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A versatile synthesis of chiral β-aminophosphines†

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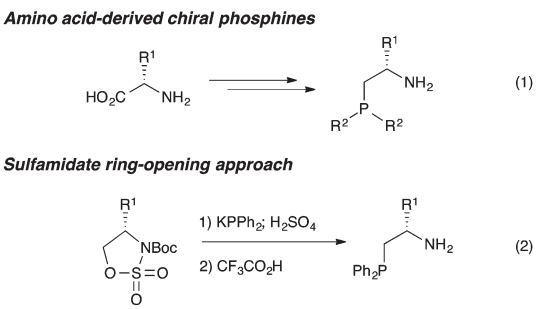
A method for the preparation of chiral β-aminophosphines having substituted *P*-aryl groups is described. Ring-opening of cyclic sulfamidates with metal diarylphosphinites yields β-aminophosphine oxides, which are then reduced to the corresponding phosphines. Effects of the diarylphosphinite countercation on the regioselectivity of the ring-opening reaction (*P- versus O*-alkylation) are discussed. This method enables the introduction of electron-deficient, electron-rich and sterically hindered diarylphosphino groups, as demonstrated by the synthesis of a series of novel, *P*-aryl-substituted β-aminophosphines derived from *tert*-leucinol, valinol and phenylglycinol. Access to these derivatives will create new opportunities for steric and electronic tuning of β-aminophosphine-derived chiral ligands and organocatalysts.

Introduction

Enantioenriched β-aminophosphines are versatile building blocks that have been employed in modular syntheses of chiral ligands and organocatalysts. Transition metal complexes of chiral β-aminophosphine-based ligands are useful for enantioselective cross-couplings,[1] hydrosilylations,[2] hydrogenations,[3] allylic substitutions[4] and conjugate additions,[5,6] while bifunctional, β-aminophosphine-derived organocatalysts have been applied in enantioselective aldol,[7] Morita–Baylis–Hillman[8] and related reactions.[9,10] An advantage of β-aminophosphines in these applications is their straightforward synthesis from readily available, chiral β-aminoalcohols, including those derived from amino acids. This enables variation of the substituent R^1 on the amine-bearing chirality center (Scheme 1, eqn (1)), the identity of which often has a significant influence on the enantioselectivity of the derived catalysts. In contrast, modification of the phosphorus-bearing substituents R^2 has largely been ignored in catalyst structure–activity relationships, despite the significant electronic and steric effects that could be anticipated. Herein, we describe a protocol for the synthesis of chiral, amino acid-derived β-aminophosphines that is compatible with the introduction of a range of phosphorus substituents R^2. The scope of this protocol is demonstrated through the preparation of several novel derivatives having electron-deficient, electron-rich and sterically hindered diarylphosphino groups.



Scheme 1 Approaches to the synthesis of chiral β-aminophosphines.

Results and discussion

Several approaches to the synthesis of enantioenriched β-aminophosphine derivatives have been explored, including substitution and aziridine ring-opening reactions using phosphorus-centered nucleophiles,[1,4,11,12] reductions of phosphonium-substituted enamines[13] and conjugate additions of amines to phosphorus-substituted alkenes.[14] For the class of β-aminoalcohol-derived phosphines shown in Scheme 1, the most commonly employed synthetic method involves the ring-opening of a cyclic sulfamidate by a metal phosphide (eqn (2)).[15]

The preparation of derivatives having substituted diarylphosphino groups has not been reported, and we encountered challenges in our attempts to make this extension. Whereas potassium diphenylphosphide is commercially available, accessing substituted diarylphosphides is less straightforward, as it generally requires the synthesis and handling of air-sensitive secondary diarylphosphines. For example, we prepared potassium bis(4-(trifluoromethyl)phenyl)phosphide by a three-step route consisting of: (i) synthesis of the corresponding secondary phosphine oxide **1a**; (ii) reduction of the phosphine

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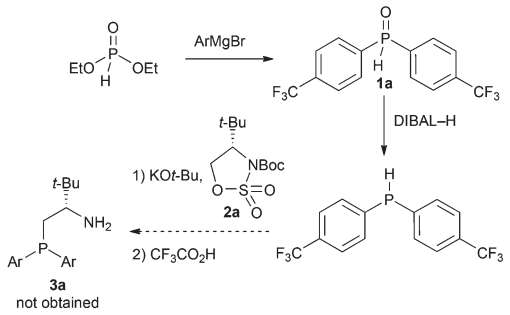
†Electronic supplementary information (ESI) available: Copies of ^{1}H, ^{13}C and ^{31}P NMR spectra of all new compounds. See DOI: 10.1039/c5ob02439k



Scheme 2 Attempted synthesis of a β-aminophosphine from a substituted diarylphosphine (Ar = 4-$CF_3C_6H_4$).

oxide with diisobutylaluminum hydride (DIBAL-H);[16] and (iii) deprotonation of the obtained secondary phosphine with potassium *tert*-butoxide. Subjecting this substituted phosphide to the sulfamidate ring-opening/*tert*-butoxycarbonyl (Boc) cleavage protocol[15] using *tert*-leucinol derivative (*S*)-**2a** led to a complex mixture of products, as judged by ^{31}P nuclear magnetic resonance (NMR) spectroscopy (Scheme 2). The observed chemical shifts were consistent with the presence of phosphine oxide derivatives, and a signal corresponding to the desired substituted β-aminophosphine **3a** was not evident in the spectrum. We note that we were able to obtain the unsubstituted diphenylphosphino derivative smoothly according to the reported protocol, regardless of whether the potassium diphenylphosphide was obtained from a commercial source or synthesized from diphenylphosphine oxide. It thus appears that the presence of the electron-withdrawing trifluoromethyl substituents has a deleterious effect on this β-aminophosphine synthesis.

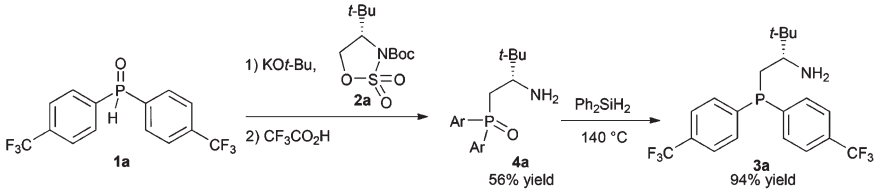
We reasoned that several advantages could arise from the use of a metal diarylphosphinite, rather than a metal diarylphosphide, as nucleophile in the sulfamidate ring-opening reaction. By deferring the reduction of the phosphine oxide until the final step of the process, such a route would minimize the handling of oxidation-prone intermediates, and would avoid the generation of the sensitive diarylphosphine intermediate entirely.[17,18] In situations where steric or electronic effects of the arylphosphine substituents resulted in a less efficient sulfamidate ring-opening, the higher stability towards purification (*e.g.*, by silica gel chromatography) of the phosphine oxides relative to the phosphines could be a decisive advantage. To test this idea, we treated secondary phosphine oxide **1a** with potassium *tert*-butoxide and sulfamidate (*S*)-**2a** in degassed THF under argon, followed by trifluoroacetic acid in dichloromethane to remove the Boc group (Scheme 3). The chiral β-aminophosphine oxide product **4a** was generated in 56% isolated yield over the two steps, after purification by flash chromatography on silica gel. Reduction of **4a** to the corresponding phosphine **3a** was accomplished in 94% yield by heating to 140 °C in diphenylsilane.[19]

While extending this protocol to the synthesis of other substituted derivatives, we observed the formation of an *O*-alkylated regioisomer from certain secondary diarylphosphine oxide/sulfamidate combinations (Scheme 4). In particular, a significant amount of phosphinate side product was observed when di-*ortho*-tolyl-substituted **1c** was used as the pro-nucleophile (eqn (1)). Presumably, the bulky aryl substituents hindered the desired *P*-alkylation reaction to the extent that *O*-alkylation became competitive, with oxidation to the phosphinate taking place upon workup. Using NaO*t*-Bu in place of KO*t*-Bu for this coupling provided inferior selectivity for *P- versus O*-alkylation, as judged by analysis of the unpurified reaction mixtures by ^{31}P NMR spectroscopy. However, the opposite trend – NaO*t*-Bu giving a higher preference for *P*-alkylation than KO*t*-Bu – was observed in the coupling of **1a** with valinol-derived sulfamidate (*S*)-**2b** (eqn (2)). In any event, case-by-case optimization of the metal counterion enabled us to accomplish ring-opening reactions of sulfamidates **2a–2c** using diarylphosphinites bearing electron-rich, electron-deficient and sterically hindered substituents (Scheme 5). Each of the obtained phosphine oxides (**4b–4h**) was reduced smoothly to the corresponding phosphine (**3b–3h**) using Ph_2SiH_2.

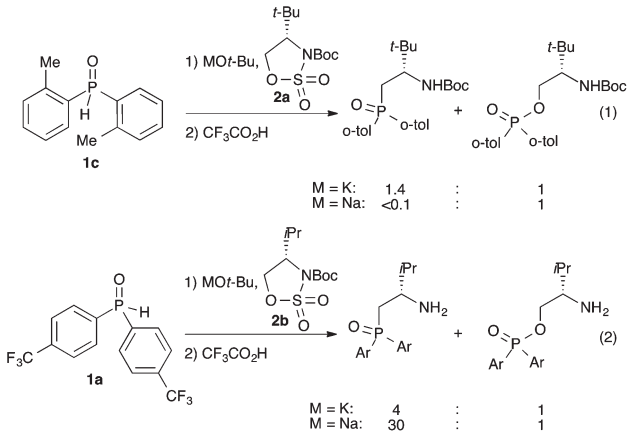
Derivatization of the amino group, which is often needed for the preparation of chiral ligands or organocatalysts, can be carried out prior to reduction of the phosphine oxide group. For example, *N*-acylation of **4a**, followed by chemoselective reduction of the phosphine oxide group, yielded the corresponding β-amidophosphines **5a** and **5b** (Scheme 6).

Conclusions

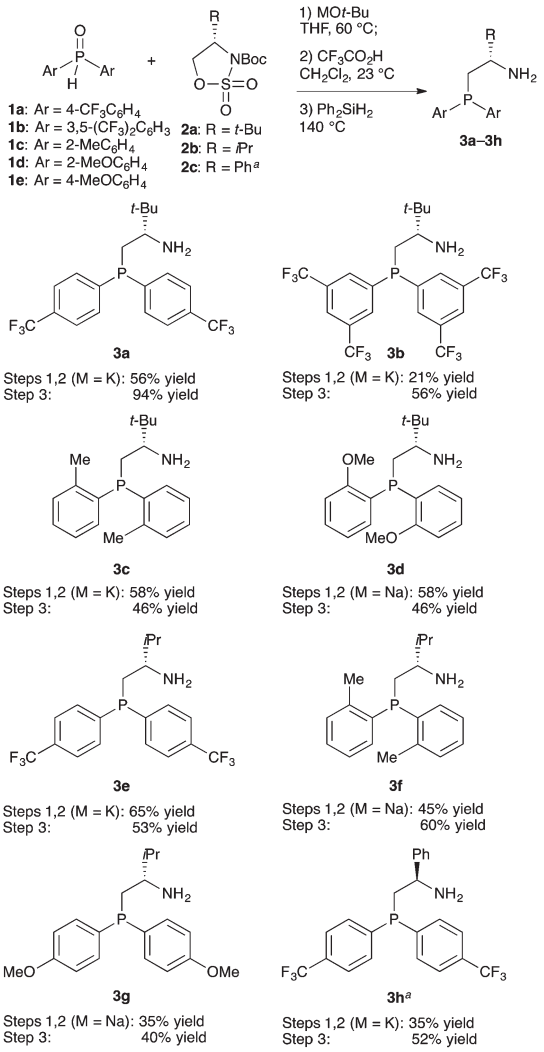
Ring-opening of cyclic sulfamidates with secondary phosphine oxide-derived nucleophiles, followed by reduction of the obtained phosphine oxide to the corresponding phosphine, provides a useful means of access to chiral β-aminophosphines having substituted *P*-aryl groups. Whether the potassium or sodium diarylphosphinite nucleophile provides higher



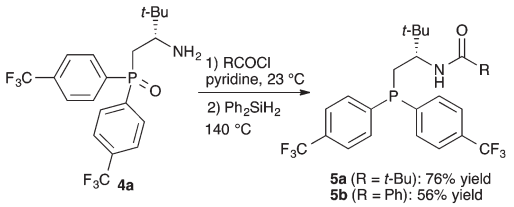
Scheme 3 Synthesis of β-aminosphosphine **3a** by diarylphosphinite/sulfamidate coupling (Ar = 4-$CF_3C_6H_4$).



Scheme 4 *P- versus O*-alkylation of metal diarylphosphinites.



Scheme 5 Synthesis of enantioenriched, substituted β-aminophosphines. [a] The phenylglycine-derived sulfamidate of *R* configuration was employed, leading to the corresponding *R*-configured β-aminophosphine.



Scheme 6 Synthesis of substituted β-amidophosphines.

