

Purification by column chromatography (light petrol : diethyl-ether 10:1, visualization by potassium permanganate stain) afforded the pure product (90% yield; 99% ee). $\boldsymbol{\alpha_D^{20}}$: +17.8 (*c* 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.34–7.29 (m, 10H, *H*-arom), 5.77–5.72 (m, 1H, CH-C*H*=CH), 5.53 (d, *J* = 12.0 Hz, 1H, CH-CH=C*H*), 5.15 (dd, *J* = 16. 0 Hz, 8.0 Hz, 4H, 2 x CH_2-arom), 3.39 (d, *J* = 8.0 Hz, 1H, C*H*-CH=CH), 2.99–2.91 (m, 1H, C*H*$(COOCH_2Ph)_2$), 1.98–1.94 (m, 2H, CH_2-CH), 1.77–1.66 (m, 2H, CH_2-CH_2-CH), 1.51–1.47 (m, 1H, CH_{2a}-$(CH_2)_2$-CH), 1.39–1.34 (m, 1H, CH_{2b}-$(CH_2)_2$-CH); **Chiral HPLC analysis:** (chiralcel IA column, ^{n}hexane : 2-propanol 90:10 V/V, 0.5 mL/min, 25 ºC, UV 254 nm) t_R = 10.8 min (*R*).

*4.6.13. (S)-N-Benzylcyclohex-2-en-1-amine (**22d**)*

Purification by column chromatography (light petrol: diethyl-ether 5:1, visualization by potassium permanganate stain) afforded the pure product as a light-yellow oil (84 mg, 89% yield; 60% ee). $\boldsymbol{\alpha_D^{20}}$: +1.8 (*c* 0.5, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)δ:** 7.25–7.17 (m, 5H, *H*-arom) 5.73–5.65 (m, 2H, CH-C*H*=CH, CH-CH=C*H*), 3.78 (dd, *J* = 16.0 Hz *J* = 8.0 Hz, 2H, CH_2-arom), 3.17–3.14 (m, 1H, C*H*-NH), 1.94–1.92 (m, 2H, CH_2-CH), 1.84–1.72 (m, 2H, CH_2-CH_2-CH), 1.70–1.65 (m, 1H, CH_{2a}-$(CH_2)_2$-CH), 1.52–1.40 (m, 1H, CH_{2b}-$(CH_2)_2$-CH); **Chiral HPLC analysis:** (chiralcel OD column, ^{n}hexane : 2-propanol 99.5:0.5 V/V, 1.0 mL/min, 25 ºC, UV 220 nm) t_R = 19.1 min (*S*), t_R = 21.1 min (*R*).

Acknowledge

Financial support by the Austrian Science Fund (project P29146-N34) is gratefully acknowledged.

Appendix A. Supplementary data

NMR spectra of all new and known chiral ligands and allylation products, chiral HPLC traces.

