# Brønsted Acid-Catalyzed Phosphoramidic Acid Additions to Alkenes: Diastereo- and Enantioselective Halogenative Cyclizations for the Synthesis of *C*- and *P*-Chiral Phosphoramidates

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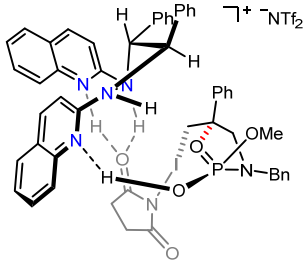
SI-I-X

**Reagent-Substrate Assembly Models for Enantioselection (proposed)**

Although not exclusive of other possibilities, the model in Figure 1 is consistent with our studies to-date. The catalyst is bifunctional, acting as both a Brønsted acid (to activate NIS) and a Brønsted base (to activate the phosphoramidic acid). Assumptions include: 1) *anti*-addition to the alkene, 2) a 1:1:1:1 complex of substrate:NIS:BAM-ligand:$Tf_2NH$, 3) a coplanar arrangement between the quinolinium ring and NIS based on double hydrogen bonding to the NIS carbonyl group, and 4) orientation of the iodine toward the chiral backbone.

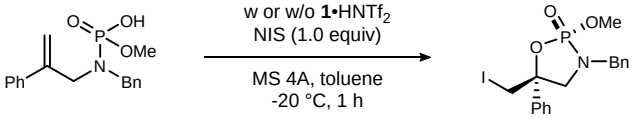
The reaction of *cis*-dimethyl-substituted alkene **4aj** provided essentially a single diastereomer, and based on the stereochemistry of the corresponding epoxide, the cyclization should undergo *anti*-addition of the phosphoryl oxygen to an iodonium intermediate. Since NBS afforded the corresponding product in good yield and with modest enantioselection, and iodine ($I_2$) gave significant low enantioselection, the succinimide moiety seems important to stereocontrol. The X-ray structure of the product implies that the substituent, which leads to the *C*-chiral center, may be located on the pseudo-axial position in the transient state.

**Figure 1.** Proposed Reagent-Substrate Assemblies




**Reaction Rate Study**

The reaction is difficult to monitor by TLC to accurately follow the consumption of starting material, so all reactions were provided a 48 hour standard reaction time. Among control experiments that established baseline reactivity is the pair detailed below. Two reactions were performed under identical conditions, differing only by the presence of the catalysts. When quenched after 1 hour, the catalyzed reaction yielded the product in 74% yield (>20:1 dr, 96% ee), whereas the non-catalyzed reaction ('background reaction') yielded product in 15% yield (2:1 dr), revealing a significant rate difference between the background reaction and the catalytic reaction.

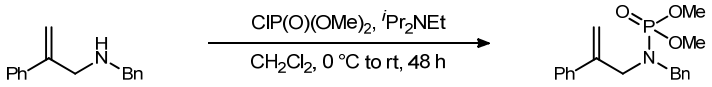



**1**•$HNTf_2$ (10 mol%): 74% (>20:1 dr, 96% ee)
without **1**•$HNTf_2$: 15% (2:1 dr)

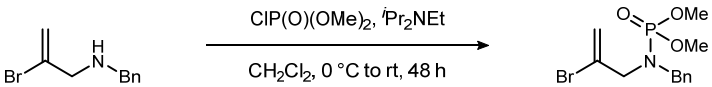
**Experimental Section**

All reagents and solvents were commercial grade and purified prior to use when necessary. Tetrahydrofuran (THF), dichloromethane ($CH_2Cl_2$) and toluene were dried by passage through a column of activated alumina as described by Grubbs.[1] *N*-Iodosuccinimide was recrystallized from dioxane and carbon tetrachloride. Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μm) plates, and flash chromatography utilized 230-400 mesh silica gel from Scientific Adsorbents. Products were visualized by UV light, iodine, and/or the use of PMA and potassium permanganate solutions were used. Melting points were measured on a Meltemp melting point apparatus and were not corrected. IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer and are reported in wavenumbers ($cm^{-1}$). All compounds were analyzed as neat films on a NaCl plate (transmission). Nuclear magnetic resonance spectra (NMR) were acquired on a Bruker DRX-400 (400 MHz), a Bruker DRX-500 (500 MHz), or a Bruker AVIII-600 (600 MHz) spectrometer. Chemical shifts are measured relative to residual solvent peaks as an internal standard set to 7.26 and 77.0 for $CDCl_3$. Mass spectra were recorded on a Thermo Electron Corporation MAT 95XP-Trap mass spectrometer by the ionization method noted. by the Indiana University Mass Spectrometry Facility. A post-acquisition gain correction was applied using sodium formate or sodium iodide as the lock mass. Optical rotations were measured on a Perkin Elmer-341 polarimeter.

**Preparation of Precursors of Starting Materials**

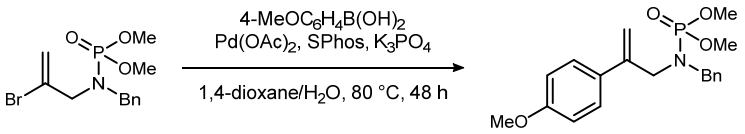



**Dimethyl benzyl(2-phenylallyl)phosphoramidate (SI-1).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (983 mg, 4.40 mmol)[2], dichloromethane (11 mL), and Hünig's base (2.30 mL, 13.2 mmol). Dimethyl chlorophosphate (712 μL, 6.60 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 30-50-70% ethyl acetate in hexanes) yielded a yellow oil (1.22 g, 84%). $R_f$ = 0.20 (50% EtOAc/hexanes) visualized with PMA; IR (film) 2949, 1255, 1059, 1028, 827, 707 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.35-7.28 (m, 8H), 5.41 (s, 1H), 5.15 (d, *J* = 1.2 Hz, 1H), 4.11 (d, *J* = 11.2 Hz, 2H), 4.00 (d, *J* = 9.2 Hz, 2H), 3.51 (d, *J* = 11.2 Hz, 6H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 144.0 (d, *J* = 2.5 Hz), 139.3, 137.0, 128.5, 128.2, 128.1, 127.6, 127.2, 126.7, 115.9, 52.9 (d, *J* = 6.3 Hz), 48.4 (d, *J* = 5.0 Hz), 48.2 (d, *J* = 3.8 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 12.2; HRMS (EI): Exact mass calcd for $C_{18}H_{22}NO_3P$ $[M]^+$ 331.1332, found 331.1332.

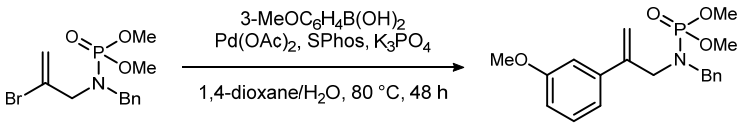



**Dimethyl benzyl(2-bromoallyl)phosphoramidate (SI-2).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (724 mg, 3.20 mmol)[3], dichloromethane (8 mL), and Hünig's base (1.67 mL, 9.60 mmol). Dimethyl chlorophosphate (518 μL, 4.80 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 25-50-75% ethyl acetate in hexanes) yielded a yellow oil (885 mg, 83%). $R_f$ = 0.33 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2952, 1259, 1059, 1029, 827, 702 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 5.76 (d, *J* = 1.2 Hz, 1H), 5.65 (s, 1H), 4.23 (d, *J* = 10.4 Hz, 2H), 3.77 (d, *J* = 11.2 Hz, 6H), 3.76 (d, *J* = 9.6 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 136.6 (d, *J* = 2.0 Hz), 129.6 (d, *J* = 3.0 Hz), 128.6, 128.5, 127.6, 119.3, 53.6 (d, *J* = 6.1 Hz), 52.6

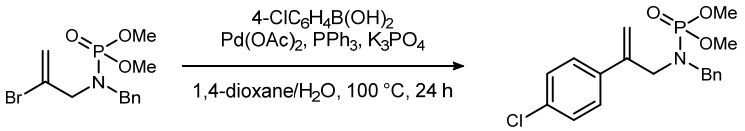
(d, $J$ = 6.1 Hz), 48.8 (d, $J$ = 4.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 12.8; HRMS (ESI): Exact mass calcd for $C_{12}H_{17}BrNNaO_3P$ $[M+Na]^+$ 356.0027, found 356.0025.




**Dimethyl benzyl(2-(4-methoxyphenyl)allyl)phosphoramidate (SI-3).** To a round-bottomed flask equipped with a stir bar was added the vinyl bromide (401 mg, 1.20 mmol), potassium phosphate (764 mg, 3.60 mmol), the boronic acid (274 mg, 1.80 mmol), 1,4-dioxane (10 mL), and water (1 mL). SPhos (25 mg, 60 µmol) and palladium acetate (6.7 mg, 30 µmol) were added, and the atmosphere was replaced with argon three times, and the reaction mixture was then stirred at 80 °C for 48 h. After cooling to room temperature, the mixture was treated with water (10 mL) and the aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 25-50-75% ethyl acetate in hexanes) yielded a yellow oil (390 mg, 90%). $R_f$ = 0.29 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1513, 1251, 1060, 1029, 827, 703 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, $J$ = 8.8 Hz, 2H), 7.33-7.25 (m, 5H), 6.87 (d, $J$ = 8.8 Hz, 2H), 4.10 (s, 1H), 5.06 (d, $J$ = 0.8 Hz, 1H), 4.10 (d, $J$ = 11.2 Hz, 2H), 3.97 (d, $J$ = 9.2 Hz, 2H), 3.80 (s, 3H), 3.54 (d, $J$ = 11.2 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 159.3, 143.3 (d, $J$ = 3.0 Hz), 137.2 (d, $J$ = 1.0 Hz), 131.8, 128.6, 128.3, 128.0, 127.3, 114.6, 113.5, 55.2, 53.1 (d, $J$ = 6.1 Hz), 48.5 (d, $J$ = 5.1 Hz), 48.3 (d, $J$ = 4.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.5; HRMS (ESI): Exact mass calcd for $C_{19}H_{24}NNaO_4P$ $[M+Na]^+$ 384.1341, found 384.1351.

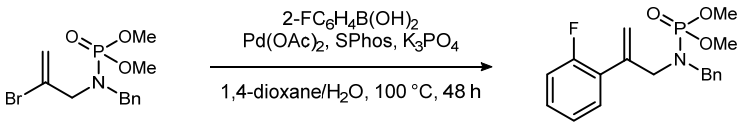



**Dimethyl benzyl(2-(3-methoxyphenyl)allyl)phosphoramidate (SI-4).** To a round-bottomed flask equipped with a stir bar was added the vinyl bromide (668 mg, 2.00 mmol), potassium phosphate (1.27 g, 6.00 mmol), the boronic acid (456 mg, 3.00 mmol), 1,4-dioxane (20 mL), and water (2 mL). SPhos (41.1 mg, 100 µmol) and palladium acetate (11.2 mg, 50.0 µmol) were added and the atmosphere was replaced with argon three times, and the reaction mixture was then stirred at 80 °C for 48 h. After cooling to room temperature, the mixture was treated with water (20 mL), and the aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 25-50-75% ethyl acetate in hexanes) yielded a yellow oil (703 mg, 97%). $R_f$ = 0.33 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2950, 1255, 1059, 1030, 827, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33-7.22 (m, 6H), 7.02-6.98 (m, 2H), 6.83 (dd, $J$ = 8.0, 2.0 Hz, 1H), 5.42 (s, 1H), 5.14 (s, 1H), 4.10 (d, $J$ = 10.8 Hz, 2H), 4.00 (d, $J$ = 9.2 Hz, 2H), 3.82 (s, 3H), 3.53 (d, $J$ = 11.2 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 159.4, 144.1 (d, $J$ = 3.0 Hz), 140.8, 137.1, 129.2, 128.6, 128.3, 127.3, 116.1, 113.5, 112.3, 55.2, 53.0 (d, $J$ = 6.1 Hz), 48.5 (d, $J$ = 5.1 Hz), 48.3 (d, $J$ = 4.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.4; HRMS (ESI): Exact mass calcd for $C_{19}H_{24}NNaO_4P$ $[M+Na]^+$ 384.1341, found 384.1330.

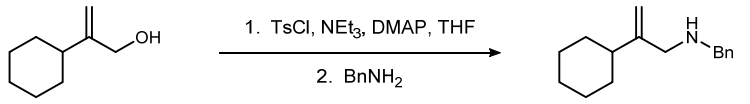



**Dimethyl benzyl(2-(4-chlorophenyl)allyl)phosphoramidate (SI-5).** To a round-bottomed flask equipped with a stir bar was added the vinyl bromide (401 mg, 1.20 mmol), potassium phosphate (764 mg, 3.60 mmol), the boronic acid (338 mg, 2.16 mmol), 1,4-dioxane (10 mL), and water (1 mL). Triphenylphosphine (62.9 mg, 240

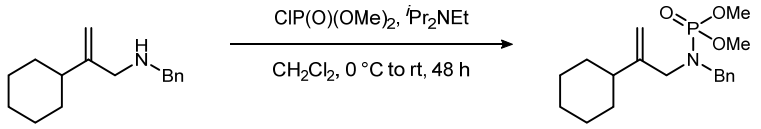
μmol) and palladium acetate (13.5 mg, 60.0 μmol) were added, the atmosphere was replaced with argon three times, and the reaction mixture was then stirred at 100 °C for 24 h. After cooling to room temperature, the mixture was treated with water (10 mL), and the aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 5-10-20% ethyl acetate in dichloromethane) yielded a yellow oil (378 mg, 86%). $R_f$ = 0.34 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2950, 1256, 1060, 1030, 827, 702 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 9H), 5.40 (s, 1H), 5.15 (s, 1H), 4.08 (d, *J* = 11.2 Hz, 2H), 3.98 (d, *J* = 9.2 Hz, 2H), 3.55 (d, *J* = 11.2 Hz, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 143.1 (d, *J* = 4.0 Hz), 137.8, 137.0, 133.6, 128.6, 128.4, 128.3, 128.2, 127.4, 116.5, 53.2 (d, *J* = 6.1 Hz), 48.5 (d, *J* = 5.1 Hz), 48.4 (d, *J* = 4.0 Hz); $^{31}P$ NMR (162 MHz, $CDCl_3$) ppm 12.1; HRMS (ESI): Exact mass calcd for $C_{18}H_{21}ClNNaO_3P$ $[M+Na]^+$ 388.0845, found 388.0860.



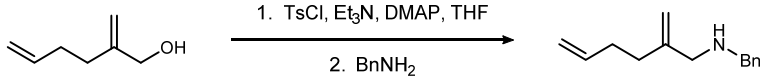

**Dimethyl benzyl(2-(2-fluorophenyl)allyl)phosphoramidate (SI-6).** To a round-bottomed flask equipped with a stir bar was added the vinyl bromide (668 mg, 2.00 mmol), potassium phosphate (1.27 g, 6.00 mmol), the boronic acid (420 mg, 3.00 mmol), 1,4-dioxane (20 mL), and water (2 mL). SPhos (41.1 mg, 100 μmol) and palladium acetate (11.2 mg, 50.0 μmol) were added, the atmosphere was replaced with argon three times, and the reaction mixture was then stirred at 100 °C for 48 h. After cooling to room temperature, the mixture was treated with water (20 mL), and the aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 25-50-75% ethyl acetate in hexanes) yielded a yellow oil (643 mg, 92%). $R_f$ = 0.34 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1257, 1061, 1030, 828, 766, 701 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.23 (m, 7H), 7.11 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.04 (ddd, *J* = 10.4, 8.0, 0.8 Hz, 1H), 5.36 (s, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 4.17 (d, *J* = 11.2 Hz, 2H), 3.91 (d, *J* = 9.6 Hz, 2H), 3.49 (d, *J* = 11.2 Hz, 6H); $^{13}C$ NMR (126 MHz, $CDCl_3$) ppm 160.2 (d, *J* = 248.2 Hz), 139.8 (d, *J* = 2.5 Hz), 137.3, 130.5 (d, *J* = 5.0 Hz), 129.2 (d, *J* = 7.6 Hz), 128.8, 128.3, 127.8 (d, *J* = 15.1 Hz), 127.4, 123.9 (d, *J* = 3.8 Hz), 119.4, 115.6 (d, *J* = 22.7 Hz), 53.0 (d, *J* = 6.3 Hz), 49.2 (dd, *J* = 3.8, 3.8 Hz), 48.5 (d, *J* = 5.0 Hz); $^{19}F$ NMR (282 MHz, $CDCl_3$) ppm -113.1; $^{31}P$ NMR (202 MHz, $CDCl_3$) ppm 13.3; HRMS (ESI): Exact mass calcd for $C_{18}H_{21}FNNaO_3P$ $[M+Na]^+$ 372.1141, found 372.1144.



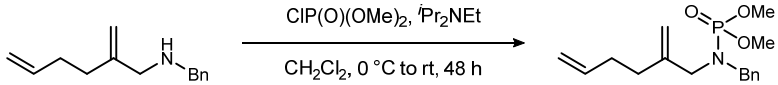

***N*-Benzyl-2-cyclohexylprop-2-en-1-amine (SI-7).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allyl alcohol (330 mg, 2.35 mmol)[4], tetrahydrofuran (9.4 mL), and triethylamine (983 μL, 7.05 mmol). 4-Toluenesulfonyl chloride (493 mg, 2.59 mmol) and 4-dimethylaminopyridine (14.4 mg, 118 μmol) were added at 0 °C and the reaction mixture was stirred at rt for 24 h. Benzylamine (1.03 mL, 9.40 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for an additional 48 h. The mixture was treated with 3 M aq sodium hydroxide (20 mL), and the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, washed with water, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 2-5-10% ethyl acetate in hexanes) yielded a yellow oil (205 mg, 38%). $R_f$ = 0.50 (20% EtOAc/hexanes) visualized with PMA; IR (film) 3336, 2925, 1450, 1114, 890, 737, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.23 (m, 5H), 4.93 (d, *J* = 1.2 Hz, 1H), 4.85 (s, 1H), 3.78 (s, 2H), 3.24 (s, 2H), 1.94 (tt, *J* = 11.2, 2.0 Hz, 1H), 1.79-1.75 (m, 4H), 1.70-1.67 (m, 1H), 1.33-1.12 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 153.2, 140.5, 128.3, 128.1, 126.9, 107.8, 53.3, 52.9, 42.4, 32.5, 26.8, 26.4; HRMS (EI): Exact mass calcd for $C_{16}H_{23}N$ $[M]^+$ 229.1830, found 229.1834.




**Dimethyl benzyl(2-cyclohexylallyl)phosphoramidate (SI-8).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (183 mg, 800 μmol), dichloromethane (2 mL), and Hünig's base (418 μL, 2.40 mmol). Dimethyl chlorophosphate (129 μL, 1.20 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 15-30-45% ethyl acetate in hexanes) yielded a yellow oil (202 mg, 75%). $R_f$ = 0.43 (50% EtOAc/hexanes) visualized with PMA; IR (film) 2925, 1258, 1062, 1031, 827, 702 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 4.94 (s, 1H), 4.89 (d, *J* = 1.2 Hz, 1H), 4.14 (d, *J* = 11.6 Hz, 2H), 3.71 (d, *J* = 11.2 Hz, 6H), 3.49 (d, *J* = 9.6 Hz, 2H), 1.87-1.66 (m, 6H), 1.29-1.06 (m, 5H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 149.8 (d, *J* = 3.0 Hz), 137.7, 128.8, 128.3, 127.3, 110.2, 53.3 (d, *J* = 6.1 Hz), 48.6 (d, *J* = 4.0 Hz), 48.5 (d, *J* = 5.1 Hz), 40.8, 32.3, 26.8, 26.3; $^{31}P$ NMR (162 MHz, $CDCl_3$) ppm 12.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{28}NNaO_3P$ $[M+Na]^+$ 360.1704, found 360.1710.

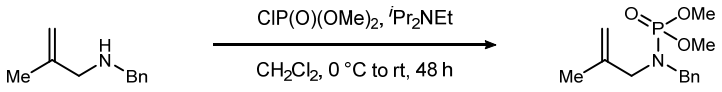



***N*-Benzyl-2-methylenehex-5-en-1-amine (SI-9).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allyl alcohol (734 mg, 6.55 mmol)[5], tetrahydrofuran (26 mL), and triethylamine (2.74 mL, 19.7 mmol). 4-Toluenesulfonyl chloride (1.37 g, 7.21 mmol) and 4-dimethylaminopyridine (40.0 mg, 328 μmol) were added at 0 °C and the reaction mixture was stirred at rt for 24 h. Benzylamine (2.86 mL, 26.2 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at room temperature for additional 48 h. The mixture was treated with 3 M aq sodium hydroxide (50 mL), and the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, washed with water, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 2-5-10% ethyl acetate in hexanes) yielded a yellow oil (475 mg, 36%). $R_f$ = 0.36 (20% EtOAc/hexanes) visualized with PMA; IR (film) 3314, 2919, 1453, 1107, 906, 738, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 5.82 (ddt, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.04 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1H), 4.98 (s, 1H), 4.97 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.88 (s, 1H), 3.78 (s, 2H), 3.23 (s, 2H), 2.25-2.16 (m, 4H), 1.35 (br s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 147.1, 140.3, 138.3, 128.4, 128.2, 126.9, 114.6, 110.4, 53.7, 53.1, 33.6, 32.0; HRMS (EI): Exact mass calcd for $C_{14}H_{19}N$ $[M]^+$ 201.1517, found 201.1518.

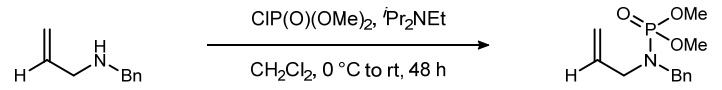



**Dimethyl benzyl(2-methylenehex-5-en-1-yl)phosphoramidate (SI-10).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (624 mg, 3.10 mmol), dichloromethane (7.8 mL), and Hünig's base (1.62 mL, 9.30 mmol). Dimethyl chlorophosphate (501 μL, 4.65 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 15-30-45% ethyl acetate in hexanes) yielded a yellow oil (834 mg, 87%). $R_f$ = 0.43 (50% EtOAc/hexanes) visualized with PMA; IR (film) 2950, 1258, 1061, 1030, 826, 702 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 5.80 (ddt, *J* = 17.2, 10.4, 6.4 Hz, 1H), 5.02 (ddt, *J* = 17.2, 2.0, 1.6 Hz, 1H), 4.97 (s, 1H), 4.96 (ddd, *J* = 10.4, 1.6, 1.6 Hz,

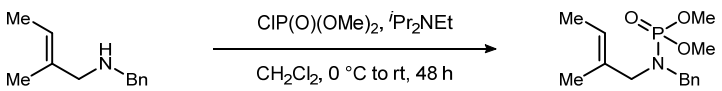
1H), 4.92 (s, 1H), 4.14 (d, *J* = 11.2 Hz, 2H), 3.71 (d, *J* = 11.2 Hz, 6H), 3.48 (d, *J* = 9.6 Hz, 2H), 2.23-2.16 (m, 2H), 2.11-2.07 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 143.9 (d, *J* = 3.0 Hz), 138.1, 137.4 (d, *J* = 2.0 Hz), 128.7, 128.3, 127.3, 114.7, 112.9, 53.3 (d, *J* = 5.1 Hz), 49.3 (d, *J* = 5.1 Hz), 48.3 (d, *J* = 5.1 Hz), 32.5, 31.6; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.8; HRMS (ESI): Exact mass calcd for $C_{16}H_{24}NNaO_3P$ $[M+Na]^+$ 332.1392, found 332.1395.




**Dimethyl benzyl(2-methylallyl)phosphoramidate (SI-11).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (452 mg, 2.80 mmol)[6], dichloromethane (7 mL), and Hünig's base (1.46 mL, 8.40 mmol). Dimethyl chlorophosphate (453 µL, 4.20 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 30-50-70% ethyl acetate in hexanes) yielded a yellow oil (625 mg, 83%). $R_f$ = 0.34 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1257, 1062, 1031, 828, 703 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 4.95 (s, 1H), 4.84 (s, 1H), 4.14 (d, *J* = 11.2 Hz, 2H), 3.71 (d, *J* = 11.2 Hz, 6H), 3.45 (d, *J* = 10.0 Hz, 2H), 1.72 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 140.7 (d, *J* = 3.0 Hz), 137.5 (d, *J* = 1.0 Hz), 128.7, 128.3, 127.3, 113.6, 53.2 (d, *J* = 6.1 Hz), 50.5 (d, *J* = 4.0 Hz), 48.3 (d, *J* = 5.1 Hz), 20.0; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.7; HRMS (ESI): Exact mass calcd for $C_{13}H_{20}NNaO_3P$ $[M+Na]^+$ 292.1078, found 292.1089.

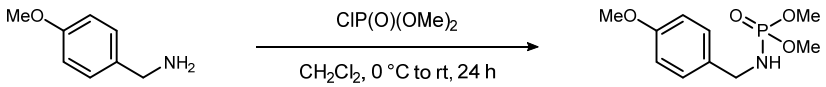



**Dimethyl allyl(benzyl)phosphoramidate (SI-12).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (412 mg, 2.80 mmol), dichloromethane (7 mL), and Hünig's base (1.46 mL, 8.40 mmol). Dimethyl chlorophosphate (453 µL, 4.20 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 40-60-80% ethyl acetate in hexanes) yielded a yellow oil (636 mg, 89%). $R_f$ = 0.32 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1257, 1058, 1032, 826, 702 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 5.75 (dddd, *J* = 16.8, 10.0, 6.4, 6.4 Hz, 1H), 5.19 (d, *J* = 10.0 Hz, 1H), 5.12 (dd, *J* = 16.8, 1.2 Hz, 1H), 4.19 (d, *J* = 10.0 Hz, 2H), 3.72 (d, *J* = 11.2 Hz, 6H), 3.49 (dd, *J* = 11.6, 6.4 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 137.6 (d, *J* = 3.0 Hz), 134.0 (d, *J* = 1.0 Hz), 128.42, 128.35, 127.3, 118.3, 53.1 (d, *J* = 6.1 Hz), 48.4 (d, *J* = 5.1 Hz), 47.3 (d, *J* = 5.1 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.7; HRMS (ESI): Exact mass calcd for $C_{12}H_{18}NNaO_3P$ $[M+Na]^+$ 278.0922, found 278.0932.

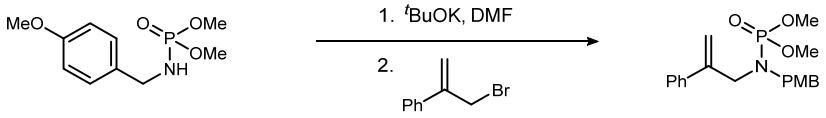



**Dimethyl (*E*)-benzyl(2-methylbut-2-en-1-yl)phosphoramidate (5).** To a flame-dried round-bottomed flask equipped with a stir bar was added the allylamine (911 mg, 5.20 mmol)[7], dichloromethane (13 mL), and Hünig's base (2.72 mL, 15.6 mmol). Dimethyl chlorophosphate (841 µL, 7.80 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 48 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted twice with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 20-40-60% ethyl

acetate in hexanes) yielded a yellow oil (1.33 g, 90%). $R_f$ = 0.30 (50% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1256, 1061, 1030, 826, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H), 5.30-5.25 (m, 1H), 4.09 (d, *J* = 11.6 Hz, 2H), 3.70 (d, *J* = 11.2 Hz, 6H), 3.43 (d, *J* = 9.2 Hz, 2H), 1.62 (d, *J* = 8.0 Hz, 3H), 1.61 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 137.9, 131.2 (d, *J* = 3.0 Hz), 128.7, 128.2, 127.1, 123.4, 53.2 (d, *J* = 6.1 Hz), 52.6 (d, *J* = 4.0 Hz), 48.1 (d, *J* = 5.1 Hz), 13.7, 13.3; $^{31}P$ NMR (162 MHz, $CDCl_3$) ppm 12.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{22}NNaO_3P$ $[M+Na]^+$ 306.1230, found 306.1226.




**Dimethyl (4-methoxybenzyl)phosphoramidate (SI-13).** To a flame-dried round-bottomed flask equipped with a stir bar was added 4-methoxybenzylamine (1.31 mL, 10.0 mmol) and dichloromethane (10 mL). Dimethyl chlorophosphate (431 μL, 4.00 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 24 h. The mixture was treated with hexanes (50 mL), and 4-methoxybenzylamine hydrochloric acid salt was removed by filtration. The filtrate was concentrated and flash column chromatography ($SiO_2$, 2-10-20% methanol in ethyl acetate) yielded a yellow oil (959 mg, 98%). $R_f$ = 0.35 (20% MeOH/EtOAc) visualized with PMA; IR (film) 3225, 2952, 1513, 1249, 1034, 830, 760 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.03 (dd, *J* = 9.6, 6.8 Hz, 2H), 3.80 (s, 3H), 3.70 (d, *J* = 11.2 Hz, 6H), 2.86 (br s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 159.0, 131.6 (d, *J* = 7.1 Hz), 128.6, 114.0, 55.3, 53.1 (d, *J* = 6.1 Hz), 44.8; $^{31}P$ NMR (162 MHz, $CDCl_3$) ppm 12.2; HRMS (ESI): Exact mass calcd for $C_{10}H_{16}NNaO_4P$ $[M+Na]^+$ 268.0709, found 268.0702.

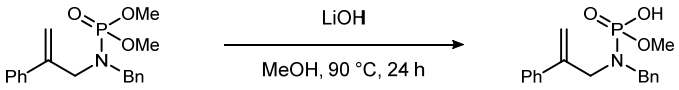



**Dimethyl (4-methoxybenzyl)(2-phenylallyl)phosphoramidate (SI-14).** To a flame-dried round-bottomed flask equipped with a stir bar was added the phosphoramidate (662 mg, 2.70 mmol) and *N*,*N*-dimethylformamide (7.7 mL). Potassium *tert*-butoxide (528 mg, 4.32 mmol) was added at 0 °C and the reaction mixture was stirred at 0 °C for 30 min. The allyl bromide (1.06 g 5.40 mmol)[8] was added at 0 °C and the reaction mixture was stirred at rt for 24 h. The mixture was quenched with satd aq ammonium chloride, and the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, washed twice with water and then brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 40-60-80% ethyl acetate in hexanes) yielded a yellow oil (703 mg, 72%). $R_f$ = 0.31 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1513, 1252, 1060, 1031, 828, 705 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.35-7.23 (m, 5H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.41 (s, 1H), 5.17 (d, *J* = 1.2 Hz, 1H), 4.05 (d, *J* = 11.2 Hz, 2H), 3.97 (d, *J* = 9.2 Hz, 2H), 3.81 (s, 3H), 3.51 (d, *J* = 11.2 Hz, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) ppm 158.9, 144.3 (d, *J* = 4.0 Hz), 139.5, 130.1, 129.2, 128.2, 127.8, 126.9, 115.9, 113.7, 55.2, 53.0 (d, *J* = 6.1 Hz), 48.3 (d, *J* = 5.1 Hz), 47.7 (d, *J* = 4.0 Hz); $^{31}P$ NMR (162 MHz, $CDCl_3$) ppm 12.2; HRMS (ESI): Exact mass calcd for $C_{19}H_{24}NNaO_4P$ $[M+Na]^+$ 384.1341, found 384.1339.

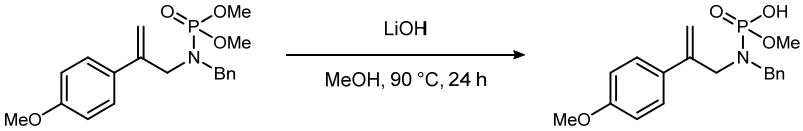
**General Procedure for Preparation of Phosphoramidic Acids**

To a sealed tube equipped with a stir bar was added the phosphoramidate (1 equiv), methanol (0.05 M) and lithium hydroxide (10 equiv), and the reaction mixture was stirred at 90 °C for 24 h. The mixture was then cooled to room temperature, treated with water, and then the aqueous solution was washed with hexanes. The aqueous layer was treated with 1 M aq HCl (until pH 2) and then extracted three times with ethyl acetate. The organic layers were combined, washed with water and brine, dried over sodium sulfate and concentrated. The phosphoramidic acids are prone to decomposition at room temperature, so the unpurified material was

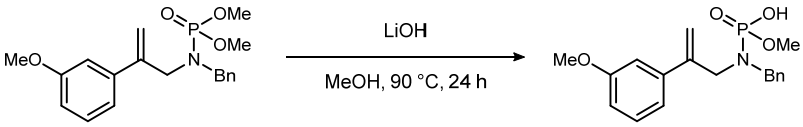
submitted to the iodocyclization as soon as possible.[9] Partial data to characterize the (unpurified) phosphoramidic acid was collected.



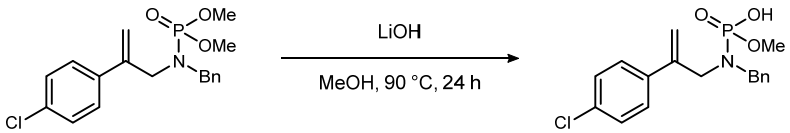

**Methyl hydrogen benzyl(2-phenylallyl)phosphoramidate (3aa).** Prepared according to the general procedure using the phosphoramidate (232 mg, 700 μmol) to afford a yellow oil (204 mg, 92%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *This phosphoramidic acid decomposes rapidly at room temperature, so only $^1$H NMR data could be obtained.* $^1$H NMR (500 MHz, $CDCl_3$) δ 8.86 (br s, 1H), 7.43-7.24 (m, 10H), 5.42 (s, 1H), 5.24 (s, 1H), 4.17 (d, *J* = 11.0 Hz, 2H), 3.97 (d, *J* = 10.0 Hz, 2H), 3.54 (d, *J* = 11.5 Hz, 3H).



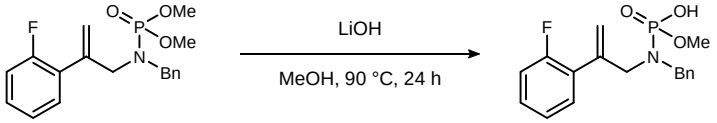

**Methyl hydrogen benzyl(2-(4-methoxyphenyl)allyl)phosphoramidate (3ab).** Prepared according to the general procedure using the phosphoramidate (50.6 mg, 140 μmol) to afford a yellow oil (46.2 mg, 95%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *This phosphoramidic acid decomposes rapidly at room temperature, so only $^1$H NMR data could be obtained.* $^1$H NMR (400 MHz, $CDCl_3$) δ 8.53 (br s, 1H), 7.35-7.24 (m, 7H), 6.83 (d, *J* = 8.8 Hz, 1H), 5.35 (s, 1H), 5.14 (d, *J* = 1.2 Hz, 1H), 4.16 (d, *J* = 10.8 Hz, 2H), 3.94 (d, *J* = 9.6 Hz, 2H), 3.78 (s, 3H), 3.57 (d, *J* = 11.6 Hz, 3H).



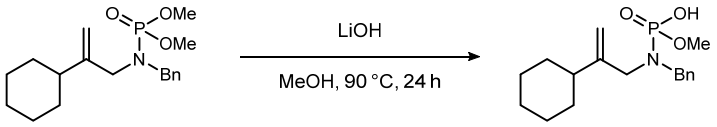

**Methyl hydrogen benzyl(2-(3-methoxyphenyl)allyl)phosphoramidate (3ac).** Prepared according to the general procedure using the phosphoramidate (54.0 mg, 149 μmol) to afford a yellow oil (43.4 mg, 94%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *This phosphoramidic acid decomposes rapidly at room temperature, so only $^1$H NMR data could be obtained.* $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.19 (m, 6H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.81 (d, *J* = 7.6, 2.0 Hz, 1H), 6.54 (br s, 1H), 5.42 (s, 1H), 5.23 (d, *J* = 0.8 Hz, 1H), 4.17 (d, *J* = 10.8 Hz, 2H), 3.95 (d, *J* = 9.6 Hz, 2H), 3.79 (s, 3H), 3.55 (d, *J* = 11.6 Hz, 3H).



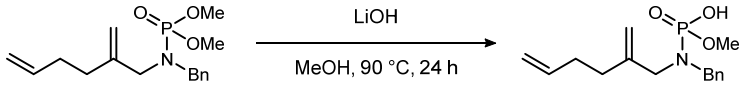

**Methyl hydrogen benzyl(2-(4-chlorophenyl)allyl)phosphoramidate (3ad).** Prepared according to the general procedure using the phosphoramidate (58.5 mg, 160 μmol) to afford a yellow oil (49.8 mg, 87%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *This phosphoramidic acid decomposes rapidly at room temperature, so only $^1$H NMR data could be obtained.* $^1$H NMR (400 MHz, $CDCl_3$) δ 10.76 (br s, 1H), 7.33-7.23 (m, 9H), 5.40 (s, 1H), 5.22 (s, 1H), 4.14 (d, *J* = 10.8 Hz, 2H), 3.94 (d, *J* = 9.6 Hz, 2H), 3.58 (d, *J* = 11.6 Hz, 3H).



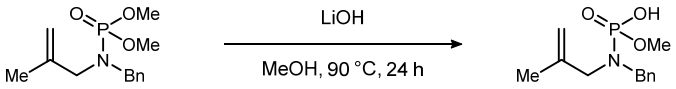

**Methyl hydrogen benzyl(2-(2-fluorophenyl)allyl)phosphoramidate (3ae).** Prepared according to the general procedure using the phosphoramidate (55.9 mg, 160 μmol) to afford a yellow oil (51.0 mg, 95%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *In order to slow the decomposition during the NMR experiments, solvents were not completely removed.* $^{1}$H NMR (400 MHz, $CDCl_3$) δ 10.79 (br s, 1H), 7.36-7.19 (m, 7H), 7.07 (dd, *J* = 7.6, 6.8 Hz, 1H), 7.01 (dd, *J* = 10.4, 8.4 Hz, 1H), 5.42 (s, 1H), 5.34 (s, 1H), 4.19 (d, *J* = 10.4 Hz, 2H), 3.90 (d, *J* = 10.4 Hz, 2H), 3.50 (d, *J* = 11.2 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 160.0 (d, *J* = 247.0 Hz), 139.9, 137.4, 130.3 (d, *J* = 3.8 Hz), 129.1 (d, *J* = 7.6 Hz), 128.6, 128.3, 128.0 (d, *J* = 10.1 Hz), 127.3, 123.9 (d, *J* = 3.8 Hz), 118.4, 115.6 (d, *J* = 22.7 Hz), 52.9 (d, *J* = 6.3 Hz), 49.0 (dd, *J* = 3.8, 3.8 Hz), 48.7 (d, *J* = 5.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.7.



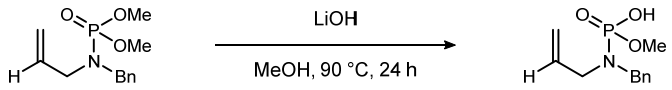

**Methyl hydrogen benzyl(2-cyclohexylallyl)phosphoramidate (3af).** Prepared according to the general procedure using the phosphoramidate (46.9 mg, 139 μmol) to afford a yellow oil (42.0 mg, 94%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.60 (br s, 1H), 7.35-7.22 (m, 5H), 4.91 (s, 2H), 4.16 (d, *J* = 11.2 Hz, 2H), 3.72 (d, *J* = 11.2 Hz, 3H), 3.72 (d, *J* = 10.4 Hz, 2H), 1.88-1.64 (m, 6H), 1.29-1.04 (m, 6H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 149.8, 137.8, 137.5, 128.6, 128.3, 127.2, 110.0, 53.2 (d, *J* = 6.3 Hz), 48.6 (d, *J* = 5.0 Hz), 48.4 (d, *J* = 5.0 Hz), 32.3, 26.7, 26.4; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.2.



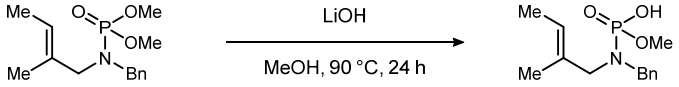

**Methyl hydrogen benzyl(2-methylenehex-5-en-1-yl)phosphoramidate (3ag).** Prepared according to the general procedure using the phosphoramidate (45.5 mg, 147 μmol) to afford a yellow oil (32.2 mg, 74%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.23 (m, 5H), 5.79 (ddt, *J* = 16.8, 10.4, 6.4 Hz, 1H), 5.01 (ddd, *J* = 17.2, 1.6, 1.6 Hz, 1H), 4.94-4.92 (m, 3H), 4.16 (dd, *J* = 10.8 Hz, 2H), 3.71 (d, *J* = 11.2 Hz, 3H), 3.49 (d, *J* = 10.4 Hz, 2H), 2.22-2.08 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 143.9, 138.2, 137.5, 128.6, 128.3, 127.2, 114.7, 112.8, 53.3 (d, *J* = 6.3 Hz), 49.4 (d, *J* = 5.0 Hz), 48.3 (d, *J* = 5.0 Hz), 32.4, 31.7; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 14.1.



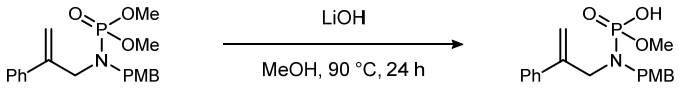

**Methyl hydrogen benzyl(2-methylallyl)phosphoramidate (3ah).** Prepared according to the general procedure using the phosphoramidate (59.2 mg, 220 μmol) to afford a yellow oil (29.6 mg, 53%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *In order to slow the decomposition during the NMR experiments, solvents were not completely removed.* $^{1}$H NMR (400 MHz, $CDCl_3$) δ 10.50 (br s, 1H), 7.36-7.25 (m, 5H), 4.92 (s, 1H), 4.83 (s, 1H), 4.16 (d, *J* = 10.8 Hz, 2H), 3.71 (d, *J* = 11.6 Hz, 3H), 3.47 (d, *J* = 10.4 Hz, 2H), 1.72 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 140.9 (d, *J* = 1.3 Hz), 137.6 (d, *J* = 2.5 Hz), 128.6, 128.3, 127.2, 113.6, 53.2 (d, *J* = 6.3 Hz), 50.6 (d, *J* = 5.0 Hz), 48.2 (d, *J* = 5.0 Hz), 20.0; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 14.1.




**Methyl hydrogen allyl(benzyl)phosphoramidate (3ai).** Prepared according to the general procedure using the phosphoramidate (63.8 mg, 250 μmol) to afford a yellow oil (30.2 mg, 50%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. *This phosphoramidic acid decomposes rapidly at room temperature, so only $^1$H NMR data could be obtained.* $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.23 (m, 5H), 5.77 (dddd, *J* = 16.8, 10.0, 6.4, 6.4 Hz, 1H), 5.16 (d, *J* = 10.0 Hz, 1H), 5.12 (dd, *J* = 16.8, 1.2 Hz, 1H), 4.87 (br s, 1H), 4.20 (d, *J* = 9.6 Hz, 2H), 3.71 (d, *J* = 11.2 Hz, 3H), 3.51 (dd, *J* = 11.6, 6.4 Hz, 2H).

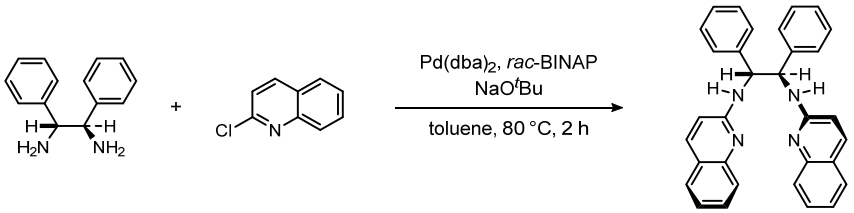



**Methyl hydrogen (*E*)-benzyl(2-methylbut-2-en-1-yl)phosphoramidate (3aj).** Prepared according to the general procedure using the phosphoramidate (45.3 mg, 160 μmol) to afford a yellow oil (40.7 mg, 94%). The phosphoramidic acid was used for the iodocyclization as soon as possible without purification. *In order to slow the decomposition during the NMR experiments, solvents were not completely removed.* $^1$H NMR (400 MHz, $CDCl_3$) δ 9.61 (br s, 1H), 7.34-7.22 (m, 5H), 5.25 (q, *J* = 5.6 Hz, 1H), 4.11 (d, *J* = 11.2 Hz, 2H), 3.70 (d, *J* = 11.6 Hz, 3H), 3.45 (d, *J* = 9.6 Hz, 2H), 1.61 (s, 3H), 1.60 (d, *J* = 5.6 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 137.9, 131.3 (d, *J* = 2.5 Hz), 128.5, 128.2, 127.0, 123.2, 53.1 (d, *J* = 6.3 Hz), 52.6 (d, *J* = 3.8 Hz), 48.0 (d, *J* = 6.3 Hz), 13.6, 13.3; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.1.



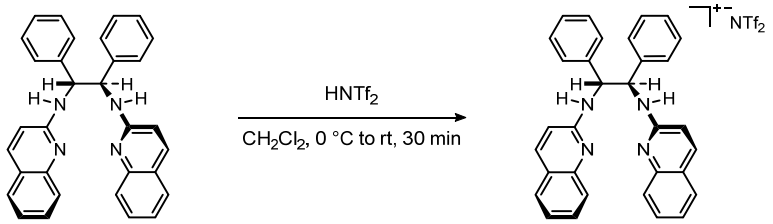

**Methyl hydrogen (4-methoxybenzyl)(2-phenylallyl)phosphoramidate (3ba).** Prepared according to the general procedure using the phosphoramidate (43.4 mg, 152 μmol) to afford a yellow oil (35.4 mg, 67%). The phosphoramidic acid was used for the iodocyclization as soon as possible without further purification. $^1$H NMR (400 MHz, $CDCl_3$) δ 9.63 (br s, 1H), 7.38-7.24 (m, 7H), 6.82 (ddd, *J* = 8.8, 2.8, 2.0 Hz , 2H), 5.43 (s, 1H), 5.25 (d, *J* = 1.2 Hz, 1H), 4.11 (d, *J* = 10.8 Hz, 2H), 3.95 (d, *J* = 9.6 Hz, 2H), 3.77 (s, 3H), 3.53 (d, *J* = 11.6 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 158.9, 143.7 (d, *J* = 3.8 Hz), 139.6, 130.0, 129.4 (d, *J* = 2.5 Hz), 128.2, 127.6, 126.6, 114.9, 113.7, 55.2, 53.2 (d, *J* = 7.6 Hz), 48.6 (d, *J* = 6.3 Hz), 48.0 (d, *J* = 6.3 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 13.7.

## Catalyst Synthesis[10]




**H,Quin-StilbBAM (2).** A round-bottomed flask equipped with a stir bar was charged with (1*R*,2*R*)-1,2-diphenylethylenediamine (1.06 g, 5.00 mmol), $Pd(dba)_2$ (43.0 mg, 80.0 μmol), *rac*-BINAP (93.0 mg, 150 μmol), sodium *tert*-butoxide (1.20 g, 12.5 mmol), and 2-chloroquinoline (1.63 g, 10.0 mmol). The reaction vessel was evacuated and placed under a nitrogen atmosphere, toluene (29 mL) was dispensed into the flask, and the

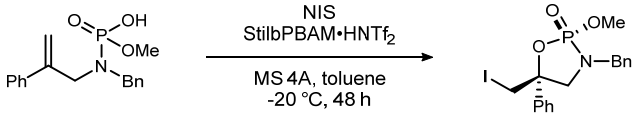
resulting solution was placed into an oil bath heated to 80 °C. After stirring for 2 h, the dark red reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a plug of Celite. The organic mixture was concentrated and the crude solid was triturated with a benzene/pentane (25/75) mixture. The solid was filtered, suspended in dichloromethane/hexanes (10/90), cooled to -20 °C and filtered. The resulting solid was dried under vacuum to give a light tan solid (2.07 g, 89%). Mp 170-172 °C; $R_f$ = 0.1 (70% EtOAc/hexanes); $[\alpha]_D^{20}$ +4.4 (*c* 1.4, $CHCl_3$); IR (film) 3238, 1619, 1573, 1508, 1426, 1352 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$) δ 7.80 (br s, 2H), 7.67 (br s, 2H) 7.58 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.31 (br s, 4H), 7.25-7.18 (m, 8H), 6.41 (br s, 4H), 5.70 (br s, 2H); $^{13}C$ NMR (151 MHz, $CDCl_3$) ppm 156.8, 147.6, 140.5, 137.0, 129.3, 128.2, 127.9, 127.4, 127.3, 126.1, 123.6, 122.4, 112.5, 62.0; HRMS (ESI) Exact mass calcd for $C_{32}H_{27}N_4$ $[M+H]^+$ 467.2236, found 467.2218.




**H,Quin-StilbBAM•$HNTf_2$ (2•$HNTf_2$)** A flame dried vial equipped with a stir bar was charged with bistrifluoromethanesulfonimide (141 mg, 500 μmol) and dichloromethane (5 mL), cooled to 0 °C, and H,Quin-StilbBAM (233 mg, 500 μmol) was added. The solution was stirred for 30 minutes before the solvent was removed *in vacuo* to give the catalyst as a beige solid that was used without any purification. *Other acid salts used in reaction optimization were made in a similar fashion using the corresponding acids and equivalents.*

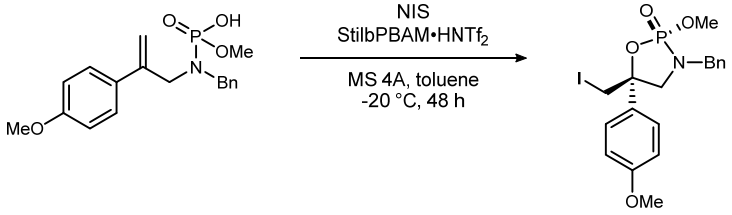
**General Procedure for Enantioselective Iodocyclizations**

To a flame-dried vial equipped with a stir bar was added the phosphoramidic acid (1 equiv), MS 4A (250 mg/mmol), toluene (0.08 M) and StilbPBAM•$HNTf_2$ (10 mol%), and the reaction was cooled to -20 ºC. *N*-Iodosuccinimide (1.5 equiv) was added and the reaction mixture was stirred without light for 48 h. The mixture was treated with 20% aq sodium thiosulfate and then the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, washed with 3 M aq sodium hydroxide, dried over sodium sulfate and concentrated. Flash column chromatography (10% $K_2CO_3/SiO_2$) yielded the product.

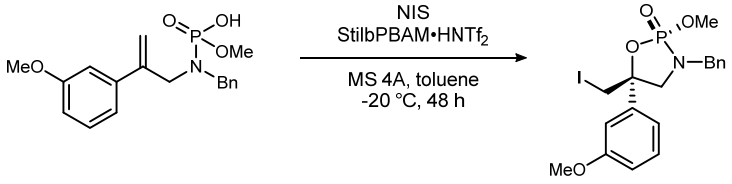



**(2*R*,5*S*)-3-Benzyl-5-(iodomethyl)-2-methoxy-5-phenyl-1,3,2-oxazaphospholidine 2-oxide (4aa).** Prepared according to the general procedure using the phosphoramidic acid (31.7 mg, 100 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (37.7 mg, 85%). The product was determined to be >20:1 dr by $^1H$ NMR and 96% ee by chiral HPLC analysis (Chiralpak AD-H, 25% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 6.4 min, $t_r(d_1e_2$, minor) = 7.2 min, $t_r(d_2e_1$, major) = 7.8 min, $t_r(d_2e_2$, minor) = 9.7 min); $R_f$ = 0.30 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -4.0 (*c* 0.92, $CHCl_3$); IR (film) 2950, 1269, 1052, 975, 826, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) ***d*₁, major** δ 7.40-7.28 (m, 10H), 4.28 (dd, *J* = 15.2, 8.8 Hz, 1H), 4.12 (dd, *J* = 15.2, 7.2 Hz, 1H), 3.70 (d, *J* = 12.0 Hz, 3H), 3.66-3.57 (m, 4H); ***d*₂, minor** δ 7.37-7.24 (m, 10H), 4.20 (dd, *J* = 15.2, 8.0 Hz, 1H), 4.08 (dd, *J* = 15.2, 8.0 Hz, 1H), 3.92 (d, *J* = 11.6 Hz, 3H), 3.75 (d, *J* = 10.8 Hz, 1H), 3.61-3.48 (m, 3H); $^{13}C$ NMR (126 MHz, $CDCl_3$) ***d*₁, major** ppm 140.4 (d, *J* = 3.8 Hz), 136.4 (d, *J* = 5.0 Hz), 128.8, 128.6, 128.5, 128.2, 127.9, 124.9, 82.4, 55.9 (d, *J* = 13.9 Hz), 54.5 (d, *J* = 7.8 Hz), 48.8 (d, *J* = 5.0 Hz), 15.4 (d, *J* = 2.5 Hz); ***d*₂, minor** ppm 140.4 (d, *J* = 5.0 Hz), 136.4 (d, *J* = 5.0 Hz),

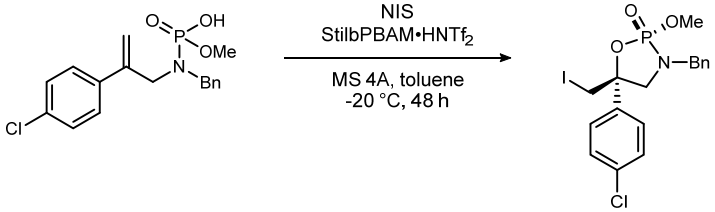
128.7, 128.5, 128.4, 127.9, 127.8, 124.7, 82.3, 56.2 (d, $J$ = 13.9 Hz), 55.1 (d, $J$ = 6.3 Hz), 48.5 (d, $J$ = 5.0 Hz), 14.7 (d, $J$ = 2.5 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ***d*$_1$, major** ppm 19.2, ***d*$_2$, minor** ppm 19.5; HRMS (ESI): Exact mass calcd for $C_{17}H_{19}INNaO_3P$ $[M+Na]^+$ 466.0045, found 466.0058.



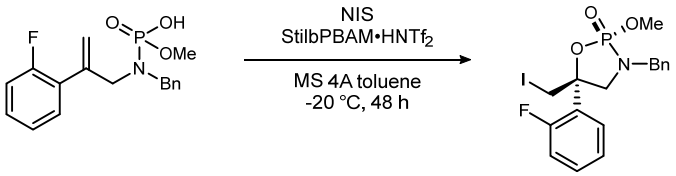

**(2*R*,5*S*)-3-Benzyl-5-(iodomethyl)-2-methoxy-5-(4-methoxyphenyl)-1,3,2-oxazaphospholidine 2-oxide (4ab).** Prepared according to the general procedure using the phosphoramidic acid (46.2 mg, 133 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, ethyl acetate) yielded a yellow oil (52.0 mg, 83%). *The product racemizes at room temperature, so the enantioenriched product could be obtained by a short column chromatography as possible.* The product was determined to be 18:1 dr by $^1$H NMR and 94% ee by chiral HPLC analysis (Chiralpak AD-H, 25% EtOH/hexanes, 1 mL/min, $t_r$(*d*$_1$*e*$_1$, major) = 8.5 min, $t_r$(*d*$_1$*e*$_2$, minor) = 9.5 min, $t_r$(*d*$_2$*e*$_1$, minor) = 10.3 min, $t_r$(*d*$_2$*e*$_2$, major) = 12.5 min)); $R_f$ = 0.30 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -13.0 (*c* 1.0, $CHCl_3$); IR (film) 2953, 1255, 1039, 975, 831, 734 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 7.22 (ddd, $J$ = 8.8, 3.2, 2.0 Hz, 2H), 6.88 (ddd, $J$ = 8.8, 3.2, 2.0 Hz, 2H), 4.26 (dd, $J$ = 14.8, 8.8 Hz, 1H), 4.12 (dd, $J$ = 14.8, 6.8 Hz, 1H), 3.80 (s, 3H), 3.67 (d, $J$ = 12.0 Hz, 3H), 3.63-3.58 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 159.6, 136.4 (d, $J$ = 5.1 Hz), 132.2 (d, $J$ = 4.0 Hz), 128.7, 128.1, 127.9, 126.2, 113.7, 82.4, 55.8 (d, $J$ = 14.1 Hz), 55.2, 54.4 (d, $J$ = 7.1 Hz), 48.7 (d, $J$ = 5.1 Hz), 15.8 (d, $J$ = 3.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 19.3; HRMS (ESI): Exact mass calcd for $C_{18}H_{21}INNaO_4P$ $[M+Na]^+$ 496.0145, found 496.0135.



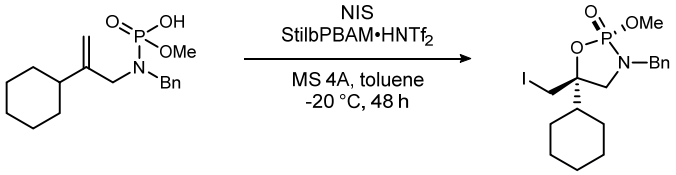

**(2*R*,5*S*)-3-Benzyl-5-(iodomethyl)-2-methoxy-5-(3-methoxyphenyl)-1,3,2-oxazaphospholidine 2-oxide (4ac).** Prepared according to the general procedure using the phosphoramidic acid (48.6 mg, 140 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (47.0 mg, 71%). The product was determined to be 18:1 dr by $^1$H NMR and 93% ee by chiral HPLC analysis (Chiralcel OZ-H, 15% EtOH/hexanes, 1 mL/min, $t_r$(*d*$_1$*e*$_1$, minor) = 12.4 min, $t_r$(*d*$_1$*e*$_2$, major) = 15.9 min, $t_r$(*d*$_2$*e*$_1$, *d*$_2$*e*$_2$) = 10.8 min); $R_f$ = 0.30 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -4.8 (*c* 1.2, $CHCl_3$); IR (film) 2951, 1275, 1050, 914, 827, 750, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.26 (m, 6H), 6.88-6.82 (m, 3H), 4.28 (dd, $J$ = 14.8, 8.8 Hz, 1H), 4.11 (dd, $J$ = 14.8, 6.8 Hz, 1H), 3.81 (s, 3H), 3.71 (d, $J$ = 12.0 Hz, 3H), 3.65-3.57 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 159.6, 142.0 (d, $J$ = 5.1 Hz), 136.4 (d, $J$ = 5.1 Hz), 129.6, 128.8, 128.2, 127.9, 117.0, 113.6, 111.2, 82.3, 56.0 (d, $J$ = 14.1 Hz), 55.3, 54.5 (d, $J$ = 7.1 Hz), 48.8 (d, $J$ = 5.1 Hz), 15.3 (d, $J$ = 3.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 19.2; HRMS (ESI): Exact mass calcd for $C_{18}H_{22}INO_4P$ $[M+H]^+$ 474.0326, found 474.0328.



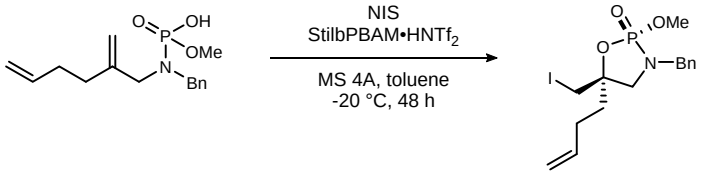

**(2*R*,5*S*)-3-Benzyl-5-(4-chlorophenyl)-5-(iodomethyl)-2-methoxy-1,3,2-oxazaphospholidine 2-oxide (4ad).** Prepared according to the general procedure using the phosphoramidic acid (49.8 mg, 139 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a white solid (49.4 mg, 74%). The product was determined to be >20:1 dr $^1$H NMR and 97% ee by chiral HPLC analysis (Chiralcel OZ-H, 12% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, minor) = 13.9 min, $t_r(d_1e_2$, major) = 14.9 min, $t_r(d_2e_1$, minor) = 11.0 min, $t_r(d_2e_2$, major) = 12.3 min); mp 144-146 °C (dec); $R_f$ = 0.33 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -18.2 (*c* 1.1, $CHCl_3$); IR (film) 2951, 1262, 1040, 975, 829, 750 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 7H), 7.23 (ddd, *J* = 8.8, 2.4, 2.0 Hz, 2H), 4.26 (dd, *J* = 14.8, 8.4 Hz, 1H), 4.11 (dd, *J* = 14.8, 6.8 Hz, 1H), 3.71 (d, *J* = 12.0 Hz, 3H), 3.63-3.52 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 138.9 (d, *J* = 5.0 Hz), 136.1 (d, *J* = 5.0 Hz), 134.6, 128.8, 128.7, 128.1, 128.0, 126.4, 82.1, 55.6 (d, *J* = 13.9 Hz), 54.6 (d, *J* = 7.6 Hz), 48.7 (d, *J* = 5.0 Hz), 14.9 (d, *J* = 2.5 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 19.1; HRMS (ESI): Exact mass calcd for $C_{17}H_{19}ClINO_3P$ $[M+H]^+$ 477.9836, found 477.9849.



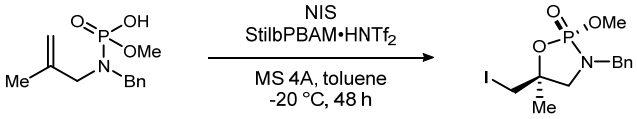

**(2*R*,5*S*)-3-Benzyl-5-(2-fluorophenyl)-5-(iodomethyl)-2-methoxy-1,3,2-oxazaphospholidine 2-oxide (4ae).** Prepared according to the general procedure using the phosphoramidic acid (51.0 mg, 152 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (56.0 mg, 80%). The product was determined to be >20:1 dr by $^1$H NMR and 96% ee by chiral HPLC analysis (Chiralpak AD-H, 15% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 7.7 min, $t_r(d_1e_2$, minor) = 9.7 min, $t_r(d_2e_1$, minor) = 8.8 min, $t_r(d_2e_2$, major) = 9.1 min); $R_f$ = 0.36 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ +40.8 (*c* 1.3, $CHCl_3$); IR (film) 2923, 1279, 1047, 982, 822, 761, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.55 (ddd, *J* = 7.6, 7.6, 2.0 Hz, 1H), 7.39-7.27 (m, 6H), 7.21 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.03 (ddd, *J* = 11.6, 7.6, 0.8 Hz, 1H), 4.28 (dd, *J* = 15.2, 9.2 Hz, 1H), 4.11 (dd, *J* = 15.2, 7.2 Hz, 1H), 3.79 (d, *J* = 11.2 Hz, 1H), 3.75 (d, *J* = 12.0 Hz, 3H), 3.69 (ddd, *J* = 16.8, 10.0, 3.2 Hz, 1H), 3.64 (d, *J* = 11.2 Hz, 1H), 3.62 (ddd, *J* = 10.0, 5.6, 1.2 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 158.3 (d, *J* = 244.4 Hz), 136.5 (d, *J* = 5.0 Hz), 130.4 (d, *J* = 8.8 Hz), 128.7, 128.3 (dd, *J* = 12.6, 5.0 Hz), 128.13, 127.9, 127.7 (d, *J* = 2.5 Hz), 124.3 (d, *J* = 2.5 Hz), 116.0 (d, *J* = 22.7 Hz), 80.6, 55.9 (dd, *J* = 13.9, 6.3 Hz), 54.6 (d, *J* = 7.6 Hz), 48.8 (d, *J* = 6.3 Hz), 13.7; $^{19}$F NMR (282 MHz, $CDCl_3$) ppm -112.8; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 18.4; HRMS (ESI): Exact mass calcd for $C_{17}H_{19}FINNaO_3P$ $[M+H]^+$ 462.0131, found 462.0151.



**(2*R*,5*S*)-3-Benzyl-5-cyclohexyl-5-(iodomethyl)-2-methoxy-1,3,2-oxazaphospholidine 2-oxide (4af).** Prepared according to the general procedure using the phosphoramidic acid (42.0 mg, 130 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (55.5 mg, 95%). The product was determined to be >20:1 dr by $^1$H NMR and 95% ee by chiral HPLC analysis (Chiralpak IB, 10% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 5.7 min, $t_r(d_1e_2$, minor) = 7.3 min, $t_r(d_2e_1$, major) = 5.5 min, $t_r(d_2e_2$, minor) = 7.7 min); $R_f$ = 0.34 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ +13.8 (*c* 0.93, $CHCl_3$); IR (film) 2929, 1260, 1048, 933, 828, 750, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 4.20 (dd, *J* = 14.8, 8.8 Hz, 1H), 4.08 (dd, *J* = 14.8, 6.8 Hz, 1H), 3.78 (d, *J* = 11.6 Hz, 3H), 3.46 (d, *J* = 10.8 Hz, 1H), 3.43 (d, *J* = 10.8 Hz, 1H), 3.22 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.00 (dd, *J* = 16.4, 9.6 Hz, 1H), 1.86-1.76 (m, 4H), 1.69-1.62 (m, 2H), 1.28-0.98 (m, 5H); δ 3.80 (d, *J* = 11.6 Hz, 3H), 3.48 (d, *J* = 10.8 Hz, 1H), 3.35 (d, *J* = 10.8 Hz, 1H), 3.15 (dd, *J* = 10.8, 9.2 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 136.6 (d, *J* = 5.1 Hz), 128.7, 128.1, 127.8, 83.6, 54.6 (d, *J* = 6.1 Hz), 51.7 (d, *J* = 15.2 Hz), 48.8 (d, *J* = 6.1 Hz), 43.8 (d, *J* = 4.0 Hz), 26.3, 26.1 (d, *J* = 6.1 Hz), 25.9 (d, *J* = 5.1 Hz), 12.3; $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 20.1; HRMS (ESI): Exact mass calcd for $C_{17}H_{25}INNaO_3P$ $[M+Na]^+$ 472.0509, found 472.0507.

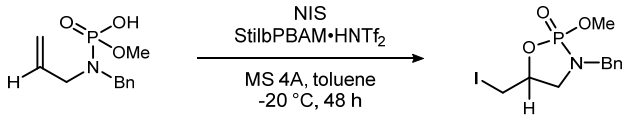



**(2*R*,5*S*)-3-Benzyl-5-(but-3-en-1-yl)-5-(iodomethyl)-2-methoxy-1,3,2-oxazaphospholidine 2-oxide (4ag).** Prepared according to the general procedure using the phosphoramidic acid (32.2 mg, 109 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (42.4 mg, 92%). The product was determined to be >20:1 dr and 98% ee by chiral HPLC analysis (Chiralpak AD-H, 10% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 8.3 min, $t_r(d_1e_2$, minor) = 10.8 min, $t_r(d_2e_1$, minor) = 9.1 min, $t_r(d_2e_2$, major) = 9.4 min); $R_f$ = 0.35 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ +5.3 (*c* 0.98, $CHCl_3$); IR (film) 2949, 1262, 1048, 960, 918, 828, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 5.79 (dddd, *J* = 17.2, 10.4, 6.4, 6.4 Hz, 1H), 5.05 (dddd, *J* = 17.2, 1.6, 1.6, 1.6 Hz, 1H), 4.99 (dddd, *J* = 10.4, 1.6, 1.2, 1.2 Hz, 1H), 4.18 (dd, *J* = 14.8, 8.8 Hz, 1H), 4.11 (dd, *J* = 14.8, 7.6 Hz, 1H), 3.77 (d, *J* = 11.6 Hz, 3H), 3.44 (d, *J* = 10.8 Hz, 1H), 3.37 (d, *J* = 10.8 Hz, 1H), 3.23 (dd, *J* = 14.4, 9.2 Hz, 1H), 3.05 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.19-2.04 (m, 2H), 2.02-1.88 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 136.8, 136.5 (d, *J* = 5.0 Hz), 128.8, 128.1, 127.9, 115.5, 82.0, 54.7 (d, *J* = 13.9 Hz), 54.5 (d, *J* = 6.3 Hz), 48.7 (d, *J* = 5.0 Hz), 37.1 (d, *J* = 3.8 Hz), 27.1, 10.6 (d, *J* = 3.8 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 20.1; HRMS (CI): Exact mass calcd for $C_{15}H_{22}INO_3P$ $[M+H]^+$ 422.0376, found 422.0388.

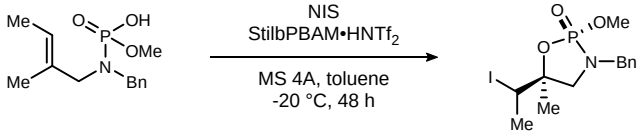



**(2*R*,5*S*)-3-Benzyl-5-(iodomethyl)-2-methoxy-5-methyl-1,3,2-oxazaphospholidine 2-oxide (4ah).** Prepared according to the general procedure using the phosphoramidic acid (29.6 mg, 116 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (40.1 mg, 91%). The product was determined to be 8:1 dr and 91% ee by chiral HPLC analysis (Chiralcel OD-H, 15% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 8.3 min, $t_r(d_1e_2$, minor) = 11.7 min, $t_r(d_2e_1$, major) = 7.9 min, $t_r(d_2e_2$, minor) = 9.2 min); $R_f$ = 0.29 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ +22.2 (*c* 1.8, $CHCl_3$); IR (film) 2952, 1258, 1044, 963, 829, 754, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 4.15 (d, *J* = 8.0 Hz, 2H), 3.76 (d, *J* = 11.6 Hz, 3H), 3.44 (d, *J* = 10.4 Hz, 1H), 3.40 (d, *J* = 10.4 Hz, 1H), 3.27 (dd, *J* = 12.4, 9.2

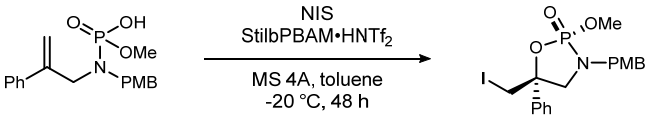
Hz, 1H) , 3.04 (dd, *J* = 9.2, 9.2 Hz, 1H), 1.60 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 136.6 (d, *J* = 5.1 Hz), 128.7, 128.1, 127.8, 80.3, 55.8 (d, *J* = 14.1 Hz), 54.5 (d, *J* = 6.1 Hz), 48.7 (d, *J* = 6.1 Hz), 25.8 (d, *J* = 3.0 Hz), 12.8 (d, *J* = 4.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 20.2; HRMS (ESI): Exact mass calcd for $C_{12}H_{17}INNaO_3P$ $[M+Na]^+$ 403.9883, found 403.9871.




**3-Benzyl-5-(iodomethyl)-2-methoxy-1,3,2-oxazaphospholidine 2-oxide (4ai).** Prepared according to the general procedure using the phosphoramidic acid (30.2 mg, 125 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (31.7 mg, 69%). The product was determined to be 1:1 dr and 68/75% ee by chiral HPLC analysis (Chiralpak AD-H, 15% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, major) = 13.3 min, $t_r(d_1e_2$, minor) = 16.7 min, $t_r(d_2e_1$, major) = 15.1 min, $t_r(d_2e_2$, minor) = 19.4 min); $R_f$ = 0.33 (50% EtOAc/hexanes) visualized with PMA; IR (film) 2951, 1273, 1050, 903, 827, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, 1:1 mixture of diastereomer) δ 7.39-7.30 (m, 10H), 4.56-4.48 (m, 2H), 4.22 (dd, *J* = 14.8, 8.8 Hz, 1H), 4.21 (dd, *J* = 14.8, 8.4 Hz, 1H), 4.11 (dd, *J* = 14.8, 7.2 Hz, 1H), 4.09 (dd, *J* = 14.8, 7.2 Hz, 1H), 3.78 (d, *J* = 11.6 Hz, 3H), 3.76 (d, *J* = 11.6 Hz, 3H), 3.43-3.33 (m, 4H), 3.24-3.19 (m, 2H), 3.04-2.98 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$, 1:1 mixture of diastereomer) ppm 136.5 (d, *J* = 5.0 Hz, 2C), 128.8 (2C), 128.12, 128.11, 127.9 (2C), 74.6, 74.3, 54.7 (d, *J* = 6.3 Hz), 54.5 (d, *J* = 6.3 Hz), 51.7 (d, *J* = 3.8 Hz), 51.6 (d, *J* = 5.0 Hz), 48.8 (d, *J* = 5.0 Hz), 48.7 (d, *J* = 5.0 Hz), 5.1 (d, *J* = 5.0 Hz), 4.7 (d, *J* = 6.3 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$, 1:1 mixture of diastereomer) ppm 21.4, 21.0; HRMS (ESI): Exact mass calcd for $C_{11}H_{15}INNaO_3P$ $[M+Na]^+$ 389.9732, found 389.9751.



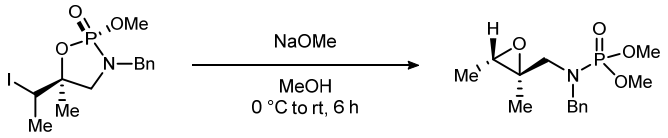

**(2*R*,5*S*)-3-Benzyl-5-((*S*)-1-iodoethyl)-2-methoxy-5-methyl-1,3,2-oxazaphospholidine 2-oxide (4aj).** Prepared according to the general procedure using the phosphoramidic acid (40.7 mg, 151 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (55.0 mg, 92%). The product was determined to be 6:1 dr and 93% ee by $^1$H NMR, $^{31}$P NMR, and chiral HPLC analysis (Chiralcel OJ-H, 3% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, minor) = 11.6 min, $t_r(d_1e_2$, major) = 14.1 min, $t_r(d_2e_1)$ = 15.1 min, $t_r(d_2e_2)$ = 19.3 min); $R_f$ = 0.35 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ +13.8 (*c* 1.1, $CHCl_3$); IR (film) 2985, 1264, 1049, 962, 824, 751, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 4.30 (q, *J* = 6.8 Hz, 1H), 4.19 (dd, *J* = 14.8, 8.4 Hz, 1H), 4.19 (dd, *J* = 14.8, 8.4 Hz, 1H), 3.75 (d, *J* = 11.6 Hz, 3H), 3.26 (dd, *J* = 9.2, 8.8 Hz, 1H), 3.05 (dd, *J* = 13.2, 9.2 Hz, 1H), 1.92 (d, *J* = 6.8 Hz, 3H), 1.59 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 136.6 (d, *J* = 5.1 Hz), 128.7, 128.0, 127.8, 83.3, 58.6 (d, *J* = 13.1 Hz), 54.6 (d, *J* = 6.1 Hz), 48.6 (d, *J* = 5.1 Hz), 32.4 (d, *J* = 5.1 Hz), 22.6, 21.2 (d, *J* = 2.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 22.1; HRMS (ESI): Exact mass calcd for $C_{13}H_{19}INNaO_3P$ $[M+Na]^+$ 418.0045, found 408.0039.



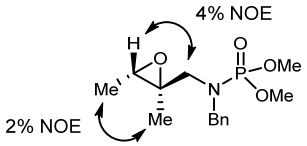

**(2*R*,5*S*)-5-(Iodomethyl)-2-methoxy-3-(4-methoxybenzyl)-5-phenyl-1,3,2-oxazaphospholidine 2-oxide (4ba).** Prepared according to the general procedure using the phosphoramidic acid (35.4 mg, 102 μmol). Flash column chromatography (10% $K_2CO_3/SiO_2$, 20-50-70% ethyl acetate in hexanes) yielded a yellow oil (41.1 mg, 85%).

The product was determined to be >20:1 dr by $^1$H NMR and 93% ee by chiral HPLC analysis (Chiralcel OJ-H, 20% EtOH/hexanes, 1 mL/min, $t_r(d_1e_1$, minor) = 13.3 min, $t_r(d_1e_2$, major) = 23.8 min, $t_r(d_2e_1$, minor) = 16.4 min, $t_r(d_2e_2$, major) = 18.4 min); $R_f$ = 0.27 (50% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -9.8 (*c* 1.0, $CHCl_3$); IR (film) 2952, 1250, 1035, 976, 824, 762, 701 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.40-7.25 (m, 7H), 6.88 (ddd, *J* = 8.8, 2.8, 2.4 Hz, 2H), 4.22 (dd, *J* = 14.8, 8.8 Hz, 1H), 4.04 (dd, *J* = 14.8, 7.2 Hz, 1H), 3.81 (s, 3H), 3.68 (d, *J* = 12.0 Hz, 3H), 3.65-3.55 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 159.3, 140.4 (d, *J* = 4.0 Hz), 129.5, 128.53, 128.45, 128.3 (d, *J* = 5.1 Hz), 124.8, 114.1, 82.4, 55.7 (d, *J* = 13.1 Hz), 55.3, 54.4 (d, *J* = 7.1 Hz), 48.1 (d, *J* = 5.1 Hz), 15.5 (d, *J* = 3.0 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 19.1; HRMS (ESI): Exact mass calcd for $C_{18}H_{22}INO_4P$ $[M+H]^+$ 474.0331, found 474.0354.

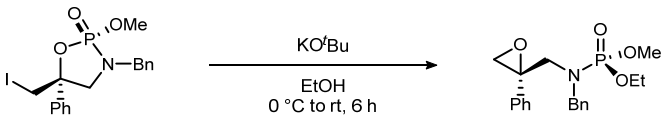
**Conversions of Cyclic Phosphoramidates**




**Dimethyl benzyl(((2*S*,3*S*)-2,3-dimethyloxiran-2-yl)methyl)phosphoramidate (6a).** To a flame-dried round-bottomed flask equipped with a stir bar was added the phosphoramidate (39.5 mg, 100 μmol) and methanol (2 mL). Sodium methoxide (54.0 mg, 1.00 mmol) was added at 0 °C and the reaction mixture was stirred at rt for 6 h. The mixture was treated with water (5 mL), and the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 45-60-75% ethyl acetate in hexanes with 1% triethylamine) yielded a yellow oil (23.9 mg, 80%). The product was determined to be 90% ee by chiral HPLC analysis (Chiralpak AD-H, 10% EtOH/hexanes, 1 mL/min, $t_r(e_1$, minor) = 7.8 min, $t_r(e_2$, major) = 9.5 min); $R_f$ = 0.34 (70% EtOAc/hexanes) visualized with PMA; $[\alpha]_D^{20}$ -1.8 (*c* 0.99, $CHCl_3$); IR (film) 2954, 1248, 1030, 828, 701 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.24 (m, 5H), 4.31 (dd, *J* = 15.2, 10.4 Hz, 1H), 4.22 (dd, *J* = 15.2, 11.6 Hz, 1H), 3.72 (d, *J* = 11.2 Hz, 6H), 3.05 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.99 (dd, *J* = 14.8, 11.2 Hz, 1H), 2.72 (q, *J* = 5.6 Hz, 1H), 1.29 (s, 3H), 1.22 (d, *J* = 5.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) ppm 137.3, 128.7, 128.4, 127.4, 59.7 (d, *J* = 3.8 Hz), 56.7, 53.3 (d, *J* = 5.0 Hz), 51.5 (d, *J* = 3.8 Hz), 50.1 (d, *J* = 5.0 Hz), 14.7, 13.6; $^{31}$P NMR (202 MHz, $CDCl_3$) ppm 13.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{22}NNaO_4P$ $[M+Na]^+$ 322.1184, found 322.1170.




The relative stereochemistry of **6a** was determined by NOE experiment.




**Ethyl methyl (*S*)-benzyl(((*S*)-2-phenyloxiran-2-yl)methyl)phosphoramidate (6b).** To a flame-dried round-bottomed flask equipped with a stir bar was added the phosphoramidate (70.9 mg, 160 μmol) and ethanol (3.2 mL). Potassium *tert*-butoxide (180 mg, 1.60 mmol) was added at 0 °C and the reaction mixture was stirred at rt for 6 h. The mixture was treated with satd aq ammonium chloride (10 mL), and the aqueous layer was extracted

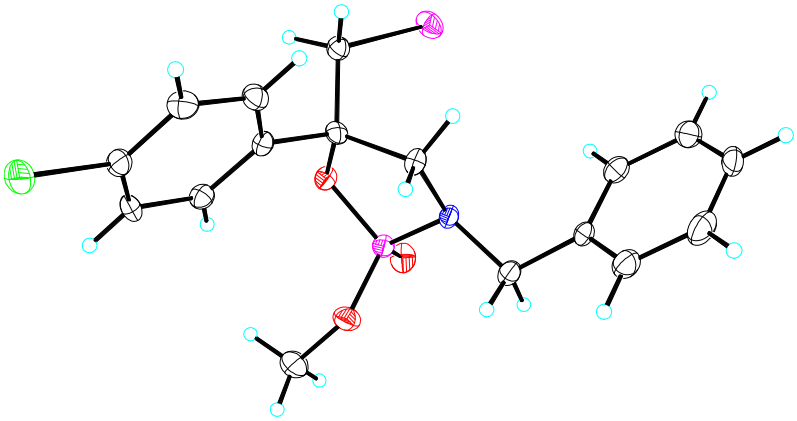
with dichloromethane. The organic layers were combined, dried over sodium sulfate and concentrated. Flash column chromatography ($SiO_2$, 20-40-60% ethyl acetate in hexanes with 1% triethylamine) yielded a yellow oil (46.8 mg, 81%). The product was determined to be 8:1 dr by $^1$H NMR and 94% ee by chiral HPLC analysis (Chiralpak IC, 4% EtOH/hexanes, 1 mL/min, $t_r$($e_1$, major) = 25.7 min, $t_r$($e_2$, minor) = 35.1 min, $t_r$($d_2e_1$, major) = 28.3 min, $t_r$($d_2e_2$, minor) = 32.4 min); $R_f$ = 0.41 (70% EtOAc/hexanes) visualized with PMA; IR (film) 2923, 1251, 1027, 956, 824, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.39-7.24 (m, 8H), 4.20-4.17 (m, 2H), 4.01-3.83 (m, 3H), 3.31 (d, $J$ = 11.2 Hz, 3H), 3.17 (dd, $J$ = 15.2, 9.2 Hz, 1H), 2.93 (d, $J$ = 5.2 Hz, 1H), 2.67 (d, $J$ = 5.2 Hz, 1H), 1.26 (ddd, $J$ = 7.2, 7.2, 0.8 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) ppm 138.1, 137.0, 129.0, 128.23, 128.22, 127.8, 127.3, 126.7, 62.5 (d, $J$ = 5.0 Hz), 60.2 (d, $J$ = 3.8 Hz), 52.6 (d, $J$ = 6.3 Hz), 52.2, 49.6 (d, $J$ = 3.8 Hz), 48.6 (d, $J$ = 5.0 Hz), 16.1 (d, $J$ = 6.3 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) ppm 10.7; HRMS (CI): Exact mass calcd for $C_{19}H_{25}NO_4P$ $[M+H]^+$ 362.1521, found 362.1509.

## Determination of the Absolute and Relative Configuration

A crystal of purified iodophosphoramidate **4ad** was grown from diethyl ether under hexanes atmosphere, and the absolute and relative stereochemistry were determined by X-ray crystallography.

| | | |
|---|---|---|
| Empirical formula | C17 H18 Cl I N O3 P | |
| Formula weight | 477.64 | |
| Crystal color, shape, size | colorless block, 0.17 × 0.15 × 0.12 mm$^3$ | |
| Temperature | 150(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system, space group | Orthorhombic, $P2_12_12_1$ | |
| Unit cell dimensions | a = 10.0282(8) Å | α= 90°. |
| | b = 12.0996(11) Å | β= 90°. |
| | c = 14.7064(12) Å | γ = 90°. |
| Volume | 1784.4(3) Å$^3$ | |
| Z | 4 | |
| Density (calculated) | 1.778 Mg/m$^3$ | |
| Absorption coefficient | 2.049 mm$^{-1}$ | |
| F(000) | 944 | |
| ***Data collection*** | | |
| Diffractometer | APEX II Kappa Duo, Bruker | |
| Theta range for data collection | 2.18 to 27.54°. | |
| Index ranges | -12<=h<=13, -15<=k<=14, -19<=l<=19 | |
| Reflections collected | 31827 | |
| Independent reflections | 4092 [R(int) = 0.0472] | |
| Observed Reflections | 3843 | |
| Completeness to theta = 27.54° | 99.9 % | |
| ***Solution and Refinement*** | | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7911 and 0.7220 | |
| Solution | Intrinsic methods | |
| Refinement method | Full-matrix least-squares on F$^2$ | |
| Weighting scheme | w = [σ$^2$Fo$^2$+ AP$^2$+ BP]$^{-1}$, with | |
| | P = (Fo$^2$+ 2 Fc$^2$)/3, A = 0.0140, B = 0.2630 | |
| Data / restraints / parameters | 4092 / 0 / 218 | |
| Goodness-of-fit on F$^2$ | 1.058 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0204, wR2 = 0.0393 | |
| R indices (all data) | R1 = 0.0231, wR2 = 0.0399 | |
| Absolute structure parameter | 0.009(11) | |
| Largest diff. peak and hole | 0.440 and -0.388 e.Å$^{-3}$ | |

Goodness-of-fit = $[\Sigma[w(F_o^2 - F_c^2)^2]/(N_{observns} - N_{params})]^{1/2}$, all data.
R1 = $\Sigma(|F_o| - |F_c|) / \Sigma |F_o|$. $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2]]^{1/2}$.



ORTEP drawing of (2*R*,5*S*)-**4ad**

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