P- versus O-alkylation regioselectivity depends on the phosphine oxide/sulfamidate combination employed, with steric factors apparently playing a role. Eight novel β-aminophosphines have been synthesized using this approach, including derivatives having electron-deficient, electron-rich and sterically hindered diarylphosphino groups. The effects of these types of substituents on the enantioselectivity and activity of aminophosphine-derived transition metal complexes and organocatalysts are worthy of further study.

Experimental

General methods

Unless otherwise stated, all reactions and purifications were carried out under argon atmosphere using Schlenk, vacuum line, or glovebox techniques in dry, oxygen-free solvents. Tetrahydrofuran (THF), diethyl ether, dichloromethane and hexanes were dried using a solvent purification system and degassed through three freeze–pump–thaw cycles. Deuterated solvents were degassed through three freeze–pump–thaw cycles. 400 MHz and 300 MHz spectrometers were employed for recording ^{1}H (400 MHz and 300 MHz), $^{13}C\{^{1}H\}$ (100 MHz and 75 MHz), and $^{31}P\{^{1}H\}$ (161 MHz and 121 MHz) NMR spectra at ambient temperature. ^{31}P chemical shifts are reported in parts per million (ppm) relative to 85% H_3PO_4 as an external reference. ^{1}H chemical shifts are reported in ppm relative to tetramethylsilane, and were measured by referencing the spectra to residual protium in the solvent. With the exception of solvents (see above), all commercially available reagents and chemicals were used as received without purification. High resolution mass spectroscopy experiments were carried out using direct analysis in real time (DART). Flash column chromatography was carried out using 35–75 μm particle size silica gel. Secondary diarylphosphine oxides **1a**,[17] **1b**,[20] **1c**,[16] **1d**[21] and **1e**,[22] and cyclic sulfamidates **2a**, **2b** and **2c**,[15] were synthesized according to published protocols.

General procedure for the ring-opening of cyclic sulfamidates with diarylphosphine oxides, followed by cleavage of the Boc group

(*S*)-(2-Amino-3,3-dimethylbutyl)bis(4(trifluoromethyl)-phenyl)-phosphine oxide (4a). To an oven-dried screw-cap reaction tube equipped with a magnetic stirring bar was charged potassium *tert*-butoxide (0.11 g, 1 mmol) in a nitrogen-filled glove-

box. THF (2 mL) was then added outside of the glovebox. Bis-(4-(trifluoromethyl)phenyl)phosphine oxide (0.34 g, 1 mmol) was dissolved in THF (2 mL) in a separate oven-dried pear-shaped flask and transferred dropwise into the reaction mixture *via* a syringe. The reaction was stirred at 23 °C for 10 min. Cyclic sulfamidate **2a** (0.28 g, 1 mmol) was dissolved in THF (2 mL) in another oven-dried pear-shaped flask and transferred dropwise into the reaction mixture *via* a syringe. The reaction tube was then sealed and stirred at 60 °C for 18 h. The reaction was quenched with 2 N H_2SO_4 (25 mL) and stirred vigorously at 23 °C for 45 min. It was then extracted two times with diethyl ether, and the combined organic extracts were washed with saturated Na_2CO_3, followed by brine. The solution was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give the crude product, which was used in the next step without further purification.

The crude product was taken up in CH_2Cl_2 (10 mL) and cooled to 0 °C. Trifluoroacetic acid (2 mL, 26 mmol) was then added dropwise. The reaction mixture was stirred at 23 °C overnight. The volatiles were then removed on the rotary evaporator the next day. The residue was taken up in diethyl ether and washed with saturated Na_2CO_3. The aqueous layer was separated and extracted with diethyl ether. The organic extracts were then combined, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography on silica gel (2–4% MeOH/CH_2Cl_2) gave the product (0.24 g, 56%) as an off-white solid. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.90 (ddd, J = 15.1, 11.0, 8.1 Hz, 4H), 7.75 (ddd, J = 16.9, 8.3, 2.4 Hz, 4H), 2.93 (ddd, J = 12.2, 11.0, 1.6 Hz, 1H), 2.50 (ddd, J = 15.0, 9.4, 1.6 Hz, 1H), 2.22 (ddd, J = 15.0, 12.8, 11.0 Hz, 1H), 0.88 (s, 9H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 138.1 (d, $^1J_{CP}$ = 97.5 Hz), 136.5 (d, $^1J_{CP}$ = 95.0 Hz), 134.1 (qd, $^2J_{CF}$ = 32.5 Hz, $^4J_{CP}$ = 2.5 Hz), 134.0 (qd, $^2J_{CF}$ = 32.5 Hz, $^4J_{CP}$ = 2.5 Hz), 131.6 (d, $^2J_{CP}$ = 8.8 Hz), 131.1 (d, $^2J_{CP}$ = 10.0 Hz), 136.0–125.7 (m), 123.6 (q, $^1J_{CF}$ = 271.3 Hz), 55.7 (d, $^2J_{CP}$ = 5.0 Hz), 35.1 (d, $^3J_{CP}$ = 11.3 Hz), 32.3 (d, $^1J_{CP}$ = 72.9 Hz), 25.8. **^{31}P NMR (160 MHz, $CDCl_3$):** δ 31.34. **IR (neat, cm^{-1}):** 1316 (s), 1183 (m), 1137 (s), 1118 (s), 1100 (s), 1060 (s), 1017 (s), 840 (m), 706 (s), 696 (m). **Optical rotation**: $[\alpha]_{589}^{20}$ = +20.5 (c = 0.12 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{20}H_{23}F_6NOP$ [(M + H)$^+$]: 438.1412. Found: 438.1416.

(*S*)-(2-Amino-3,3-dimethylbutyl)bis(3,5-bis(trifluoromethyl)-phenyl)phosphine oxide (4b). Synthesized according to the general procedure using bis(3,5-bis(trifluoromethyl)-phenyl)-phosphine oxide (**1b**) and *tert*-butyl (*S*)-4-(*tert*-butyl)-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**2a**). The intermediate was treated with trifluoroacetic acid and the crude product was purified by flash chromatography on silica gel (1–2% MeOH/CH_2Cl_2) to give the product as a white solid in 21% yield over two steps. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.24 (t, J = 11.2 Hz, 4H), 8.06 (d, J = 17.6 Hz, 2H), 2.96 (ddd, J = 12.4, 11.0, 1.8 Hz, 1H), 2.55 (ddd, J = 15.2, 10.7, 1.8 Hz, 1H), 2.28 (dt, J = 15.1, 11.3 Hz, 1H), 0.91 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 136.8 (d, $^1J_{CP}$ = 97.3 Hz), 135.8 (d, $^1J_{CP}$ = 95.2 Hz), 132.7 (m), 130.9 (m), 126.2 (m), 122.8 (q, J = 272.0 Hz), 55.9 (d, $^2J_{CP}$ = 5.3 Hz), 35.3 (d, $^3J_{CP}$ = 12.1 Hz), 32.9 (d, $^1J_{CP}$ = 74.7 Hz), 25.7. **^{31}P NMR (160 MHz, $CDCl_3$):** δ 29.55. **^{19}F NMR (376 MHz, $CDCl_3$):** δ −62.95, −62.97. **IR (neat, cm^{-1}):** 1360 (m), 1278 (s), 1183 (s), 1170 (s), 1124 (s), 915 (m), 843 (m), 707 (m), 681 (s). **Optical rotation**: $[\alpha]_{589}^{20}$ = +9.4 (c = 0.09 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{22}H_{21}F_{12}NOP$ [(M + H)$^+$]: 574.1163. Found: 574.1164.

(*S*)-(2-Amino-3,3-dimethylbutyl)di-*o*-tolylphosphine oxide (4c). Synthesized according to the general procedure using di-*o*-tolylphosphine oxide (**1c**) and *tert*-butyl (*S*)-4-(*tert*-butyl)-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**2a**). The intermediate treated with trifluoroacetic acid and the crude product was purified by flash chromatography on silica gel (3–10% MeOH/CH_2Cl_2) to give the product as a colorless oil in 58% yield over two steps. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.85 (ddd, J = 12.5, 7.7, 1.5 Hz, 1H), 7.63 (ddd, J = 12.8, 7.7, 1.4 Hz, 1H), 7.45–7.36 (m, 2H), 7.35–7.29 (m, 1H), 7.29–7.23 (m, 1H), 7.19 (dd, J = 7.5, 4.1 Hz, 2H), 2.93 (ddd, J = 12.1, 10.6, 1.2 Hz, 1H), 2.50 (ddd, J = 14.8, 8.6, 1.2 Hz, 1H), 2.34 (s, 3H), 2.31–2.21 (m, 1H), 2.24 (s, 3H), 0.87 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 141.9 (d, J = 8.1 Hz), 141.3 (d, J = 8.7 Hz), 132.9, 132.7 (d, J = 9.4 Hz), 132.1–131.9 (m), 132.0 (d, J = 2.7 Hz), 131.3 (d, J = 11.2 Hz), 130.3, 55.6 (d, $^2J_{CP}$ = 4.1 Hz), 35.0 (d, $^3J_{CP}$ = 12.1 Hz), 31.0 (d, $^1J_{CP}$ = 71.7 Hz), 25.9, 21.4 (d, J = 3.9 Hz), 21.3 (d, J = 4.4 Hz). **^{31}P NMR (160 MHz, $CDCl_3$):** δ 35.59. **IR (neat, cm^{-1}):** 2959 (s), 1593 (m), 1395 (s), 1365 (m), 1174 (s), 1138 (s), 1086 (w), 1071 (w), 754 (s), 741 (s). **Optical rotation**: $[\alpha]_{589}^{20}$ = +49.7 (c = 0.15 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{20}H_{29}NOP$ [(M + H)$^+$]: 330.1981. Found: 330.1981.

(*S*)-(2-Amino-3,3-dimethylbutyl)bis(2-methoxyphenyl)-phosphine oxide (4d). Synthesized according to the general procedure using bis(2-methoxyphenyl)phosphine oxide (**1d**), *tert*-butyl (*S*)-4-(*tert*-butyl)-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**2a**) and sodium *tert*-butoxide. The intermediate was treated with trifluoroacetic acid and the crude product was purified by flash chromatography on silica gel (3–10% MeOH/CH_2Cl_2) to give the product as a colorless oil in 36% yield over two steps. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92 (ddd, J = 12.9, 7.5, 1.8 Hz, 1H), 7.57–7.48 (m, 1H), 7.46–7.36 (m, 1H), 7.26 (ddd, J = 14.0, 7.6, 2.0 Hz 1H), 7.14–7.07 (m, 1H), 6.94–6.85 (m, 3H), 3.82 (s, 3H), 3.66 (s, 3H), 2.82–2.65 (m, 2H), 2.47 (td, J = 15.2, 11.1 Hz, 1H), 0.82 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 161.3 (d, $^4J_{CP}$ = 3.0 Hz), 159.8 (d, $^4J_{CP}$ = 3.8 Hz), 135.5 (d, J = 5.6 Hz), 133.9 (d, J = 2 Hz), 133.5 (d, J = 2.1 Hz), 121.7 (d, J = 100.8 Hz), 121.1 (d, J = 10.9 Hz), 120.5 (d, J = 11.9 Hz), 119.3 (d, J = 98.4 Hz), 56.3 (d, $^2J_{CP}$ = 5.0 Hz), 55.8, 55.3, 34.7 (d, $^3J_{CP}$ = 13.4 Hz), 31.3 (d, $^1J_{CP}$ = 74.1 Hz), 25.9. **^{31}P NMR (160 MHz, $CDCl_3$):** δ 35.18. **IR (neat, cm^{-1}):** 2958 (m), 1590 (s), 1576 (m), 1478 (s), 1432 (s), 1277 (s), 1246 (s), 1163 (s), 1137 (s), 1073 (m), 1020 (m), 801 (m), 758 (s). **Optical rotation**: $[\alpha]_{589}^{20}$ = +38.2 (c = 0.11 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{20}H_{29}NO_3P$ [(M + H)$^+$]: 362.1889. Found: 362.1885.

(*S*)-(2-Amino-3-methylbutyl)bis(4-(trifluoromethyl)phenyl)-phosphine oxide (4e). Synthesized according to the general procedure using bis(4-(trifluoromethyl)phenyl)phosphine oxide (**1a**) and *tert*-butyl (*S*)-4-isopropyl-1,2,3-oxathiazolidine-

3-carboxylate 2,2-dioxide (**2b**). The intermediate was purified by flash chromatography on silica gel (20% EtOAc/CH_2Cl_2) before treatment with trifluoroacetic acid. Product was obtained in 65% yield over two steps as a colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.98–7.82 (m, 4H), 7.79–7.68 (m, 4H), 3.07 (m, 1H), 2.67–2.18 (m, 2H), 1.91 (s, 2H), 1.67 (m, 1H), 0.88 (app dd, J = 6.8, 5.6 Hz, 6H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 137.7 (d, $^1J_{CP}$ = 95.4 Hz), 136.5 (d, $^1J_{CP}$ = 96.3 Hz), 134.5–134.0 (m), 134.0–133.6 (m), 131.4 (d, J = 9.5 Hz), 131.0 (d, J = 9.8 Hz), 126.3–125.5 (m), 124.8, 122.1, 52.0 (d, $^3J_{CP}$ = 4.6 Hz), 34.7 (d, $^2J_{CP}$ = 12.7 Hz), 33.8 (d, $^1J_{CP}$ = 72.9 Hz), 18.3, 17.5. **^{31}P NMR (120 MHz, $CDCl_3$):** δ 30.79. **IR (neat, cm^{-1}):** 3044 (w), 2961 (w), 1684 (w), 1400 (m), 1317 (s), 1183 (m), 1163 (s), 1117 (s), 1100 (s), 1060 (s), 1017 (s), 840 (m), 790 (m), 764 (m), 708 (s), 670 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +26.8 (c = 0.08 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{21}F_6NOP$ [$(M + H)^+$]: 424.1265. Found 424.1267.

(*S*)-(2-Amino-3-methylbutyl)di-*o*-tolylphosphine oxide (4f). Synthesized according to the general procedure using di-*o*-tolylphosphine oxide (**1c**), *tert*-butyl (*S*)-4-isopropyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**2b**) and sodium *tert*-butoxide. The intermediate was purified by flash chromatography on silica gel (25% EtOAc/CH_2Cl_2) before treatment with trifluoroacetic acid. Product was obtained in 45% yield over two steps as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.81 (ddd, J = 12.5, 7.7, 1.5 Hz, 1H), 7.64 (ddd, J = 12.9, 7.7, 1.4 Hz, 1H), 7.46–7.34 (m, 2H), 7.34–7.24 (m, 2H), 7.24–7.12 (m, 2H), 3.21–2.89 (m, 1H), 2.49–2.45 (m, 2H), 2.46–2.34 (m, 2H), 2.31 (s, 3H), 2.22 (s, 3H), 1.79–1.61 (m, 1H), 0.87 (app t, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 141.7 (d, J = 8.4 Hz), 141.2 (d, J = 8.8 Hz), 132.4 (d, J = 9.6 Hz), 132.0 (d, J = 96.4 Hz), 132.0, 131.9, 131.9, 131.9, 131.3 (d, J = 11.1 Hz), 130.7 (d, $^1J_{CP}$ = 95.3 Hz), 125.8 (d, J = 6.6 Hz), 125.7 (d, J = 7.0 Hz), 52.2 (d, J = 4.0 Hz), 34.5 (d, J = 12.8 Hz), 32.4 (d, $^1J_{CP}$ = 71.9 Hz), 21.3 (d, J = 4.0 Hz), 21.2 (d, J = 4.4 Hz), 18.2, 17.9. **^{31}P NMR (160 MHz, $CDCl_3$):** δ 35.29. **IR (neat, cm^{-1}):** 2957 (m), 2871 (w), 1593 (m), 1568 (m), 1452 (s), 1385 (m), 1283 (m), 1174 (s), 1138 (s), 1084 (w), 1071 (w), 927 (m), 805 (m), 751 (s), 730 (s), 688 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +68.7 (c = 0.19 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{27}F_6NOP$ [$(M + H)^+$]: 316.1830. Found 316.1834.

(*S*)-(2-Amino-3-methylbutyl)bis(4-methoxyphenyl)-phosphine oxide (4g). Synthesized according to the general procedure using bis(4-methoxyphenyl)phosphine oxide (**1e**), *tert*-butyl (*S*)-4-isopropyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**2b**) and sodium *tert*-butoxide. The intermediate was purified by flash chromatography on silica gel (2% MeOH/CH_2Cl_2) before treatment with trifluoroacetic acid. Product was obtained in 35% yield over two steps as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.69–7.54 (m, 4H), 6.93 (m, 4H), 3.80 (s, 3H), 3.77 (s, 3H), 3.00 (dddd, J = 11.7, 9.6, 4.9, 2.6 Hz, 1H), 2.69 (s, 3H), 2.36–2.09 (m, 2H), 1.65 (pd, J = 6.8, 4.8 Hz, 1H), 0.83 (app t, J = 6.7 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 162.3 (d, J = 2.8 Hz), 162.2 (d, J = 2.9 Hz), 132.7 (d, J = 10.5 Hz), 132.3 (d, J = 10.8 Hz), 125.4 (d, $^1J_{CP}$ = 105.3 Hz), 123.4 (d, J = 104.8 Hz), 55.3 (d, J = 1.6 Hz), 55.3 (d, J = 1.7 Hz), 52.0 (d, J = 4.3 Hz), 34.4 (d, J = 12.7 Hz), 33.9 (d, $^1J_{CP}$ = 72.8 Hz), 18.2, 17.7. **^{31}P NMR (160 MHz, $CDCl_3$):** δ 33.14. **IR (neat, cm^{-1}):** 2956 (m), 2839 (w), 1596 (s), 1570 (m), 1503 (s), 1463 (m), 1408 (m), 1292 (s), 1253 (s), 1173 (s), 1119 (s), 1026 (s), 930 (m), 829 (s), 802 (s), 762 (m), 729 (m), 660 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +36.1 (c = 0.12 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{27}NO_3P$ [$(M + H)^+$]: 348.1729. Found 348.1733.

(*R*)-(2-Amino-2-phenylethyl)bis(4-(trifluoromethyl)phenyl)-phosphine oxide (4h). Synthesized according to the general procedure using bis(4-(trifluoromethyl)phenyl)phosphine oxide (**1a**) and *tert*-butyl (*R*)-4-phenyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (**1c**). The intermediate was purified by flash chromatography on silica gel (10% EtOAc/CH_2Cl_2) before treatment with trifluoroacetic acid. Product was obtained in 35% yield over two steps as a white solid. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.93–7.77 (m, 4H), 7.77–7.65 (m, 4H), 7.39–7.11 (m, 5H), 4.51 (ddd, J = 10.5, 9.0, 4.0 Hz, 1H), 2.90–2.60 (m, 2H), 1.94 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 145.0 (s), 144.9 (s), 131.3 (d), 130.9 (d), 128.8, 127.8, 126.1, 125.7 (dt, J = 11.9, 3.8 Hz), 51.3 (d, J = 3.4 Hz), 39.5 (d, $^1J_{CP}$ = 69.9 Hz). **^{31}P NMR (120 MHz, $CDCl_3$):** δ 28.52. IR (neat, cm^{-1}): 2900 (w), 1496 (w), 1456 (w), 1400 (m), 1321 (s), 1165 (s), 1120 (s), 1100 (s), 1061 (s), 1017 (s), 835 (m), 789 (m), 768 (m), 742 (m), 708 (m), 696 (s). **Optical rotation:** $[\alpha]_{589}^{20}$ = −18.7 (c = 0.10 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{22}H_{19}F_6NOP$ [$(M + H)^+$]: 458.1108. Found 458.1109.

General procedure for reduction of β-aminophosphine oxides

(*S*)-1-(Bis(4-(trifluoromethyl)phenyl)-phosphanyl)-3,3-dimethylbutan-2-amine (3a). To a 0.5-dram vial equipped with a magnetic stirring bar was added (*S*)-(2-amino-3,3-dimethylbutyl)bis(4-(trifluoromethyl)phenyl)phosphine oxide (**3a**, 0.3 g, 0.68 mmol). Ph_2SiH_2 (0.89 mL, 4.78 mmol) was added and the vial was sealed. Allowed reaction to stir vigorously at 140 °C for 20 h. The product was then purified by flash chromatography on silica gel using a positive pressure of N_2 and solvents presparged with N_2 (2.0–3.5% MeOH/CH_2Cl_2) to give the product (0.27 g, 94%) as a yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.68–7.61 (m, 4H), 7.52–7.43 (m, 4H), 2.62–2.59 (m, 1H), 2.46–2.42 (m, 2H), 0.94 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 141.2 (d, $^1J_{CP}$ = 16.7 Hz), 134.7 (d, $^2J_{CP}$ = 20.4 Hz), 132.3 (d, J = 16.9 Hz), 130.6 (d, $^2J_{CF}$ = 32.4 Hz), 125.5 (m), 125.3 (m), 124.0 (q, $^1J_{CF}$ = 257.3 Hz), 58.6 (d, $^2J_{CP}$ = 13.2 Hz), 34.8 (d, $^3J_{CP}$ = 5.5 Hz), 30.6 (d, $^1J_{CP}$ = 15.7 Hz), 26.2. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −29.92. **^{19}F NMR (376 MHz, $CDCl_3$):** δ −62.95, −63.04. IR (neat, cm^{-1}): 1607 (w), 1323 (s), 1166 (m), 1125 (s), 1061 (s), 1016 (m), 831 (w), 699 (w). **Optical rotation:** $[\alpha]_{589}^{20}$ = +20.1 (c = 0.14 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{20}H_{23}F_6NP$ [$(M + H)^+$]: 422.1469. Found: 438.1472.

(*S*)-1-(Bis(3,5-bis(rifluoromethyl)phenyl)phosphanyl)-3,3-dimethylbutan-2-amine (3b). Synthesized according to the general procedure using (*S*)-(2-amino-3,3-dimethylbutyl)-bis-(3,5-bis(trifluoromethyl)phenyl)phosphine oxide (**4b**). The crude product was purified by flash chromatography on silica gel (0.3–0.5% MeOH/CH_2Cl_2) to give the product in 56% yield as a yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.93 (m, 3H),

7.85–7.76 (m, 3H), 2.53–2.37 (m, 2H), 1.94 (ddd, J = 13.6, 11.8, 5.2 Hz, 1H), 0.90 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 142.6 (d, $^1J_{CP}$ = 20.0 Hz), 140.5 (d, $^2J_{CP}$ = 21.4 Hz), 133.5 (m), 132.9–131.6 (m), 123.8 (quint, J = 3.8 Hz), 123.2 (qd, $^1J_{CF}$ = 271.0 Hz, $^4J_{CP}$ = 3.1 Hz), 122.9 (quint. J = 3.7 Hz), 58.5 (d, $^2J_{CP}$ = 11.8 Hz), 35.4 (d, $^3J_{CP}$ = 6.2 Hz), 32.4 (d, $^1J_{CP}$ = 11.3 Hz), 25.8. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −15.68. **^{19}F NMR (376 MHz, $CDCl_3$):** δ −63.06. **IR (neat, cm^{-1}):** 1352 (s), 1274 (s), 1172 (m), 1118 (s), 1094 (s), 893 (m), 844 (m), 702 (s), 681 (s). **Optical rotation:** $[\alpha]_{589}^{20}$ = +33.7 (c = 0.05 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{22}H_{21}F_{12}NP$ [(M + H)$^+$]: 558.1221. Found: 558.1220.

(*S*)-1-(Di-*o*-tolylphosphanyl)-3,3-dimethylbutan-2-amine (3c). Synthesized according to the general procedure using (*S*)-(2-amino-3,3-dimethylbutyl)di-*o*-tolylphosphine oxide (**4c**). The crude product was purified by flash chromatography on silica gel (2% MeOH/CH_2Cl_2) to give the product in 46% yield as a yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.24–7.12 (m, 8H), 2.51 (ddd, J = 11.1, 9.1, 1.8 Hz, 1H), 2.45 (s, 3H), 2.44 (s, 3H), 2.35 (ddd, J = 13.7, 4.1, 1.8 Hz, 1H), 1.68 (ddd, J = 13.8, 11.4, 4.9 Hz, 1H), 0.89 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 143.2 (d, J = 25.6 Hz), 142.0 (d, J = 25.3 Hz), 137.7 (d, J = 12.1 Hz), 136.2 (d, J = 13.8 Hz), 131.4 (d, J = 13.3 Hz), 130.2 (d, J = 1.7 Hz), 130.2 (d, J = 1.4 Hz), 128.6 (d, J = 24.4 Hz), 126.1 (d, J = 8.4 Hz), 57.8 (d, $^2J_{CP}$ = 12.8 Hz), 35.1 (d, $^3J_{CP}$ = 6.2 Hz), 31.2 (d, $^1J_{CP}$ = 10.9 Hz), 26.1, 21.6 (d, J = 11.2 Hz), 21.4 (d, J = 10.6 Hz). **^{31}P NMR (160 MHz, $CDCl_3$):** δ −42.08. **IR (neat, cm^{-1}):** 2956 (s), 1469 (s), 1452 (s), 1363 (m), 1272 (w), 1200 (w), 1130 (s), 1068 (w), 1031 (w), 839 (w), 804 (w), 746 (s), 719 (s). **Optical rotation:** $[\alpha]_{589}^{20}$ = +86.1 (c = 0.05 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{20}H_{29}NP$ [(M + H)$^+$]: 314.2034. Found: 314.2038.

(*S*)-1-(Bis(2-methoxyphenyl)phosphanyl)-3,3-dimethylbutan-2-amine (3d). Synthesized according to the general procedure using (*S*)-(2-amino-3,3-dimethylbutyl)di-*o*-tolylphosphine oxide (**4d**). The crude product was purified by flash chromatography on silica gel (3–10% MeOH/CH_2Cl_2) to give the product in 51% yield as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36 (ddd, J = 8.2, 7.4, 1.7 Hz, 1H), 7.33–7.23 (m, 2H), 7.05 (ddd, J = 7.3, 5.2, 1.7 Hz, 1H), 6.95 (td, J = 7.4, 1.0 Hz, 1H), 6.91–6.82 (m, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 2.59 (ddd, J = 11.6, 9.2, 2.0 Hz, 1H), 2.53–2.46 (ddd, J = 13.6, 4.8, 2.0 Hz, 1H), 1.87 (ddd, J = 14.0, 12.0, 3.6 Hz, 1H), 0.92 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 134.4, 133.7 (d, J = 9.2 Hz), 132.7 (d, J = 4.4 Hz), 130.6, 130.0, 121.0 (d, J = 16.7 Hz), 110.5 (d, J = 15.4 Hz), 58.6, 58.4, 55.7 (d, $^2J_{CP}$ = 10.7 Hz), 35.0 (d, $^3J_{CP}$ = 6.3 Hz), 29.1 (d, $^1J_{CP}$ = 9.8 Hz), 26.3. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −39.00. **IR (neat, cm^{-1}):** 1584 (m), 1573 (m), 1463 (s), 1430 (s), 1271 (m), 1239 (s), 1129 (w), 1072 (w), 1024 (s), 793 (w), 753 (s). **Optical rotation:** $[\alpha]_{589}^{20}$ = +38.2 (c = 0.12 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{20}H_{29}NO_3P$ [(M + H)$^+$]: 362.1889. Found: 362.1885.

(*S*)-1-(Bis(4-(trifluoromethyl)phenyl)phosphanyl)-3-methylbutan-2-amine (3e). Synthesized according to the general procedure using (*S*)-(2-amino-3-methylbutyl)bis(4-(trifluoromethyl)phenyl)phosphine oxide (**4e**). The crude product was purified by flash chromatography on silica gel (2% MeOH/CH_2Cl_2) to give the product in 53% yield as a colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.78–7.41 (m, 8H), 2.63 (m, 1H), 2.33 (m, 1H), 2.04 (m, 1H), 1.72 (m, 1H), 0.90 (app dd, J = 7.9, 6.8 Hz, 6H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 143.8 (d, J = 15.5 Hz), 142.6 (d, J = 16.8 Hz), 133.5 (d, J = 19.8 Hz), 132.6 (d, J = 18.4 Hz), 131.2 (d, J = 32.4 Hz), 130.7 (d, J = 32.6 Hz), 125.9 −124.9 (m), 54.2 (d, J = 13.1 Hz), 34.6 (d, J = 7.4 Hz), 34.4 (d, J = 12.3 Hz), 18.8, 17.0. **^{31}P NMR (120 MHz, $CDCl_3$):** δ −20.39. **IR (neat, cm^{-1}):** 1606 (w), 1396 (w), 1319 (s), 1164 (m), 1121 (s), 1059 (s), 1015 (m), 829 (m), 710 (w), 697 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +23.2 (c = 0.13 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{21}F_6NP$ [(M + H)$^+$]: 408.1316. Found 408.1315.

(*S*)-1-(Di-*o*-tolylphosphanyl)-3-methylbutan-2-amine (3f). Synthesized according to the general procedure using (*S*)-(2-amino-3-methylbutyl)di-*o*-tolylphosphine oxide (**4f**). The crude product was purified by flash chromatography on silica gel (2% MeOH/CH_2Cl_2) to give the product in 60% yield as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.25–7.10 (m, 8H), 2.81–2.63 (m, 1H), 2.45 (s, 3H), 2.43 (s, 3H), 2.25 (ddd, J = 13.8, 4.4, 1.6 Hz, 1H), 1.94 (ddd, J = 13.8, 9.2, 2.9 Hz, 1H), 1.83 (m, 1H), 0.95 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 142.7 (d, J = 25.7 Hz), 142.0 (d, J = 25.6 Hz), 137.2 (d, J = 12.3 Hz), 136.4 (d, J = 13.4 Hz), 131.2 (d, J = 7.7 Hz), 130.1 (d, J = 2.2 Hz), 130.1 (d, J = 2.0 Hz), 128.4 (d, J = 11.7 Hz), 126.1 (d, J = 0.8 Hz), 126.0 (d, J = 0.8 Hz), 54.0 (d, J = 14.0 Hz), 34.3 (d, J = 7.4 Hz), 33.4 (d, J = 12.1 Hz), 21.4 (d, J = 7.7 Hz), 21.2 (d, J = 7.4 Hz), 19.0, 17.0. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −44.02. **IR (neat, cm^{-1}):** 3055 (w), 2956 (m), 1589 (w), 1466 (m), 1451 (m), 1378 (m), 1270 (w), 1200 (w), 1130 (m), 1032 (m), 910 (w), 747 (s), 719 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +82.4 (c = 0.10 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{27}NP$ [(M + H)$^+$]: 300.1881. Found 300.1889.

(*S*)-1-(Bis(4-methoxyphenyl)phosphanyl)-3-methylbutan-2-amine (3g). Synthesized according to the general procedure using (*S*)-(2-amino-3-methylbutyl)bis(4-methoxyphenyl)-phosphine oxide (**4g**). The crude product was purified by flash chromatography on silica gel (3% MeOH/CH_2Cl_2) to give the product in 40% yield as a colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.44–7.31 (m, 4H), 6.93–6.80 (m, 4H), 3.80 (s, 3H), 3.78 (s, 3H), 2.66 (m, 1H), 2.25 (m, 1H), 1.99 (m, 1H), 1.75 (m, 1H), 1.26 (br s, 2H), 0.91 (d, J = 9.1 Hz, 3H), 0.88 (d, J = 9.0 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 160.3, 159.9, 134.5 (d, J = 20.6 Hz), 133.8 (d, J = 19.5 Hz), 130.2 (d, J = 9.3 Hz), 129.1 (d, J = 10.4 Hz), 114.2 (d, J = 4.7 Hz), 114.1 (d, J = 4.1 Hz), 55.2, 54.2, 54.1, 35.1 (d, J = 11.1 Hz), 34.2 (d, J = 7.6 Hz), 18.9, 17.2. **^{31}P NMR (120 MHz, $CDCl_3$):** δ −25.59. **IR (neat, cm^{-1}):** 2956 (m), 2835 (w), 1593 (s), 1568 (m), 1497 (s), 1462 (m), 1441 (m), 1401 (w), 1282 (s), 1245 (s), 1176 (s), 1094 (s), 1030 (s), 910 (w), 825 (s), 797 (m), 732 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +71.4 (c = 0.05 g mL^{-1}, $CHCl_3$). **HRMS (DART, m/z):** calculated for $C_{19}H_{27}NO_2P$ [(M + H)$^+$]: 332.1779. Found 332.1781.

(*R*)-2-(Bis(4-(trifluoromethyl)phenyl)phosphanyl)-1-phenylethan-1-amine (3h). Synthesized according to the general procedure using (*R*)-(2-amino-2-phenylethyl)bis(4-(trifluoromethyl)phenyl)phosphine oxide (**4h**). The crude product was

purified by silica gel chromatography (2% MeOH/CH_2Cl_2) to give the product in 52% yield as a yellow oil. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.63–7.55 (m, 4H), 7.55–7.44 (m, 4H), 7.41–7.16 (m, 5H), 4.03 (m, 1H), 2.67–2.41 (m, 2H), 1.82 (s, 2H). **^{13}C NMR (75 MHz, $CDCl_3$):** δ 133.3 (d, J = 19.6 Hz), 132.8 (d, J = 18.9 Hz), 128.7 (s), 127.5 (s), 126.1 (s), 125.3 (m), 53.9 (d, J = 16.5 Hz), 39.43 (d, J = 14.7 Hz). **^{31}P NMR (120 MHz, $CDCl_3$):** δ −21.05. **IR (neat, cm^{-1}):** 2935 (w), 2870 (w), 1606 (m), 1454 (w), 1398 (m), 1321 (s), 1165 (s), 1119 (s), 1104 (s), 1059 (s), 1015 (s), 952 (m), 879 (m), 828 (s), 769 (m), 724 (m), 699 (s). **Optical rotation:** $[\alpha]_{589}^{20}$ = −26.0 (c = 0.07 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{22}H_{19}F_6NP$ [(M + H)$^+$]: 442.1153. Found 442.1159.

General procedure for acylation and reduction of β-aminophosphine oxides

(*S*)-*N*-(1-(Bis(4-(trifluoromethyl)phenyl)phosphanyl)-3,3-dimethylbutan-2-yl)pivalamide (5a). To an oven-dried round-bottom flask equipped with a magnetic stirring bar was added (*S*)-(2-amino-3,3-dimethylbutyl)bis(4-(trifluoromethyl)phenyl)-phosphine oxide (**4a**, 20 mg, 46 μmol). Pyridine (0.1 mL) was added and the reaction mixture was cooled to 0 °C. Trimethylacetyl chloride (6 μL, 50 μmol) was added dropwise *via* a microsyringe. The reaction was stirred at room temperature overnight. The reaction mixture was then quenched with H_2O and extracted two times with EtOAc. The combined organic extracts were washed once with saturated $NaHCO_3$, twice with 10% $CuSO_4$, then once with brine. The solution was then dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography on silica gel (2.5% MeOH/CH_2Cl_2) gave the intermediate as a white solid.

The phosphine oxide intermediate was reduced following the general procedure for reduction of β-aminophosphine oxides. The crude product was purified by flash chromatography on silica gel (0.2% MeOH/CH_2Cl_2) to afford the product (17.6 mg, 76% over two steps) as a white solid. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.60–7.58 (m, 4H), 7.56–7.44 (m, 4H), 5.46 (d, J = 10.2 Hz, 1H), 3.89 (dddd, J = 11.6, 10.2, 8.7, 2.8 Hz, 1H), 2.43 (ddd, J = 13.8, 4.4, 2.8 Hz, 1H), 1.98 (ddd, J = 13.8, 11.9, 4.5 Hz, 1H), 1.16 (s, 9H), 0.88 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 177.5, 133.8 (d, J = 19.8 Hz), 132.7 (d, J = 18.7 Hz), 125.4 (m), 53.6 (d, $^2J_{CP}$ = 13.0 Hz), 39.0, 35.6 (d, $^3J_{CP}$ = 6.3 Hz), 31.1 (d, $^1J_{CP}$ = 13.6 Hz), 27.7, 26.3. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −21.03. **^{19}F NMR (376 MHz, $CDCl_3$):** δ −62.89. **IR (neat, cm^{-1}):** 1647 (m), 1513 (m), 1320 (s), 1168 (s), 1118 (s), 1103 (s), 1059 (s), 838 (m), 827 (m), 696 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +25.4 (c = 0.07 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{25}H_{31}F_6NOP$ [(M + H)$^+$]: 506.2044. Found 506.2047.

(*S*)-*N*-(1-(Bis(4-(trifluoromethyl)phenyl)phosphanyl)-3,3-dimethylbutan-2-yl)benzamide (5b). Synthesized according to the general procedure using (*S*)-(2-amino-3,3-dimethylbutyl)bis-(4-(trifluoromethyl)phenyl)phosphine oxide (**4a**) and benzoyl chloride. The intermediate was purified by flash chromatography on silica gel (2.5% MeOH/CH_2Cl_2) before treatment with Ph_2SiH_2. Flash chromatography on silica gel (0.2% MeOH/CH_2Cl_2) gave the product in 56% yield over two steps as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.62–7.52 (m, 6H), 7.52–7.42 (m, 5H), 5.74 (d, J = 10.2 Hz, 1H), 4.20 (dddd, J = 13.1, 11.1, 8.4, 2.8 Hz, 1H), 2.52 (td, J = 13.9, 2.8 Hz, 1H), 2.17 (ddd, J = 14.2, 12.0, 2.5 Hz, 1H), 0.97 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.0, 134.7, 133.5 (d, J = 19.3 Hz), 133.1 (d, J = 19.4 Hz), 131.6, 128.7, 126.8, 125.5 (m), 55.0 (d, $^2J_{CP}$ = 14.7 Hz), 35.9 (d, $^3J_{CP}$ = 6.8 Hz), 30.9 (d, $^1J_{CP}$ = 14.3 Hz), 26.4. **^{31}P NMR (160 MHz, $CDCl_3$):** δ −20.19. **^{19}F NMR (376 MHz, $CDCl_3$):** δ −62.90. **IR (neat, cm^{-1}):** 1641 (m), 1520 (m), 1321 (s), 1162 (s), 1120 (s), 1106 (s), 1059 (s), 830 (m), 818 (m), 691 (m). **Optical rotation:** $[\alpha]_{589}^{20}$ = +22.7 (c = 0.04 g mL^{-1}, $CHCl_3$). **HRMS (DART, *m*/*z*):** calculated for $C_{27}H_{27}F_6NOP$ [(M + H)$^+$]: 526.1736. Found 526.1734.

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