References

1. Yoshizaki, H.; Satoh, H.; Sato, Y.; Nukui, S.; Shibasaki, M.; Mori, M. *J. Org. Chem*. **1995**, *60*, 2016-2021.
2. Kobayashi, J.; Ishibashi, M.;Nakamura, H.; Ohizumi, Y. *Tetrahedron Lett.* **1986**, *27*, 5755-5758.
3. Trost, B. M.; Chisholm, J. D.; Wrobleski, S. J.; Jung, M. *J. Am. Chem. Soc*. **2002**, *124*, 12420-12421.
4. Trost, B. M.; Crawley, M. L. *Chem. Rev*. **2003**, *103*, 2921-2944.
5. For selected reviews, see:
   a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev*. **1996**, *96*, 395-422. b) Trost, B. M. *Tetrahedron*, **2015**, *71*, 5708-5733.
   c) Mohr, J. T.; Stoltz, B. M. *Chem-Asian J*. **2007**, *2*, 1486-1491.
   d) Poli, G.; Prestat, G.; Liron, F.; Kammerer-Pentier, C. *Top. Organomet. Chem.* **2011**, *38*, 1-64.
6. For selected advances with *P*,*P*-bidentate ligands, see:
   a) Trost, B. M.; Schroeder, G. M. *J. Am. Chem. Soc*. **1999**, *121*, 6759-6760.
   b) Trost, B. M.; Patterson, D. E.; Hembre, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 10834-10835.
   c) Trost, B. M.; Radinov, R.; Grenzer, E. M. *J. Am. Chem. Soc.* **1997**, *119*, 7879-7880.
   d) Trost, B. M. *Chem. Pharm. Bull*. **2002**, *50*, 1-14.
   e) Lu, Z.; Ma, S. *Angew. Chem. Int. Ed*. **2008**, *47*, 258-297.
7. Reeves, C. M.; Behenna, D. C.; Stotz, B. M. *Org. Lett.* **2014**, *16*, 2314-2317.
8. Mohr, J. T.; Behenna, D. C.; Harned, A. M.; Stoltz, B. M. *Angew. Chem. Int. Ed*. **2005**, *44*, 6924-6927.
9. Tanaka, Y.; Mino, T.; Akita, K; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2004**, *69*, 6679-6687.
10. Mahadik, G. S.; Hitchcock, S. R. *Tetrahedron: Asymmetry **2010**, 1*, 33-38.
11. Kuwano, R.; Uchida, K-I.; Ito, Y. *Org. Lett*. **2003**, *5*, 2177-2179.
12. Ogasawara, M.; Ngo, H. L.; Sakamoto, T.; Takashashi, T. *Org. Lett*. **2005**, *7*, 2881-2884.
13. Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron Lett.* **1996**, *44*, 7995-7998.
14. Liu, D.; Xie, F.; Zhang, W. *J. Org. Chem.* **2007**, *72*, 6992-6997.
15. Trost, B. M.; Breit, B.; Organ, M. G. *Tetrahedron Lett.* **1994**, *35*, 5817-5820.
16. Kim, Y. K.; Lee, S. J.; Ahn, K. H. *J. Org. Chem.* **2000**, *65*, 7807-7813.
17. Pálvölgyi, Á. M.; Bitai, J.; Zeindlhofer, V.; Schröder, C.; Bica, K. *ACS Sustainable Chem. Eng*. **2019**, *7*, 3414-3423.
18. Lloyd-Jones, G. C.; Stephen, S. C.; Fairlamb, I. J. S.; Martorell, A.; Dominguez, B.; Tomlin, P. M.; Murray, M; Fernandez, J. M.; Jeffery, J. C.; Riis-Johannes, T.; Guerziz, T. *Pure Appl. Chem.* **2004**, *76*, 589-601.
19. Lee, D. W.; Ha, H.; Lee, W. K. *Synth. Commun.* **2007**, *37*, 252-255.
20. Kucherenko, A. S.; Siyutkin, D. E.; Nigmatov, S. G.; Chizhov, A. O.; Zlotin, S. G. *Adv. Synth. Catal*. **2012**, *16*, 3078-3086.
21. Xiong, Y; Du, Z.; Chen, H.; Yang, Z.; Tan, Q.; Zhang, C.; Zhu, L.; Zhang, M. *J. Am. Chem. Soc*. **2019**, *141*, 961-971.
22. Watson, I. D. G.; Styler, S.A.; Yudin, A. K. *J. Am. Chem. Soc.* **2004**, *126*, 5086-5087.
23. Fuchs, S.; Berl, V.; Lepoittevin, J-P. *Eur. J. Org. Chem.* **2007**, 1145-1152.
24. Du, X.; Liu, H.; Du, D.- M. *Eur. J. Org. Chem.* **2010**, 786-793.
25. Von Matt, P.; Pfaltz, A. *Angew. Chem.* **1993**, *105*, 614-615.
26. Blay, G.; Cardona, L.; Pedro, J. R. *Chem. Eur. J*. **2012**, *18*, 12966-12969.
27. Smyth, D.; Tye, H.; Eldred, C.; Alcock, N.W.; Wills, M. *J. Chem. Soc. Perkin Trans.* **2001**, 2840-2849.
28. Ma, J.; Li, C.; Zhang, D.; Lei, Y.; Li, M.; Jiang, R.; Chen, W. *RSC Adv*. **2015**, *5*, 35888-35892.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: