Enantioselective Alkylation of 2-Alkyl Pyridines Controlled by Organolithium Aggregation

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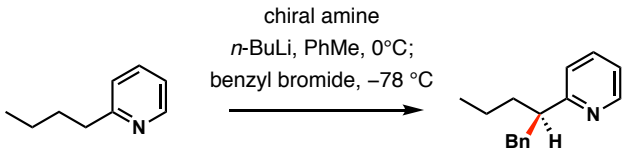
Supplementary Information I

Contents

General Information. All reactions were carried out under an inert atmosphere of dry argon in oven or flame-dried glassware, unless the reaction procedure states otherwise. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium-benzophenone in a continuous still under an atmosphere of argon. Toluene was distilled over sodium under an inert atmosphere of argon. Diisopropylamine and triethylamine were distilled from calcium hydride in a continuous still under an atmosphere of argon. Reaction temperatures were controlled by IKA ETS-D4 fuzzy thermo couples. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with Silica Gel 60 F_{254} (EMD no. 5715-7) and visualized using combinations of UV, anisaldehyde, ceric ammonium molybdate (CAM), potassium permanganate, and iodine staining. Flash column chromatography was performed using 40-63 μm silica gel (Merck, Geduran, no. 11567-1) as the stationary phase. Proton nuclear magnetic resonance spectra were recorded at 400, 500, and 600 MHz on Varian Unity Inova spectrometers. Carbon nuclear magnetic resonance spectra were recorded at 100 MHz, 125 MHz, and 150 MHz on Varian Unity Inova spectrometers. All chemical shifts were reported in δ units relative to tetramethylsilane. Optical Rotations were measured on a Rudolph Autopol III polarimeter. High resolution mass spectral data were obtained by the Mass Spectrometry laboratory at the University of California, Santa Barbara.

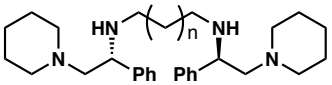
Reaction Development

Table S1. Screen of Chiral Amides.

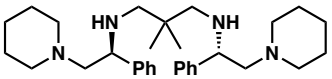


entry	chiral amine	yield (%)[a]	er
1	(*R*)-[1]**TA**	31(38)	74:26
2	(*R*)-[2]**TA**	45(53)	78:22
3	(*S*)-[3]**TA**	20(37)	53:47
4	(*R*)-[1]**TA**[b]	24(44)	97:3
5	(*R*)-[2]**TA**[b]	10(13)	57:43
6	(*S*)-[3]**TA**[b]	25(37)	56:44
7	(*S*)-[4]**TA**	32(40)	63:37
8	(*R*)-[5]**TA**	21(36)	56:44
9	(*R*)-[1]**DA**	22(25)	87:13
10	(*R*)-[2]**DA**	25(43)	64:36
11	(*R*)-[2]**DA**[b]	41(44)	63:37
12	(*R*)-[3]**DA**	21(32)	73:27
13	(*S*)-[4]**DA**	32(57)	79:21
14	(*S*)-[4]**DA**[b]	45(57)	73:27
15	(*S*)-[5]**DA**	17(40)	59:41
16	(*S*)-[6]**DA**	31(37)	67:33
17	(*S*)-[6]**DA**[b]	32(36)	85:15
18	(*S*)-[7]**DA**	30(39)	75:25
19	(*S*)-[7]**DA**[b]	38(47)	87:13
20	(*S*)-[8]**DA**	15(34)	50:50
21	(*S*)-[9]**DA**	22(37)	59:41
22	(*S*)-[9]**DA**[b]	32(52)	61:39
23	(*S*)-[10]**DA**	19(21)	62:38

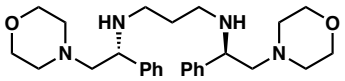
chiral amine:



n = 0, (*R*)-[1]**TA**
n = 1, (*R*)-[2]**TA**
n = 2, (*S*)-[3]**TA**

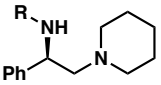


(*R*)-[4]**TA**



(*S*)-[5]**TA**

tetraamines (**TA**)



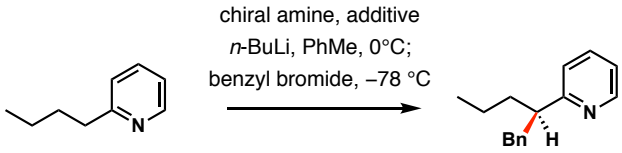
diamines (**DA**)

(*R*)-[1]**DA:** R = *t*-butyl
(*R*)-[2]**DA:** R = Et
(*R*)-[3]**DA:** R = adamantyl
(*S*)-[4]**DA:** R = $MeOCH_2CH_2$
(*S*)-[5]**DA:** R = F_3CCH_2
(*S*)-[6]**DA:** R = Bn
(*S*)-[7]**DA:** R = neopentyl
(*S*)-[8]**DA:** R = *i*-Pr
(*S*)-[9]**DA:** R = $MeOCH_2CH_2CH_2$
(*S*)-[10]**DA:** R = Cy

All reactions were carried out according to **general procedure III** (vide infra) using 0.44 mmol of 2-butylpyridine (**1a**), 0.45 mmol of chiral amine (1.03 equiv, unless otherwise noted), 0.90 mmol of *n*-BuLi for diamines (2.03 equiv) or 1.35 mmol for tetraamines (3.03 equiv), and 0.53 mmol of benzyl bromide (1.2 equiv)

in 5.0 mL of toluene. 2-Butylpyridine (**1a**) was distilled over CaH_2 and stored in a desiccator. Toluene was distilled over Na and stored in a Schlenk flask under an atmosphere of argon. Benzyl bromide was distilled over CaH_2 and stored in a desiccator. *n*-Butyllithium (2.5 M in hexanes) was purchased from Sigma-Aldrich and transferred to a Schlenk tube for storage prior to use. Chiral amines were prepared according to published procedures, dried under high vacuum for 12 h prior to use, and stored in a desiccator. [a] Conversion measured by NMR spectroscopy is shown in parenthesis. [b] 2 equiv of the chiral amine were used with an additional equivalent of *n*-BuLi for diamines and two additional equivalents of *n*-BuLi for tetraamines.

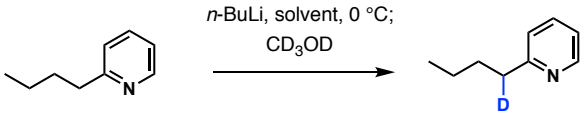
Table S2. Screen of Additives



entry	additive[a]	chiral amine[b]	yield (%)[c]	er
1	none	(*R*)-^{1}**DA**	22(25)	87:13
2	HMPA (0.5)	(*R*)-^{1}**DA**	67(70)	97:3
3	HMPA (0.75)	(*R*)-^{1}**DA**	68(78)	77:23
4	HMPA (0.75)	(*R*)-^{1}**DA** (2.03)	78(89)	95:5
5	HMPA (0.75)	(*R*)-^{1}**DA** (1.4)	75(85)	95:5
6	TMEDA (1.0)	(*R*)-^{1}**DA**	77(84)	50:50
7	TMEDA (0.5)	(*R*)-^{1}**DA**	68(70)	50:50
8	DMPU (0.5)	(*R*)-^{1}**DA**	25(28)	80:20
9	LiCl (1.0)	(*R*)-^{1}**DA**	8(9)	75:25
10	LiBr (1.0)	(*R*)-^{1}**DA**	11(11)	91:9
11	pyridine (1.0)	(*R*)-^{1}**DA**	16(43)	66:34
12	Et_3N (1.0)	(*R*)-^{1}**DA**	24(35)	87:13
13	DABCO (1.0)	(*R*)-^{1}**DA**	16(36)	59:41
14	none	(*R*)-^{3}**DA**	21(32)	73:27
15	HMPA (0.5)	(*R*)-^{3}**DA**	39(88)	87:13
16	Et_2O (0.5)	(*R*)-^{3}**DA**	14(24)	80:20
17	H_2O (1.0)	(*R*)-^{3}**DA**	16(18)	74:26
18	THF (0.5)	(*R*)-^{3}**DA**	37(60)	60:40

All reactions were carried out according to **general procedure III** (vide infra) using 0.44 mmol of 2-butylpyridine (**1a**), 0.45 mmol of chiral amine (1.03 equiv, unless otherwise noted), 0.90 mmol of *n*-BuLi (2.03 equiv, additional equivalents were added when excess chiral amine was used), and 0.53 mmol of benzyl bromide (1.2 equiv) in 5.0 mL of toluene. [a]Equivalents shown in parenthesis. [b]Equivalents of chiral amine are shown in parenthesis when the amount deviated from 1.03 equiv. [c] Conversion measured by NMR spectroscopy is shown in parenthesis.

Table S3. Lithiation Study.



entry	reaction conditions	lithiation time	deuteration (%)[a]
1	*n*-BuLi (1.1 equiv), THF	10 min	64
2	*n*-BuLi (1.1 equiv), THF	1 h	95
3	*n*-BuLi (3.0 equiv), THF	10 min	100
4	*n*-BuLi (1.1 equiv), PhMe	1 h	44
5	*n*-BuLi (1.1 equiv), PhMe	2 h	43
6	*n*-BuLi (3.0 equiv), PhMe	1 h	8
7	*n*-BuLi (1.1 equiv), HMPA (0.75 equiv), PhMe	10 min	71
8	*n*-BuLi (1.1 equiv), HMPA (0.75 equiv), PhMe	1 h	76
9	*n*-BuLi (3.0 equiv), HMPA (0.75 equiv), PhMe	1 h	55
10[b]	(^{i}Pr)$_2$NH (1.2 equiv), *n*-BuLi (2.3 equiv), PhMe	1 h	48
11[b]	(^{i}Pr)$_2$NH (1.2 equiv), *n*-BuLi (2.3 equiv), HMPA (0.75 equiv), PhMe	1 h	72
12	chiral amine (1.2 equiv), *n*-BuLi (2.3 equiv), PhMe	10 min	25
13	chiral amine (1.2 equiv), *n*-BuLi (2.3 equiv), PhMe	1 h	57
14	chiral amine (1.2 equiv), *n*-BuLi (2.3 equiv), HMPA (0.75 equiv), PhMe	10 min	81
15	chiral amine (1.2 equiv), *n*-BuLi (2.3 equiv), HMPA (0.75 equiv), PhMe	1 h	82
16	*n*-BuLi (1.1 equiv), HMPA (2.0 equiv), PhMe	1 h	68
17	chiral amine (1.2 equiv), *n*-BuLi (2.3 equiv), HMPA (2.0 equiv), PhMe	1 h	100

Deuteration procedure: A round bottom flask equipped with a stir bar is flame dried under vacuum and cooled under an atmosphere of dry argon. Chiral amine is added and the flask is backfilled with argon three times. 2-Butylpyridine (**1a**, 60 mg, 0.44 mmol) and HMPA are added by syringe and dissolved in solvent (5.0 ml). The solution is cooled to 0 °C and *n*-BuLi is added dropwise. The solution is stirred at 0 °C for the indicated period of time, and then quenched by addition of CD_3OD. After stirring for 10 min, the solution was diluted with ethyl acetate (3 mL) and DI water (3 mL) and transferred to a separatory funnel. The layers were separated, and the aqueous phase was extracted with ethyl acetate. Combined organics were washed with brine, dried over anhydrous Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (5% EtOAc in Hexane). [b]A solution of LDA was prepared in PhMe at –78 °C; HMPA and 2-

Butylpyridine (60 mg, 0.44 mmol) were added to this solution at 0 °C. [b]Deuterium incorporation was quantified by integration of ^{1}H NMR spectra obtained on a 500 MHz Varian Unity Inova spectrometer. All ^{1}H spectra were obtained in $CDCl_3$ with a relaxation delay of 30 sec (8 scans).

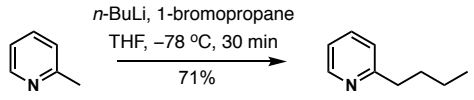
Comments:

Lithiation of **1a** with 1.1 equiv of *n*-butyllithium in tetrahydrofuran (THF) led to 64% incorporation of deuterium after a 10 min interval. Full lithiation was observed after 1 h of lithiation in THF. Lithiation in toluene (PhMe) resulted in a maximum of 43% deuterium incorporation within a 1 h interval. Addition of excess *n*-butyllithium (3 equiv) inhibited lithiation of **1a** in PhMe (entry 6), while quantitative lithiation was observed following lithiation with excess *n*-butyllithium (3 equiv) in THF (entry 3). The addition of HMPA (0.75 equiv) increased substrate lithiation in toluene to 75% after a 10-minute interval, with no further lithiation observed even after several hours. Incorporation of the chiral lithium amide into the reaction mixture resulted in an increase in lithiation to 81%, which correlates with conversion by NMR analysis observed for the asymmetric alkylation of **1a** with benzyl bromide. This enhancement in lithiation is unique to the subset of chiral lithium amides tested for this procedure, lithium diisopropylamide did not affect the same result (entries 10, 11). Complete deuteration of **1a** was only achieved in PhMe when 2.0 equiv of HMPA were used in conjunction with a chiral lithium amide base, however, under these conditions alkylation of **1a** with benzyl bromide resulted in a racemic mixture of products.

Experimental Procedures

The known chiral amine **(*R*)-^{1}DA**[1] was prepared according to the literature procedure in ref. 1 from commercially available (*R*)-styrene oxide and characterization data match reported literature.[2] 2-Methyl pyridine, 2-methylquinoline, 2-methyl-6-chloropyridine, 2-methyl-6-fluoropyridine, 2-methyl-6-methoxypyridine, 3-(pyridine-2-yl)-propanol, 2-ethyl pyridine, 5,6,7,8-tetrahydroquinoline, and pyridine-2-carbaldehyde were purchased from commercial sources and distilled over CaH_2 prior to use. Allyl bromide, methyl iodide, methallyl bromide, and benzyl bromide were purchased from commercial sources and distilled over CaH_2 prior to use. 1-Bromopropane, 1-bromohexane, 1-iodo-2-methylpropane, cyclopropylmethyl bromide, 2-iodopropane, 1-iodocyclopentane, cinnamyl bromide, 1-bromo-4-methylpent-3-ene, 1-bromo-3-(bromomethyl)benzene, 1-(bromomethyl)-3-(trifluoromethyl)benzene, and 1-(bromomethyl)naphthalene were purchased from commercial sources and used without further purification. Known compounds **1a**[3], **1e**[4], **1g**[4], **1i**[5], **1j**[6], **1k**[7], and **1l**[8] were prepared according to **general procedure I** and distilled over CaH_2 prior to use. Known compound **1m**[9] was prepared according to **general procedure II** and distilled over CaH_2 prior to use. Known compounds 4-(2-iodo-ethyl)-morpholine[10], 2-iodo-1-methoxyethane[11], 4-pyridin-2-ylbutan-2-one[12], 2-hydroxymethyl-4-(2′-pyridyl)-1-butanol[13], 4-(bromomethyl)benzene-1-sulfonylmorpholine[14], 3,4-

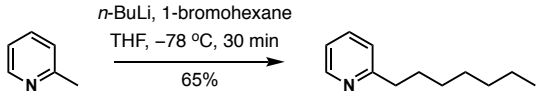
methylenedioxybenzyl bromide[15], 2-(4-(bromomethyl)phenyl)-1,3-dioxolane[16], 2-(bromomethyl)-1,3-benzothiazole[19], and [2-((*S*)-4-Benzyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl)-2-oxoethyl]phosphonic acid diethyl ester[20] were synthesized according to literature procedures. Known compounds 2-(bromomethyl)thiophene[17] and 2-(bromomethyl)pyridine[18] were prepared according to literature procedures and used immediately (without purification) as solutions in toluene.



1a

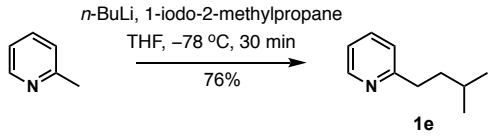
General Procedure I:

2-Butylpyridine (1a). A solution of *n*-BuLi (52 mL, 2.18 M in hexanes, 112.75 mmol, 1.05 equiv) was added dropwise to a solution of 2-methylpyridine (10.0 g, 107.38 mmol) in THF (215.0 mL) at –78 °C and the reaction mixture was allowed to stir at this temperature for 15 min. The solution was then brought to 0 °C for 15 min, after which 1-bromopropane (9.8 mL, 107.38 mmol, 1.0 equiv) was added at –78 °C. The resultant mixture was stirred for 30 min at –78 °C, quenched with MeOH (2 mL), brought to room temperature, and diluted with H_2O (50 mL) and EtOAc (50 mL). The reaction mixture was extracted with ethyl acetate, and combined organics were washed with brine, dried over anhydrous Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (2-8% EtOAc in Hexane) to afford the product **1a** (10.24 g, 75.73 mmol, 71% yield). Product was further distilled over CaH_2 (120 °C, at 10 tor) to obtaine pure compound as a colorless oil. Spectral data matches that reported in literature[3].



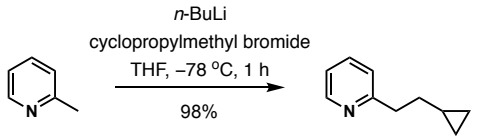
1b

2-Heptylpyridine (1b). The title compound was prepared according to **general procedure I** using 2-methylpyridine (1.00 g, 10.73 mmol), *n*-BuLi (4.5 mL, 2.5 M in hexanes, 11.27 mmol, 1.05 equiv) in THF (36.0 mL) followed by addition of 1-bromohexane (1.58 mL, 11.27 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 30 min and product **1b** (1.24 g, 6.99 mmol, 65%) was obtained after purification by column chromatography on silica gel (2-6% EtOAc in hexane) as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.51(m, 1H), 7.56 (td, *J* = 7.7, 1.9 Hz, 1H), 7.13 (m, 1H), 7.09-7.06 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 2.77 (m, 2H), 1.74-1.67 (m, 2H), 1.38-1.23 (m, 8H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 162.5, 149.2, 136.2, 122.6, 120.8, 38.5, 31.8, 29.9, 29.4, 29.2, 22.6, 14.1. HRMS (TOF MS EI) calcd for $C_{12}H_{19}N$ $[M]^+$ 177.1517, found 177.1515.



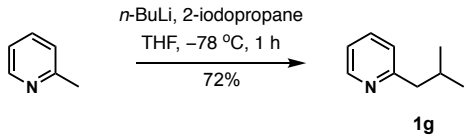
1e

2-Isopentylpyridine (1e). The title compound was prepared according to **general procedure I** using 2-methylpyridine (1.00 g, 10.73 mmol), *n*-BuLi (4.5 mL, 2.5 M in hexanes, 11.27 mmol, 1.05 equiv) in THF (36.0 mL) followed by addition of 1-iodo-2-methylpropane (1.3 mL, 11.27 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 0.5 h and product **1e** (1.214 g, 8.13 mmol, 76%) was obtained after purification by column chromatography on silica gel (2-6% EtOAc in hexane) as yellow oil. Spectral data matches that reported in the literature[4].



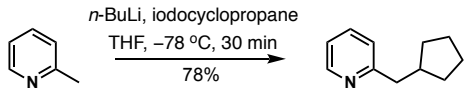
1f

2-(2-Cyclopropylethyl)pyridine (1f). The title compound was prepared according to **general procedure I** using 2-methylpyridine (1.00 g, 10.74 mmol), *n*-BuLi (4.3 mL, 2.5 M in hexanes, 10.74 mmol, 1.0 equiv) in THF (25.0 mL) followed by addition of cyclopropylmethyl bromide (1.04 mL, 10.74 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 1 h and product **1f** (1.581 g, 10.73 mmol, 98%) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 4.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.08 (t, *J* = 7.0 Hz, 1H), 2.89 (t, *J* = 7.5 Hz, 2H), 1.64 (m, 2H), 0.72 (m, 1H), 0.40 (m, 2H), 0.04 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 162.1, 149.0, 136.1, 122.7, 120.7, 38.3, 34.9, 10.6, 4.4. HRMS (TOF MS EI) calcd for $C_{10}H_{12}N$ $[M-H]^+$ 146.0970, found 146.0972.



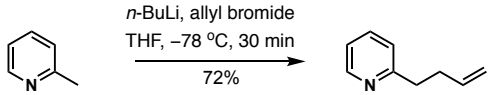
1g

2-Isobutylpyridine (1g). The title compound was prepared according to **general procedure I** using 2-methylpyridine (0.500 g, 5.37 mmol), *n*-BuLi (2.66 mL, 2.08 M in hexanes, 5.53 mmol, 1.03 equiv) in THF (15.0 mL) followed by addition of 2-iodopropane (0.561 mL, 5.63 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 1 h and product **1g** (0.521 g, 3.85 mmol, 72%) was obtained after purification by column chromatography on silica gel (3-10% EtOAc in hexane) as colorless oil. Spectral data matches that reported in the literature[4].



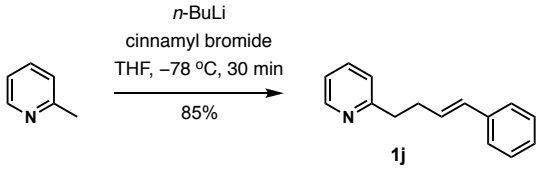
1h

2-(Cyclopentylmethyl)pyridine (1h). The title compound was prepared according to **general procedure I** using 2-methylpyridine (0.500 g, 5.37 mmol), *n*-BuLi (2.66 mL, 2.08 M in hexanes, 5.52 mmol, 1.03 equiv) in THF (15.0 mL) followed by addition of 1-iodocyclopentane (0.621 mL, 5.37 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 0.5 h and product **1h** (0.675 g, 4.19 mmol, 78%) was obtained after purification by column chromatography on silica gel (2-10% EtOAc in hexane) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.51 (m, 1H), 7.55 (td, *J* = 7.6, 1.8 Hz, 1H), 7.10 (m, 1H), 7.06 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 2.76(d, *J* = 7.5 Hz, 2H), 2.29-2.21 (m, 1H), 1.72-1.66(m, 2H), 1.65-1.59 (m, 2H), 1.54-1.47 (m, 2H), 1.25-1.16 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 162.0, 149.1, 136.0, 123.0, 120.8, 44.4, 40.6, 32.4, 24.9. HRMS (TOF MS EI) calcd for $C_{11}H_{14}N$ $[M-H]^+$ 160.1126, found 160.1130.



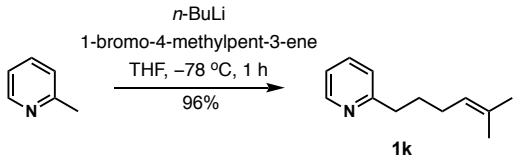
1i

2-(But-3-en-1-yl)pyridine (1i). The title compound was prepared according to **general procedure I** using 2-methylpyridine (1.00 g, 10.73 mmol), *n*-BuLi (4.5 mL, 2.5 M in hexanes, 11.27 mmol, 1.05 equiv) in THF (28.0 mL) followed by addition of allyl bromide (0.973 mL, 11.27 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 0.5 h and product **1i** (1.027 g, 7.71 mmol, 72%) was obtained after purification by column chromatography on silica gel (2-5% EtOAc in hexane) as colorless oil. Spectral data matches that reported in the literature[5].



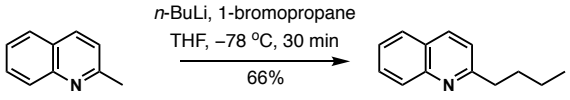
1j

(*E*)-2-(4-Phenylbut-3-en-1-yl)pyridine (1j). The title compound was prepared according to **general procedure I** using 2-methylpyridine (0.707 g, 7.591 mmol), *n*-BuLi (3.03 mL, 2.5 M in hexanes, 7.591 mmol, 1.0 equiv), in THF (25 mL) followed by addition of cinnamyl bromide (1.496 g, 7.591 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 0.5 h and product **1j** (1.353 g, 6.45 mmol, 85%) was obtained after purification by column chromatography on silica gel (2-5% EtOAc in hexanes) as a brown oil. Spectral data matches that reported in the literature[6].



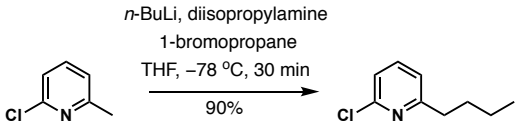
1k

2-(5-Methylhex-4-en-1-yl)pyridine (1k). The title compound was prepared according to **general procedure I** using 2-methylpyridine (0.500 g, 5.36 mmol), *n*-BuLi (2.14 mL, 2.5 M in hexanes, 5.36 mmol, 1.0 equiv), in THF (25 mL) followed by addition of 1-bromo-4-methylpent-3-ene (0.73 g, 5.36 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 1 h and product **1k** (0.903 g, 5.14 mmol, 96%) was obtained after purification by column chromatography on silica gel (2-5% EtOAc in hexanes) as a clear yellow oil. Spectral data matches that reported in the literature[7].



1l

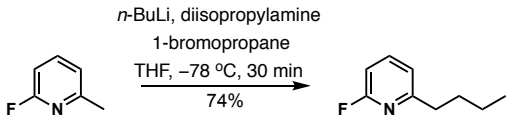
2-Butylquinoline (1l). The title compound was prepared according to **general procedure I** using 2-methylquinoline (1.00 g, 6.98 mmol), *n*-BuLi (2.93 mL, 2.5 M in hexanes, 7.33 mmol, 1.05 equiv) in THF (15.0 mL) followed by addition of 1-bromopropane (0.667 mL, 7.33 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 30 min and product **1l** (0.853 g, 4.6 mmol, 66%) was obtained after purification by column chromatography on silica gel (2-5% EtOAc in hexane) as yellow oil. Spectral data matches that reported in the literature[8].



1m

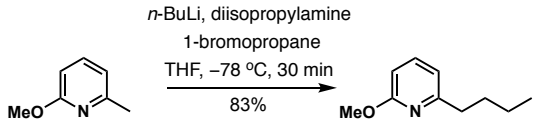
General procedure II:

2-Butyl-6-chloropyridine (1m). A solution of *n*-BuLi (3.17 mL, 2.08 M in hexanes, 6.58 mmol, 1.2 equiv) was added dropwise to a solution of diisopropylamine (0.929 mL, 6.58 mmol, 1.2 equiv) in THF (20.0 mL) at –78 °C and the reaction mixture was allowed to stir at this temperature for 30 min. A solution of 2-methyl-6-chloropyridine (0.70 g, 5.49 mmol) in THF (10 mL) was added dropwise. The resultant mixture was brought to 0 °C and stirred for 30 min after which 1-bromopropane (0.525 mL, 5.76 mmol, 1.05 equiv) was added at –78 °C. After stirring for 30 min at –78 °C, the reaction mixture was quenched with MeOH and brought to room temperature. The reaction was diluted with H_2O and extracted with ethyl acetate. Combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (1% EtOAc in Hexane) to afford the pure product **1m** (0.838 g, 4.9 mmol, 90%) as a colorless oil. Spectral data matches that reported in the literature[9].



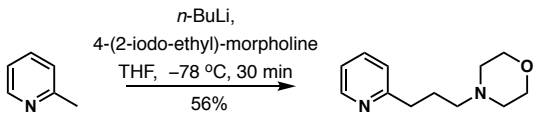
1n

2-Butyl-6-fluoropyridine (1n). The title compound was prepared according to **general procedure II** using 2-methyl-6-fluoropyridine (1.00 g, 9.0 mmol), *n*-BuLi (4.32 mL, 2.5 M in hexanes, 10.8 mmol, 1.2 equiv), and diisopropylamine (1.52 mL, 10.8 mmol, 1.2 equiv) in THF (20.0 mL) followed by addition of 1-bromopropane (0.861 mL, 9.45 mmol, 1.05 equiv), at –78 °C. The reaction was quenched after 30 min and product **1n** (1.023 g, 6.67 mmol, 74% yield) was obtained after purification by column chromatography on silica gel (1% EtOAc in hexane) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.65 (td, *J* = 8.2, 7.4 Hz, 1H), 7.00 (dd, *J* = 7.4, 2.5 Hz, 1H), 6.72 (dd, *J* = 8.2, 2.9 Hz, 1H), 2.72 (m, 2H), 1.72-1.66 (m, 2H), 1.40-1.33 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 163.2 (d, *J* = 236 Hz), 161.8 (d, J = 13.0 Hz), 140.0 (d, *J* = 7.6 Hz), 119.7 (d, *J* = 4.12 Hz), 106.2 (d, *J* = 37 Hz), 37.3, 31.6, 22.3, 13.9. ^{19}F NMR (376 MHz, CDCl3) δ (ppm): -67.9 (d, J = 6.6 Hz). HRMS (TOF MS EI) calcd for $C_9H_{11}FN$ $[M-H]^+$ 152.0876, found 152.0878.



1o

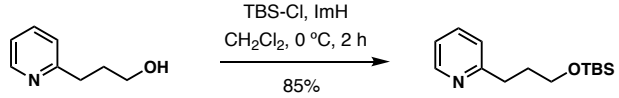
2-Butyl-6-methoxypyridine (1o). The title compound was prepared according to **general procedure I** using 2-methyl-6-methoxypyridine (0.700 g, 5.68 mmol), *n*-BuLi (2.73 mL, 2.08 M in hexanes, 5.68 mmol, 1.0 equiv) in THF (20.0 mL) followed by addition of 1-bromopropane (0.517 mL, 5.68 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 30 min and product **1o** (0.774 g, 4.68 mmol, 83%) was obtained after purification by column chromatography on silica gel (2-10% EtOAc in hexane) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.44 (dd, *J* = 8.2, 7.3 Hz, 1H), 6.68 (d, *J* = 7.2 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 3.90 (s, 3H), 2.67 (m, 2H), 1.71-1.66 (m, 2H), 1.40-1.33 (m, 2H), 0.93 (t, *J* = 7.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.6, 160.4, 138.5, 115.0, 107.0, 53.1, 37.6, 31.5, 22.4, 14.0. HRMS (TOF MS EI) calcd for $C_{10}H_{15}NO$ $[M]^+$ 165.1154, found 165.1149.



1p

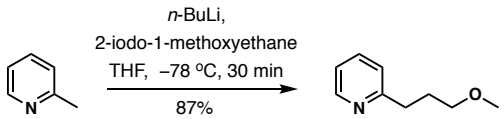
4-(3-Pyridin-2-ylpropyl)morpholine (1p). The title compound was prepared according to **general procedure I** using 2-methylpyridine (0.500 g, 5.36 mmol), *n*-BuLi (2.71 mL, 2.18 M in hexanes, 5.90 mmol, 1.1 equiv) in THF (25.0 mL) followed by addition of 4-(2-iodo-ethyl)-morpholine[10](1.42 g, 5.90 mmol, 1.1 equiv), at –78 °C.

The reaction was quenched after 30 min and product **1p** (0.619 g, 3.00 mmol, 56%) was obtained after purification by column chromatography on silica gel (5% MeOH in CH_2Cl_2) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 4.7 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.10 (t, *J* = 6.0 Hz, 1H), 3.71 (s, 4H), 2.82 (t, *J* = 7.6 Hz, 2H), 2.43 (d, *J* = 17.3 Hz, 6H), 2.05 – 1.80 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 161.67, 149.10, 136.25, 122.75, 120.97, 66.87, 58.27, 53.58, 35.95, 26.49. HRMS (TOF MS ES) calcd for $C_{12}H_{18}N_2OH$ $[M+H]^+$ 207.1497, found 207.1488.



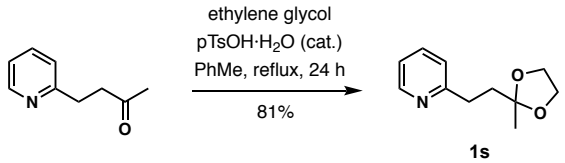
1q

***Tert*-butyl-dimethyl-(3-pyridin-2-ylpropoxy)silane (1q).** 3-(pyridine-2-yl)-propanol (1.05 g, 7.65 mmol) was dissolved in CH_2Cl_2 (75 mL) and cooled to 0 °C. Imidazole (1.042 g, 15.30 mmol, 2.0 equiv) was added followed by TBS-Cl (1.10 g, 7.26 mmol, 0.95 equiv) and the solution stirred for 2 h until completion was observed by TLC. H_2O was added to the mixture and the aqueous layer was extracted with CH_2Cl_2. Combined organics were rinsed with brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography on silica gel (5% EtOAc in hexanes) to afford the product **1q** (1.62 g, 6.17 mmol, 85%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 6.7 Hz, 1H), 7.63 – 7.53 (m, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.12 – 7.05 (m, 1H), 3.66 (t, *J* = 6.3 Hz, 2H), 2.93 – 2.79 (m, 2H), 2.01 – 1.89 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 161.99, 149.20, 136.18, 122.80, 120.88, 62.51, 34.68, 32.72, 25.95, 18.32, 5.31. HRMS (TOF MS EI) calcd for $C_{13}H_{22}NOSi$ $[M-CH_3]^+$ 236.1471, found 236.1471.

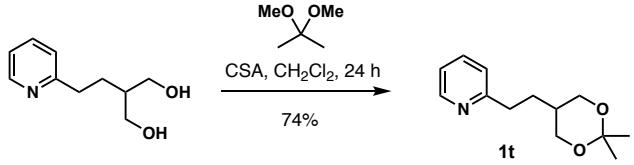


1r

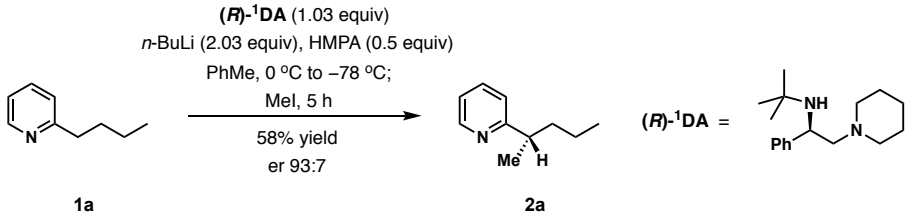
2-(3-Methoxypropyl)pyridine (1r). The title compound was prepared according to **general procedure I** using 2-methylpyridine (1.00 g, 10.7 mmol), *n*-BuLi (4.3 mL, 2.5 M in hexanes, 10.7 mmol, 1.0 equiv) in THF (53.0 mL) followed by addition of 2-iodo-1-methoxyethane[11](1.99 g, 10.7 mmol, 1.0 equiv), at –78 °C. The reaction was quenched after 0.5 h and product **1r** (1.419 g, 9.38 mmol, 87%) was obtained after purification by column chromatography on silica gel (20% EtOAc in Hexanes) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.51 (d, *J* = 5.7 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.12 – 7.06 (m, 1H), 3.41 (t, *J* = 6.4 Hz, 2H), 3.33 (s, 3H), 2.85 (t, *J* = 7.3 Hz, 2H), 2.06 – 1.96 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 161.63, 149.20, 136.22, 122.80, 120.94, 71.92, 58.46, 34.73, 29.52. HRMS (TOF MS EI) calcd for $C_8H_{10}NO$ $[M-CH_3]^+$ 136.0762, found 136.0766.



2-(2-(2-Methyl-1,3-dioxolan-2-yl)ethyl)pyridine (1s). 4-Pyridin-2-ylbutan-2-one[12] (0.380 g, 2.55 mmol), ethylene glycol (5.7 mL, 101.9 mmol, 40 equiv), and *p*-toluenesulfonic acid monohydrate (49 mg, 0.255 mmol, 0.1 equiv) were dissolved in toluene (30 mL) in a reaction vessel equipped with a Dean-Stark trap. The solution was heated to reflux for 24 h, cooled to room temperature, poured into a solution of sat $NaHCO_3$ and extracted with CH_2Cl_2. Combined organics were dried with anhydrous $NaSO_4$, concentrated, and purified by column chromatography on silica gel (10% EtOAc in Hexanes) affording **1s** (0.399 g, 2.06 mmol, 81%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 5.7 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.07 (m, 1H), 4.01 – 3.93 (m, 4H), 2.95 – 2.85 (m, 2H), 2.16 – 2.06 (m, 2H), 1.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 161.79, 149.17, 136.32, 122.68, 120.96, 109.69, 64.74, 38.81, 32.83, 23.96. HRMS (TOF MS EI) calcd for $C_{10}H_{12}NO_2$ $[M\text{-}CH_3]^+$ 178.0868, found 178.0870.

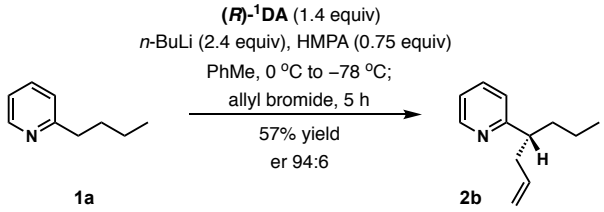


2-(2-(2,2-Dimethyl-1,3-dioxan-5-yl)ethyl)pyridine (1t). Dimethoxy propane (1.7 mL, 13.92 mmol, 6 equiv) was added to a solution of 2-hydroxymethyl-4-(2′-pyridyl)-1-butanol[13] (0.422 g, 2.32 mmol) and CSA (0.324 g, 1.39 mmol, 0.6 equiv) in CH_2Cl_2 (77 mL). After stirring for 24 h the solution was quenched with 1 M NaOH and extracted with CH_2Cl_2. Combined organics were dried over anhydrous $NaSO_4$, concentrated, and the crude residue was purified by column chromatography on silica gel (20% EtOAc in Hexanes) affording **1t** (0.380 g, 1.71 mmol, 74%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 4.8 Hz, 1H), 7.59 (d, *J* = 6.3 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 7.13 – 7.08 (m, 1H), 3.88 (dd, *J* = 12.0, 4.7 Hz, 2H), 3.63 (d, *J* = 8.2 Hz, 2H), 2.78 (d, *J* = 8.8 Hz, 2H), 1.95 – 1.83 (m, 1H), 1.71 – 1.64 (m, 2H), 1.41 (d, *J* = 15.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 161.29, 149.27, 136.41, 122.68, 121.16, 97.77, 64.68, 35.17, 33.88, 28.62, 27.28, 20.57. HRMS (TOF MS EI) calcd for $C_{12}H_{16}NO_2$ $[M\text{-}CH_3]^+$ 206.1181, found 206.1190.



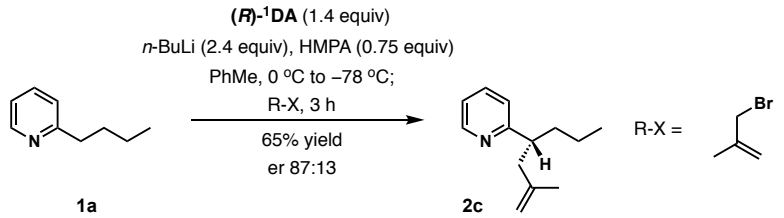
General procedure III:

(*S*)-2-(Pentan-2-yl)pyridine (2a). A round bottom flask equipped with a stir bar was flame dried under vacuum and cooled under an atmosphere of dry argon. **(*R*)-^{1}DA** (0.118 g, 0.46 mmol, 1.03 equiv) is added and the flask is backfilled with argon three times. 2-Butylpyridine (60 mg, 0.44 mmol) and HMPA (0.344 mL, 0.639 M in toluene, 0.22 mmol, 0.50 equiv) (***caution**: possible carcinogen*) were added by syringe and dissolved in toluene (4.8 ml). The solution was cooled to 0 °C and *n*-BuLi (0.390 mL, 2.29 M in hexanes, 0.893 mmol, 2.03 equiv) was added dropwise. The solution was stirred for 15 min, then cooled to –78 °C and stirred for an additional 15 min. Methyl iodide (69 µL, 1.1 mmol, 2.5 equiv) was added at –78 °C, and the solution was stirred at this temperature for 5 h. Upon completion, the reaction was quenched with 300 µL of methanol at –78 °C and the solution was stirred for 15 min before being brought to room temperature. The reaction was diluted with deionized H_2O (5 mL) and EtOAc (2 mL) and transferred to a separatory funnel. The aqueous layer was extracted 3 times with EtOAc (5 mL). Combined organic layers were rinsed with a 10 mL portion of deionized H_2O containing 0.552 mmol of HCl to recover **(*R*)-^{1}DA.** Organic layers were rinsed with brine, dried over anhydrous Na_2SO_4, concentrated, and the crude extract is purified by column chromatography on silica gel (1-2% EtOAc in hexane) to afford **2a** (38 mg, 0.255 mmol, 55% yield, 93:7 e.r.) as a colorless oil. E.r.: 93:7 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 5.18 min (major); t_1 = 4.93 min). $[\alpha]_D^{24}$ + 10.0° (*c* 0.865, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.53 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.58 (td, *J* = 7.7, 1.9 Hz, 1H), 7.11 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 2.91-2.84 (m, 1H), 1.75-1.68 (m, 1H), 1.59-1.52 (m, 1H), 1.33-1.25 (m, 1H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.24-1.13 (m, 1H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 166.7, 149.1, 136.2, 121.5, 120.9, 41.8, 39.4, 20.8, 20.7, 14.1. HRMS (TOF MS EI) calcd for $C_{10}H_{15}N$ $[M]^+$ 149.1205, found 149.1199.

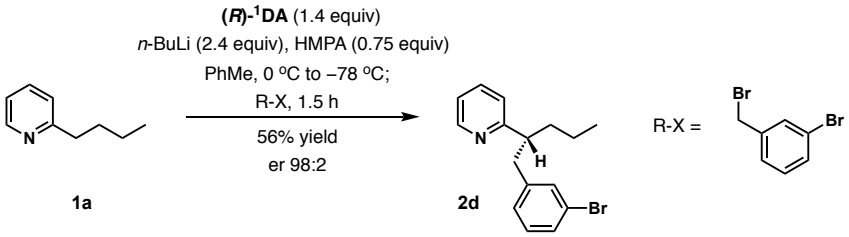


(*R*)-2-(Hept-1-en-4-yl)pyridine (2b). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of allyl bromide (57 µL, 0.66 mmol, 1.5 equiv) at –78 °C. The

reaction was quenched after 5 h at –78 °C and product **2b** (46 mg, 0.262 mmol, 60% yield) was obtained as colorless oil after purification by column chromatography on silica gel (1-2% EtOAc in hexane). Er: 94:6 (Chiralcel® AD-H; 0.1% *i*-PrOH in hexanes with 0.05% Et_3N; flow rate = 0.5 mL/min; detection at 254 nm; t_1 = 14.56 min (major); t_2 = 15.62 min). $[\alpha]_D^{20}$ + 7.8° (*c* 0.3, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.56-8.54 (m, 1H), 7.58-7.55(m, 1H), 7.09-7.06 (m, 2H), 5.71-5.62 (m, 1H), 4.96-4.91 (m, 1H), 4.90-4.87 (m, 1H), 2.84-2.78 (m, 1H), 2.51-2.36 (m, 2H), 1.75-1.62 (m, 2H), 1.25-1.08 (m, 2H), 0.85 (t, *J* = 7.32 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.7, 149.3, 136.9, 135.9, 122.7, 121.1, 115.8, 47.5, 40.0, 37.1, 20.6, 14.1. HRMS (TOF MS EI) calcd for $C_{11}H_{14}N$ $[M\text{-}CH_3]^+$ 160.1126, found 160.1124.

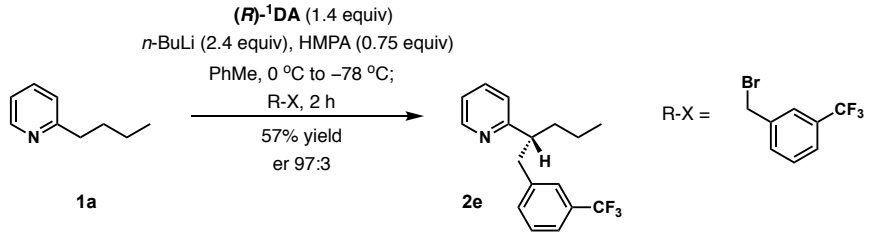


(*R*)-2-(2-Methylhept-1-en-4-yl)pyridine (2c). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of methallyl bromide (66 µL, 0.66 mmol, 1.5 equiv) at –78 °C. The reaction was quenched after 3 h at –78 °C and product **2c** (54 mg, 0.285 mmol, 65% yield) was obtained as a colorless oil after purification by column chromatography on silica gel (1-2% EtOAc in hexane). Er: 87:13 (Chiralcel® OD-H; 0.1% *i*-PrOH in hexanes with 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 10.78 min (major); t_2 = 11.23 min). $[\alpha]_D^{22}$ – 2.4° (*c* 0.93, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.55-8.54 (m, 1H), 7.56 (td, *J* = 7.6, 1.8 Hz, 1H), 7.09-7.06 (m, 2H), 4.64-4.63 (m, 1H), 4.58-4.57 (m, 1H), 2.98-2.92 (m, 1H), 2.46-2.33 (m, 2H), 1.72-1.59 (m, 5H), 1.25-1.07 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.0, 149.2, 144.0, 135.9, 122.6, 121.0, 111.9, 45.7, 44.1, 37.4, 22.4, 20.6, 14.1. HRMS (TOF MS EI) calcd for $C_{13}H_{19}N$ $[M]^+$ 189.1517, found 189.1516.

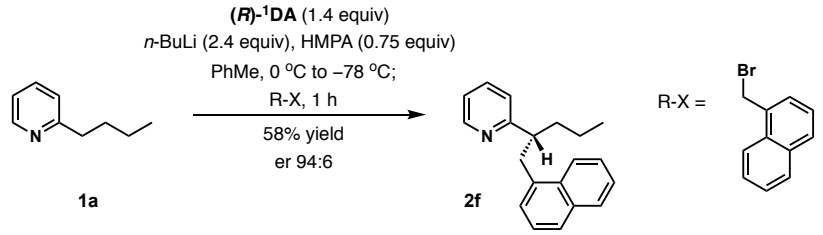


(*R*)-2-(1-(3-Bromophenyl)pentan-2-yl) pyridine (2d). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.461 mL, 2.29 M in hexanes, 1.065 mmol,

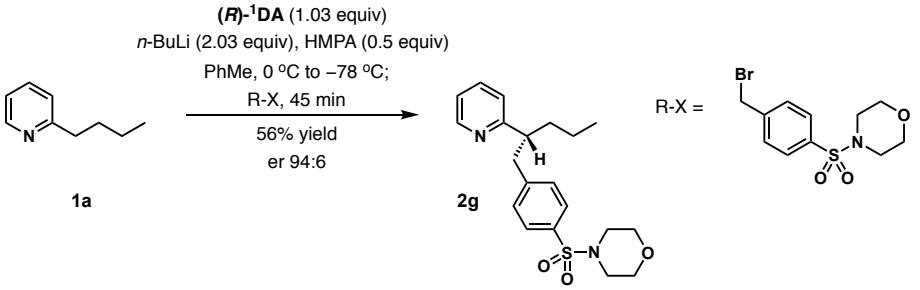
2.4 equiv) in toluene (4.6 ml) followed by the addition of a solution of 1-bromo-3-(bromomethyl)benzene (132 mg, 0.528 mmol, 1.2 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 1.5 h at –78 °C and product **2d** (75 mg, 0.252 mmol, 56% yield) was obtained as colorless oil after purification by column chromatography on silica gel (1-3% EtOAc in hexane). Er: 98:2 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 6.27 min (major); t_1 = 5.87 min). $[\alpha]_D^{21}$ – 81.7° (*c* 0.98, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.50 (td, *J* = 7.6, 1.9 Hz, 1H), 7.24 (ddd, *J* = 8.1, 2.1, 1.1 Hz, 1H), 7.17 (t, *J* = 1.8 Hz, 1H), 7.08 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.02 (t, *J* = 7.7 Hz, 1H), 6.91-6.89 (m, 2H), 3.03-2.93 (m, 2H), 2.91-2.88 (m, 1H), 1.83-1.75 (m, 1H), 1.67-1.60 (m, 1H), 1.22-1.09 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.7, 149.4, 143.2, 135.9, 132.0, 129.5, 128.8, 127.7, 123.3, 122.1, 121.3, 49.5, 41.7, 37.0, 20.6, 14.1. HRMS (TOF MS EI) calcd for $C_{16}H_{18}BrN$ $[M]^+$ 303.0623, found 303.0624.



(*R*)-2-(1-(3-(Trifluoromethyl)phenyl)pentan-2-yl)pyridine (2e). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.461 mL, 2.29 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of 1-(bromomethyl)-3-(trifluoromethyl)benzene (0.1 mL, 0.66 mmol, 1.5 equiv) at –78 °C. The reaction was quenched after 2 h at –78 °C and product **2e** (74 mg, 0.252 mmol, 57% yield) was obtained as yellow oil after purification by column chromatography on silica gel (1-3% EtOAc in hexane). Er: 97:3 (Chiralcel® AD-H; 0.5% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 7.83 min (major); t_1 = 6.46 min). $[\alpha]_D^{20}$ – 81.3° (*c* 1.085, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (ddd, *J* = 4.8,1.8, 0.9 Hz, 1H), 7.47 (td, *J* = 7.6, 1.9 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.28-7.25 (m, 1H), 7.20 (m, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 6.88-6.86 (m, 1H), 3.13-3.08 (m, 1H), 3.02-2.96 (m, 2H), 1.87-1.79 (m, 1H), 1.69-1.62 (m, 1H), 1.26-1.11 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.5, 149.5, 141.6, 135.9, 132.4 (q, *J* = 1.4 Hz), 130.1, 128.4, 125.7 (q, *J* = 3.9 Hz), 123.4, 122.5 (q, *J* = 3.8 Hz), 121.3, 49.6, 41.9, 37.1, 20.6, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): -62.6. HRMS (TOF MS EI) calcd for $C_{17}H_{18}F_3N$ $[M]^+$ 293.1391, found 293.1394.

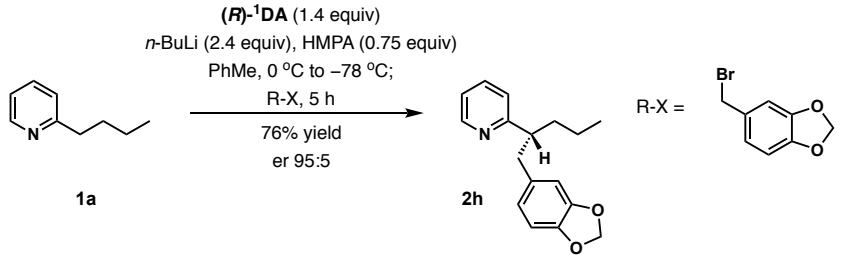


(*R*)-2-(1-(Naphthalen-1-yl)pentan-2-yl)pyridine (2f). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-[1]DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of a solution of 1-(bromomethyl)naphthalene (117 mg, 0.528 mmol, 1.2 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 1 h at –78 °C and product **2f** (56 mg, 0.254 mmol, 58% yield) was obtained as yellow oil after purification by column chromatography on silica gel (1-2% EtOAc in hexane). Er: 94:6 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 28.12 min (major); t_1 = 11.41 min). $[\alpha]_D^{21}$ – 103.4° (*c* 0.48, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.62 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 8.07-8.05 (m, 1H), 7.83-7.82 (m, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.51-7.41 (m, 3H), 7.25 (dd, *J* = 8.2, 7.0 Hz, 1H), 7.08-7.05 (m, 2H), 6.82 (dt, *J* = 7.7, 1.1 Hz, 1H), 3.44 (qd, *J* = 13.9, 7.9 Hz, 2H), 3.21-3.16 (m, 1H), 1.96-1.89 (m, 1H), 1.77-1.70 (m, 1H), 1.21-1.13 (m, 2H), 0.85 (t, *J* = 7.30 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.4, 149.5, 136.7, 135.8, 133.8, 132.1, 128.7, 127.2, 126.6, 125.7, 125.3, 125.2, 123.9, 123.4, 121.1, 48.7, 39.4, 37.3, 20.8, 14.2. HRMS (TOF MS EI) calcd for $C_{20}H_{21}N$ $[M]^+$ 275.1674, found 275.1672.

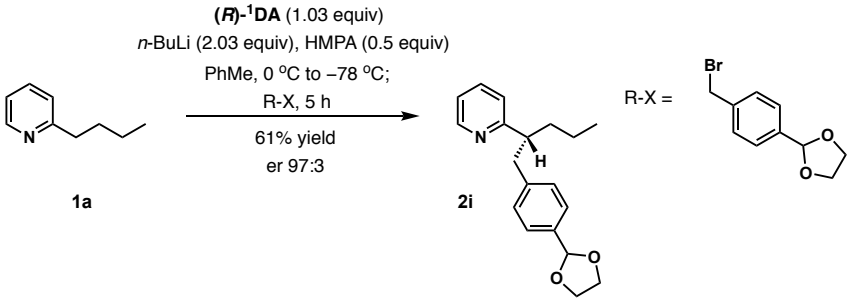


(*R*)-4-((4-(2-(Pyridine-2-yl)pentyl)phenyl)sulfonyl)morpholine (2g). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.35 mL, 0.639 M in toluene, 0.22 mmol, 0.5 equiv), and **(*R*)-[1]DA** (0.119 g, 0.457 mmol, 1.03 equiv), *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.2 ml) followed by the addition of a solution of 4-(bromomethyl)benzene-1-sulfonylmorpholine[14] (130 mg, 0.406 mmol, 0.91 equiv) in toluene (1 mL) at –78 °C. The reaction was quenched after 45 min at –78 °C and product **2g** (85 mg, 0.248 mmol, 56% yield) was obtained as a yellow oil after purification by column chromatography on silica gel (30% EtOAc in hexane). Er: 94:6 (Chiralcel® OD-H; 10% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 21.32 min (major); t_1 = 20.01 min). $[\alpha]_D^{23}$ – 76.1° (*c* 1.20, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (d, *J* = 4.8 Hz,

1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.48 (td, *J* = 7.7, 1.9 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.07 (dt, *J* = 4.8, 2.5, 0.9 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.71 (t, *J* = 4.7 Hz, 4H), 3.13 (dd, *J* = 12.8, 8.8 Hz, 1H), 3.07 – 2.97 (m, 2H), 2.95 – 2.88 (m, 4H), 1.90 – 1.79 (m, 1H), 1.72 – 1.62 (m, 1H), 1.26 – 1.12 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.35, 149.72, 147.00, 136.30, 132.46, 129.95, 127.79, 123.47, 121.63, 66.26, 49.66, 46.17, 42.07, 37.48, 20.81, 14.24. HRMS (TOF MS EI) calcd for $C_{20}H_{26}N_2O_3S$ $[M]^+$ 374.1664, found 374.1653.

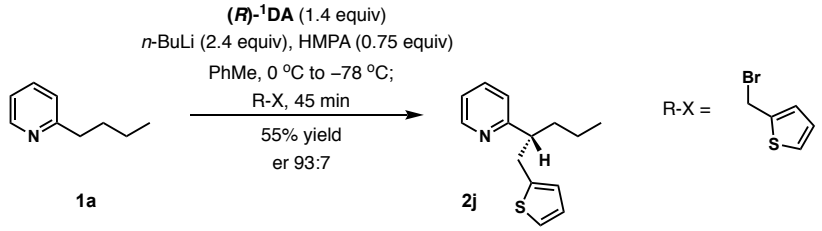


(*R*)-2-(1-(1,3-Benzodioxol-5-yl)pentan-2-yl)pyridine (2h). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.52 mL, 0.639 M in toluene, 0.333 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.622 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by the addition of a solution of 3,4-methylenedioxybenzyl bromide[15] (0.114 g, 0.533 mmol, 1.2 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 5 h at –78 °C and product **2h** (93 mg, 0.337 mmol, 76% yield) was obtained as a colorless oil after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 94:6 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 11.30 min (major); t_1 = 9.90 min). $[\alpha]_D^{26}$ – 92.0° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (d, *J* = 4.8 Hz, 1H), 7.50 (td, *J* = 7.6, 1.9 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 6.93 (dt, *J* = 7.8, 1.0 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 6.51 (d, *J* = 1.6 Hz, 1H), 6.46 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.87 (s, 2H), 3.00 – 2.91 (m, 2H), 2.89 – 2.80 (m, 1H), 1.83 – 1.73 (m, 1H), 1.68 – 1.60 (m, 1H), 1.21 – 1.08 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.26, 149.37, 147.23, 145.45, 135.86, 134.58, 123.27, 121.89, 121.13, 109.41, 107.84, 100.62, 49.88, 41.89, 36.91, 20.68, 14.10. HRMS (TOF MS EI) calcd for $C_{17}H_{19}NO_2$ $[M]^+$ 269.1416, found 269.1412.

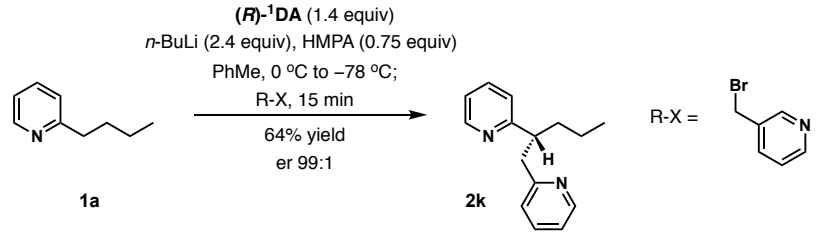


(*R*)-2-(1-(4-(1,3-Dioxolan-2-yl)phenyl)pentan-2-yl)pyridine (2i). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.42 mL, 0.522 M in toluene, 0.22

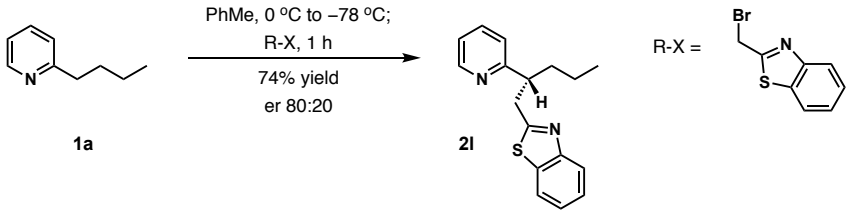
mmol, 0.5 equiv), and **(*R*)-^{1}DA** (0.119 g, 0.457 mmol, 1.03 equiv), *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.1 ml) followed by the addition of a solution of 2-(4-(bromomethyl)phenyl)-1,3-dioxolane[16] (130 mg, 0.533 mmol, 1.2 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 5 h at –78 °C and product **2i** (81 mg, 0.270 mmol, 61% yield) was obtained as a colorless oil after purification by column chromatography on silica gel (5% EtOAc in hexane). Er: 97:3 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 20.96 min (major); t_1 = 20.35 min). $[\alpha]_D^{24}$ – 70.6° (*c* 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.56 (d, *J* = 4.1 Hz, 1H), 7.47 (td, *J* = 7.6, 1.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.08 – 7.01 (m, 3H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.72 (s, 1H), 4.16 – 4.07 (m, 2H), 4.06 – 3.96 (m, 2H), 3.04 (dd, *J* = 12.7, 7.8 Hz, 1H), 3.01 – 2.95 (m, 1H), 2.92 (dd, *J* = 12.8, 6.4 Hz, 1H), 1.83 – 1.71 (m, 1H), 1.66 – 1.59 (m, 1H), 1.20 – 1.06 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.14, 149.33, 141.92, 135.90, 135.15, 129.07, 126.23, 123.26, 121.15, 103.79, 65.24, 49.53, 41.89, 36.95, 30.89, 20.64, 14.06. HRMS (TOF MS EI) calcd for $C_{19}H_{23}NO_2$ $[M]^+$ 297.1729, found 297.1725.



(*R*)-2-(1-(Thiophen-2-yl)pentan-2-yl)pyridine (2j). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of a solution of 2-(bromomethyl)thiophene[17] (117 mg, 0.66 mmol, 1.5 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 45 min at –78 °C and product **2j** (56 mg, 0.242 mmol, 55% yield) was obtained as yellow oil after purification by column chromatography on silica gel (1-2% EtOAc in hexane). Er: 93:7 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 8.55 min (major); t_1 = 7.79 min). $[\alpha]_D^{22}$ – 69.1° (*c* 0.66, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.51 (td, *J* = 7.6, 1.8 Hz, 1H), 7.08 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H0, 7.01 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.98 (dt, *J* = 7.8, 1.0 Hz, 1H), 6.79 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.59-6.58 (m, 1H), 3.29-3.13 (m, 2H), 3.03-2.99 (m, 1H), 1.81-1.75(m, 1H), 1.71-1.64 (m, 1H), 1.24-1.11 9m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.8, 149.4, 143.3, 135.9, 126.4, 125.1, 123.4, 123.1, 121.3, 49.9, 37.1, 35.8, 20.6, 14.0. HRMS (TOF MS EI) calcd for $C_{14}H_{17}NS$ $[M]^+$ 231.1082, found 231.1082.

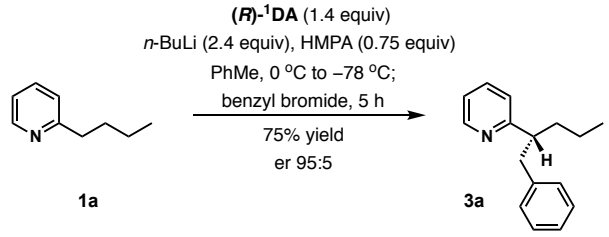


(*R*)-2,2'-(Pentane-1,2-diyl) dipyridine (2k). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-[1]DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of 2-(bromomethyl)pyridine[18] (0.210 mL, 2.51 M in toluene, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 15 min at –78 °C and product **2k** (64 mg, 0.283 mmol, 64% yield) was obtained as yellow oil after purification by column chromatography on silica gel (20-30% EtOAc in hexane). Er: 99:1 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes with 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 17.46 min (major); t_1 = 16.35 min). $[\alpha]_D^{24}$ + 102.2° (*c* 0.33, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.56 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 8.49 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.46 (td, *J* = 7.6, 1.8 Hz, 1H), 7.41 (td, *J* = 7.6, 1.9 Hz, 1H), 7.04 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.00 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 6.95 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.86 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.33-3.27 (m, 1H), 3.22 – 3.10 (m, 2H), 1.89–1.79 (m, 2H), 1.68-1.61 (m, 1H), 1.25 – 1.09 (m, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.1, 160.7, 149.4, 149.2, 135.86, 135.88, 123.7, 123.5, 121.1, 120.9, 47.9, 44.3, 37.3, 20.6, 14.1. HRMS (TOF MS EI) calcd for $C_{15}H_{18}N_2$ $[M]^+$ 226.1470, found 226.1468.

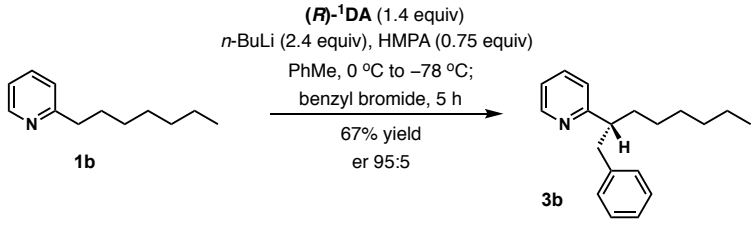


(*R*)-2-(2-(Pyridin-2-yl)pentyl)benzothiazole (2l). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-[1]DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by the addition of 2-(bromomethyl)-1,3-benzothiazole[19] (0.111 g, 0.488 mmol, 1.1 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 1 h at –78 °C and product **2l** (92 mg, 0.328 mmol, 74% yield) was obtained as an orange oil after purification by column chromatography on silica gel (10% EtOAc in hexane). Er: 80:20 (Chiralcel® OD-H; 1% *i*-PrOH in hexanes with 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 14.23 min (major); t_2 = 15.48 min). $[\alpha]_D^{24}$ – 80.6° (*c* 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.59 (d, *J* = 5.4 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.51

(td, *J* = 7.6, 1.8 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.33 – 7.25 (m, 1H), 7.12 – 7.05 (m, 2H), 3.61 (dd, *J* = 14.4, 8.8 Hz, 1H), 3.46 (dd, *J* = 14.5, 6.0 Hz, 1H), 3.43 – 3.34 (m, 1H), 1.92 – 1.82 (m, 1H), 1.81 – 1.70 (m, 1H), 1.27 – 1.13 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 170.76, 163.02, 153.33, 149.79, 136.34, 135.49, 125.91, 124.74, 123.85, 122.68, 121.80, 121.57, 48.01, 39.93, 37.88, 20.67, 14.23. HRMS (TOF MS EI) calcd for $C_{17}H_{18}N_2S$ $[M]^+$ 282.1191, found 282.1183.

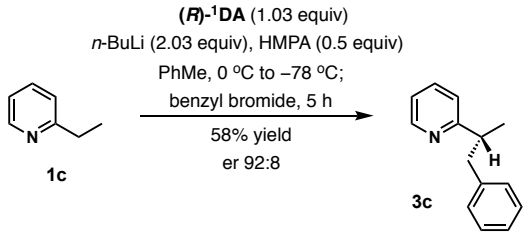


(*R*)-2-(1-Phenylpentan-2-yl) pyridine (3a). The title compound was prepared according to **general procedure III** using 2-butylpyridine (60 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by the addition of benzyl bromide (78 µL, 0.66 mmol, 1.5 equiv) at –78 °C. The reaction was quenched after 5 h and the product **3a** (75 mg, 0.33 mmol, 75% yield) was obtained as a colorless oil after purification by column chromatography on silica gel (2% EtOAc in hexane). Er: 95:5 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 11.88 min (major); t_1 = 10.98 min). $[\alpha]_D^{23}$ – 90.8° (*c* 1.25, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.48 (td, *J* = 7.6, 1.9, Hz, 1H), 7.20–7.15 (m, 2H), 7.14–7.09 (m, 1H), 7.08-7.05 (m, 1H), 7.04–7.00 (m, 2H), 6.92 (dt, *J* = 7.8, 1.0 Hz, 1H), 3.07–2.97 (m, 2H), 2.94 (m, 1H), 1.82-1.76 (m, 1H), 1.69-1.62 (m, 1H), 1.22–1.08 (m, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.3, 149.4, 140.7, 135.8, 129.1, 128.0, 125.7, 123.2, 121.1, 49.7, 42.2, 37.0, 20.7, 14.1. HRMS (TOF MS EI) calcd for $C_{16}H_{19}N$ $[M]^+$ 225.1517, found 225.1520.

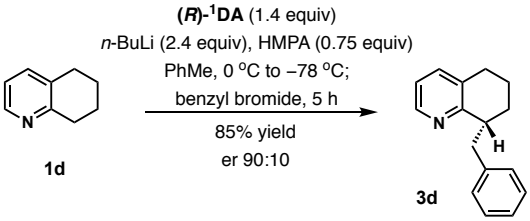


(*R*)-2-(1-Phenyloctan-2-yl)pyridine (3b). The title compound was prepared according to **general procedure III** using 2-heptylpyridine (**1b**) (78 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.461 mL, 2.29 M in hexanes, 1.056 mmol, 2.4 equiv) in toluene (4.5 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h at –78 °C and product **3b** (79 mg, 0.294 mmol, 67% yield) was obtained after purification by column chromatography on silica gel (1-2% EtOac in dichloromethane). Er: 95:5

(Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 7.74 min (major); t_1 = 6.88 min). $[\alpha]_D^{23}$ – 62.8° (*c* 1.145, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.48 (td, *J* = 7.6, 1.9 Hz, 1H), 7.21–7.14 (m, 2H), 7.14–7.09 (m, 1H), 7.06 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.04–6.99 (m, 2H), 6.91 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.12–2.86 (m, 3H), 1.83-1.76 (m, 1H), 1.73–1.63 (m, 1H), 1.29–1.03 (m, 8H), 0.82 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.4, 149.3, 140.8, 135.8, 129.1, 128.0, 125.7, 123.2, 121.1, 49.9, 42.2, 34.8, 31.7, 29.3, 27.5, 22.6, 14.0. HRMS (TOF MS EI) calcd for $C_{19}H_{25}N$ $[M]^+$ 267.1987, found 267.1989.

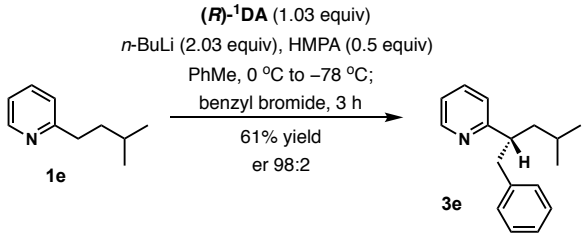


(*R*)-2-(1-Phenylpropan-2-yl)pyridine (3c). The title compound was prepared according to **general procedure III** using 2-ethylpyridine (48 mg, 0.44 mmol), HMPA (0.35 mL, 0.639 M in toluene, 0.22 mmol, 0.5 equiv), **(*R*)-^{1}DA** (0.119 g, 0.457 mmol, 1.03 equiv), and *n*-BuLi (0.39 mL, 2.29 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.2 ml) followed by addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3c** (51 mg, 0.25 mmol, 58% yield) was obtained after purification by column chromatography on silica gel (3% EtOac in hexane). Er: 92:8 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 215 nm; t_2 = 19.34 min (major); t_1 = 12.88 min). $[\alpha]_D^{23}$ – 73.6° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 5.6 Hz, 1H), 7.54 (td, *J* = 7.7, 1.8 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 3H), 7.03 (d, *J* = 7.8 Hz, 1H), 3.22 – 3.06 (m, 2H), 2.84 (dd, *J* = 13.3, 8.0 Hz, 1H), 1.29 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.52, 149.20, 140.64, 136.22, 129.12, 128.10, 125.82, 121.93, 121.21, 43.82, 43.33, 20.00. HRMS (TOF MS EI) calcd for $C_{14}H_{15}N$ $[M]^+$ 197.1205, found 197.1201.

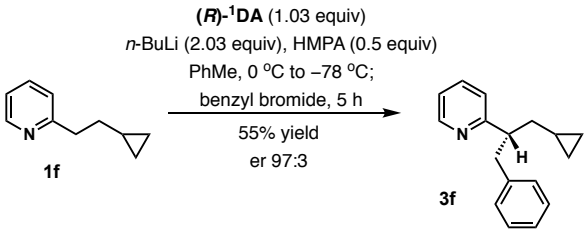


(*R*)-8-Benzyl-5,6,7,8-tetrahydro-quinoline (3d). The title compound was prepared according to **general procedure III** using 5,6,7,8-tetrahydroquinoline (59 mg, 0.44 mmol), HMPA (0.52 mL, 0.638 M in toluene, 0.33 mmol, 0.75 equiv), **(*R*)-^{1}DA** (0.161 g, 0.457 mmol, 1.4 equiv), and *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at

–78 °C. The reaction was quenched after 5 h and product **3d** (84 mg, 0.377 mmol, 85% yield) was obtained after purification by column chromatography on silica gel (5% EtOac in hexane). Er: 90:10 (Chiralcel® OJ-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 8.53 min (major); t_1 = 7.56 min). $[\alpha]_D^{26}$ + 23.8° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.46 (d, *J* = 6.4 Hz, 1H), 7.37 (d, *J* = 9.2 Hz, 1H), 7.32 – 7.24 (m, 5H), 7.23 – 7.18 (m, 1H), 7.06 (dd, *J* = 7.6, 4.6 Hz, 1H), 3.56 (dd, *J* = 13.5, 3.9 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.81 – 2.72 (m, 2H), 2.66 (dd, *J* = 13.5, 11.2 Hz, 1H), 1.92 – 1.82 (m, 1H), 1.79 – 1.71 (m, 1H), 1.71 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 159.44, 146.63, 140.78, 136.56, 132.12, 129.07, 127.94, 125.56, 120.78, 42.27, 40.89, 28.98, 26.24, 19.26. HRMS (TOF MS EI) calcd for $C_{16}H_{17}N$ $[M]^+$ 223.1361, found 223.1363.

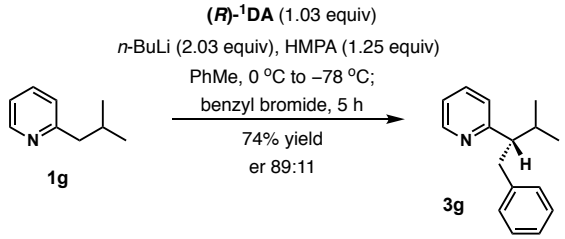


(*R*)-2-(1-Phenylpropan-2-yl)pyridine (3e). The title compound was prepared according to **general procedure III** using 2-isopentylpyridine (**1e**) (66 mg, 0.44 mmol), HMPA (0.344 mL, 0.639 M in toluene, 0.22 mmol, 0.5 equiv), **(R)-^{1}DA** (0.118 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.357 mL, 2.5 M in hexanes, 0.893 mmol, 2.03 equiv) in toluene (4.5 ml) followed by the addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 3 h and product **3e** (64 mg, 0.268 mmol, 61% yield) was obtained after purification by column chromatography on silica gel (1-2% EtOAc in dichloromethane). Er: 98:2 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 10.85 min (major); t_1 = 8.64 min). $[\alpha]_D^{23}$ – 75.8° (*c* 0.645, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): δ 8.58 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.47 (td, *J* = 7.6, 1.9 Hz, 1H), 7.18 – 7.14 (m, 2H), 7.12 – 7.09 (m, 1H), 7.06 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.01 – 6.97 (m, 2H), 6.90 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.13-3.07 (m, 1H), 3.01 (dd, *J* = 13.3, 8.3 Hz, 1H), 2.90 (dd, *J* = 13.3, 6.4 Hz, 1H), 1.82 (ddd, *J* = 13.4, 9.9, 5.0 Hz, 1H), 1.48 (ddd, *J* = 13.7, 9.0, 5.0 Hz, 1H), 1.38-1.30 (m, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.4, 149.4, 140.7, 135.8, 129.0, 128.0, 125.7, 123.3, 121.1, 47.7, 44.1, 42.6, 25.6, 23.5, 21.9. HRMS (TOF MS EI) calcd for $C_{17}H_{21}N$ $[M]^+$ 239.1674, found 239.1673.

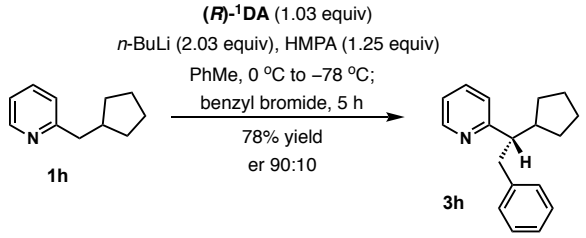


(*R*)-2-(1-Cyclopropyl-3-phenylpropan-2-yl)pyridine (3f). The title compound was prepared according to **general procedure III** using 2-(2-cyclopropylethyl)pyridine (**1f**) (65 mg, 0.44 mmol), HMPA (0.34 mL, 0.639 M

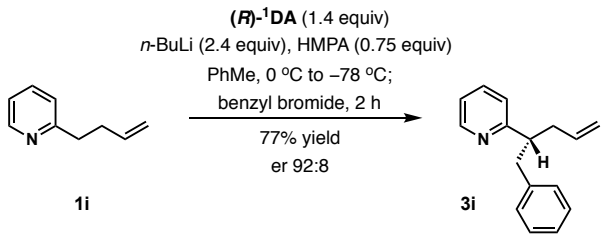
in toluene, 0.22 mmol, 0.5 equiv), **(*R*)-^{1}DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.2 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3f** (58 mg, 0.244 mmol, 55% yield) was obtained after purification by column chromatography on silica gel (5% EtOAc in hexane). Er: 97:3 (Chiralcel® OJ-H; 0.5% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_1 = 14.71 min (major); t_2 = 16.03 min). $[\alpha]_D^{25}$ – 53.9° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 5.5 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.17 (t, *J* = 7.6 Hz, 2H), 7.15 – 7.00 (m, 3H), 6.97 (d, *J* = 8.6 Hz, 1H), 3.20 – 3.10 (m, 1H), 3.10 – 2.94 (m, 2H), 1.87 – 1.76 (m, 1H), 1.52 – 1.43 (m, 1H), 0.55 – 0.44 (m, 1H), 0.37 – 0.29 (m, 1H), 0.28 – 0.19 (m, 1H), -0.01 – -0.09 (m, 1H), -0.11 – -0.20 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.13, 148.97, 140.50, 135.60, 128.79, 127.79, 125.44, 123.27, 120.90, 50.11, 41.43, 39.77, 9.11, 4.47, 4.15. HRMS (TOF MS EI) calcd for $C_{17}H_{19}N$ $[M]^+$ 237.1517, found 237.1520.



(*S*)-2-(3-Methyl-1-phenylbutan-2-yl)pyridine (3g). The title compound was prepared according to **general procedure III** using 2-isobutylpyridine (**1g**) (60 mg, 0.44 mmol), HMPA (0.87 mL, 0.639 M in toluene, 0.55 mmol, 1.25 equiv), **(*R*)-^{1}DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.39 mL, 2.29 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (4.6 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3g** (72 mg, 0.316 mmol, 72% yield) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 89:11 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_1=5.38 min (major); t_2=6.37 min). $[\alpha]_D^{27}$ + 110.8° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.56 (d, *J* = 5.6 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 2H), 7.07 – 6.99 (m, 2H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.81 (d, *J* = 7.7 Hz, 1H), 3.16 (dd, *J* = 13.5, 4.7 Hz, 1H), 3.04 (dd, *J* = 13.4, 10.4 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.17 – 2.07 (m, 1H), 1.08 (d, *J* = 6.7 Hz, 3H), 0.78 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.26, 148.99, 141.19, 135.41, 128.91, 127.89, 125.44, 124.34, 120.96, 56.94, 38.54, 32.43, 21.02, 20.70. HRMS (TOF MS EI) calcd for $C_{16}H_{19}N$ $[M]^+$ 225.1517, found 225.1517.

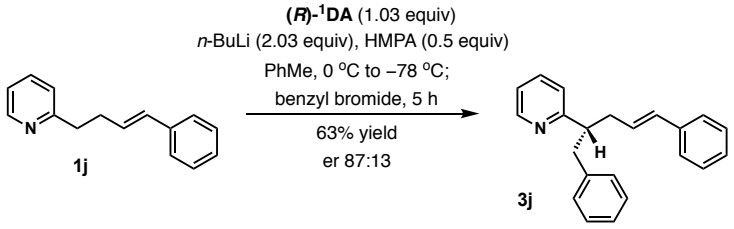


(*S*)-2-(1-Cyclopentyl-2-phenylethyl)pyridine (3h). The title compound was prepared according to **general procedure III** using 2-(cyclopentylmethyl)pyridine (**1h**) (72 mg, 0.44 mmol), HMPA (0.87 mL, 0.639 M in toluene, 0.55 mmol, 1.25 equiv), **(*R*)-[1]DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.39 mL, 2.29 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (4.6 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3h** (87 mg, 0.346 mmol, 78% yield) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 90:10 (Chiralcel® OJ-H; 0.5% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_2 = 12.09 min (major); t_1 = 11.45 min). $[\alpha]_D^{25}$ + 92.9° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.55 (d, *J* = 4.8 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 2H), 7.07 – 6.99 (m, 2H), 6.88 (d, *J* = 7.1 Hz, 2H), 6.75 (d, *J* = 7.8 Hz, 1H), 3.13 (dd, *J* = 13.4, 4.2 Hz, 1H), 3.10 – 3.01 (m, 1H), 2.76 (td, *J* = 10.0, 4.1 Hz, 1H), 2.32 (h, *J* = 9.5 Hz, 1H), 2.11 – 2.01 (m, 1H), 1.73 – 1.63 (m, 1H), 1.64 – 1.51 (m, 2H), 1.51 – 1.42 (m, 1H), 1.39 – 1.31 (m, 2H), 1.07 – 0.96 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.91, 149.12, 140.93, 135.49, 128.93, 127.86, 125.46, 123.91, 120.96, 56.30, 45.24, 40.83, 31.69, 31.37, 25.28, 25.06. HRMS (TOF MS EI) calcd for $C_{18}H_{21}N$ $[M]^+$ 251.1674, found 251.1673.

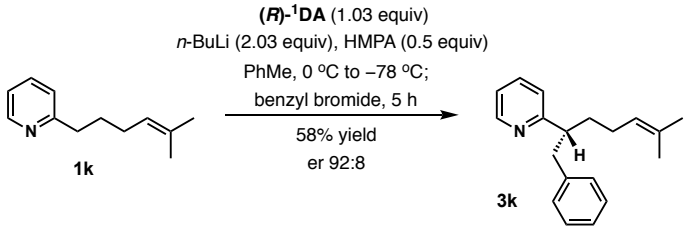


(*R*)-2-(1-Phenylpent-4-en-2-yl)pyridine (3i). The title compound was prepared according to **general procedure III** using 2-(but-3-en-1-yl)pyridine (**1i**) (59 mg, 0.44 mmol), HMPA (0.52 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-[1]DA** (0.161 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv, neat) at –78 °C. The reaction was quenched after 2 h and product **3i** (75 mg, 0.34 mmol, 77% yield) was obtained after purification by column chromatography on silica gel (1-2% EtOAc in dichloromethane). Er: 92:8 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 12.49 min (major); t_1 = 10.68 min). $[\alpha]_D^{24}$ – 69.1° (*c* 0.765, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.59 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.48 (td, *J* = 7.6, 1.8 Hz, 1H), 7.19-7.16 (m, 2H), 7.13-7.10 (m, 1H), 7.07 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.02 (m, 2H), 6.89 (dt, *J* = 7.8, 1.0 Hz, 1H), 5.71-5.63 (m, 1H), 4.97-4.93 (m, 1H), 4.92-4.90 (m, 1H),

3.13-2.97 (m, 3H), 2.60-2.43 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.4, 149.4, 140.4, 136.6, 135.8, 129.1, 128.1, 125.8, 123.4, 121.3, 116.3, 49.6, 41.3, 39.0. HRMS (TOF MS EI) calcd for $C_{16}H_{17}N$ $[M]^+$ 223.1361, found 223.1354.

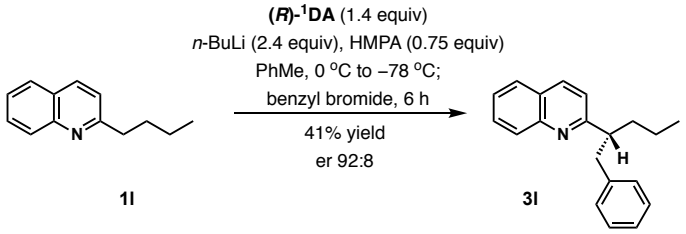


(*R*,*E*)-2-(1,5-Diphenylpent-4-en-2-yl)pyridine (3j). The title compound was prepared according to **general procedure III** using (E)-2-(4-phenylbut-3-en-1-yl)pyridine (**1j**) (93 mg, 0.44 mmol), HMPA (0.35 mL, 0.639 M in toluene, 0.22 mmol, 0.5 equiv), **(*R*)-^{1}DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.2 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3j** (83 mg, 0.279 mmol, 63% yield) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 87:13 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 14.99 min (major); t_1 = 13.88 min). $[\alpha]_D^{22}$ – 1.28° (*c* 1.16, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.60 (d, *J* = 5.6 Hz, 1H), 7.48 (t, *J* = 6.8 Hz, 1H), 7.25 – 7.10 (m, 8H), 7.08 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.05 (dt, *J* = 15.5, 7.1 Hz, 1H), 3.17 (q, *J* = 7.5 Hz, 1H), 3.13 – 2.98 (m, 2H), 2.77 – 2.67 (m, 1H), 2.66 – 2.58 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.10, 148.81, 140.16, 137.59, 136.60, 131.72, 129.13, 128.42, 128.27, 128.18, 126.96, 126.00, 125.95, 123.62, 121.59, 49.66, 41.35, 38.18. HRMS (TOF MS EI) calcd for $C_{22}H_{21}N$ $[M]^+$ 299.1674, found 299.1682.

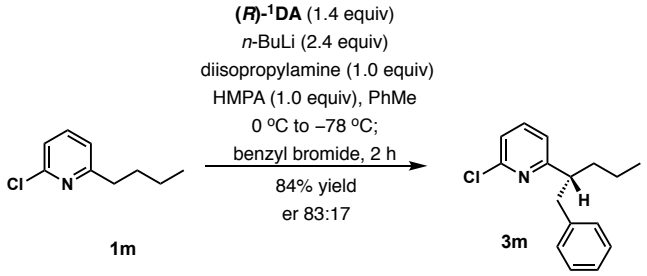


(*R*)-2-(6-Methyl-1-phenylhept-5-en-2-yl)pyridine (3k). The title compound was prepared according to **general procedure III** using 2-(5-methylhex-4-en-1-yl)pyridine (**1k**) (78 mg, 0.44 mmol), HMPA (0.35 mL, 0.639 M in toluene, 0.22 mmol, 0.5 equiv), **(*R*)-^{1}DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.2 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3k** (68 mg, 0.257 mmol, 58% yield) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 92:8 (Chiralcel® OJ-H; 0.5% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_1 = 12.88 min

(major); t_2 = 14.12 min). $[\alpha]_D^{23}$ – 36.8° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 5.7 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.17 (t, *J* = 7.3 Hz, 2H), 7.14 – 7.04 (m, 2H), 7.01 (d, *J* = 7.1 Hz, 2H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.03 (t, *J* = 7.4 Hz, 1H), 3.09 – 2.88 (m, 3H), 1.90 – 1.77 (m, 3H), 1.76 – 1.68 (m, 1H), 1.63 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.07, 149.27, 140.60, 135.90, 131.53, 129.07, 128.01, 125.70, 124.23, 123.40, 121.17, 49.33, 42.18, 34.74, 25.98, 25.68, 17.62. HRMS (TOF MS EI) calcd for $C_{19}H_{23}N$ $[M]^+$ 265.1830, found 265.1836.

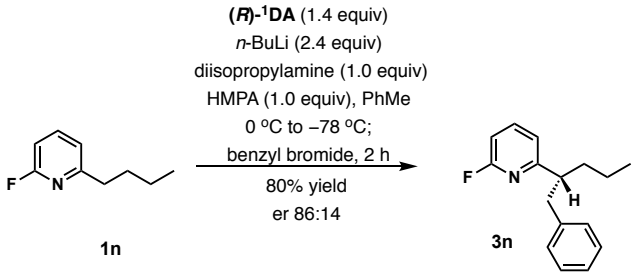


(*R*)-2-(1-Phenylpentan-2-yl)quinoline (3l). The title compound was prepared according to **general procedure III** using 2-butylquinoline (**1l**) (82 mg, 0.44 mmol), HMPA (0.516 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.422 mL, 2.5 M in hexanes, 1.056 mmol, 2.4 equiv) in toluene (4.6 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 6 h and product **3l** (50 mg, 0.18 mmol, 41% yield) was obtained after purification by column chromatography on silica gel (1-2% EtOAc in hexane). Er: 92:8 (Chiralcel® OD-H; 0.25% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_2 = 22.8 min (major); t_1 = 21.3 min). $[\alpha]_D^{25}$ – 101.3° (*c* 0.57, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.07 (d, *J* = 8.51 Hz, 1H), 8.00 (d, *J* = 8.46 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.68 (ddd, *J* = 6.9, 1.6, 1.5 Hz, 1H), 7.48 (ddd, *J* = 6.9, 1.2, 1.2 Hz, 1H), 7.19-7.15 (m, 3H), 7.13-7.09 (m, 3H), 3.30-3.24 (m, 1H), 3.18 (dd, *J* = 13.4, 7.7 Hz, 1H), 3.01 (dd, *J* = 13.5, 7.1 Hz, 1H), 1.90-1.82 (m, 1H), 1.77-1.70 (m, 1H), 1.28-1.13 (m, 2H), 0.83 (t, *J* = 7.31 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.1, 148.0, 140.6, 135.8, 129.2, 129.13, 129.08, 128.0, 127.5, 126.9, 125.7, 125.6, 121.0, 50.3, 41.9, 37.0, 20.7, 14.1. HRMS (TOF MS EI) calcd for $C_{20}H_{21}N$ $[M]^+$ 275.1674, found 275.1677.



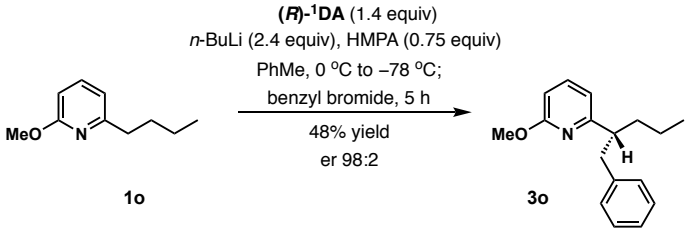
(*R*)-2-Chloro-6-(1-phenylpentan-2-yl)pyridine (3m). *n*-BuLi (0.422 mL, 2.50 M in hexanes, 1.056 mmol, 2.4 equiv) was added dropwise to a solution of diisopropyl amine (0.062 mL, 0.44 mmol, 1 equiv), HMPA (0.688 mL, 0.639 M in toluene, 0.44 mmol, 1.0 equiv), and **(*R*)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv) in toluene (4.4 ml) at 0 °C and stirring was continued for 15 min. Then 2-butyl-6-chloropyridine (**1m**) (75 mg, 0.44 mmol) was added and the resulting mixture was allowed to stir for 15 min. The reaction mixture was then cooled to –78

°C and stirred for 10 min. Benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) was added to the reaction mixture dropwise. The resultant mixture was stirred for 2 h at –78 °C before quenching with MeOH (300 µL). After 10 min, the reaction mixture was warmed to room temperature and diluted with water and ethyl acetate. The aqueous layer was separated and the organic layer was acidified with aq. HCl (0.125 mL, 6 M in H_2O, 1.7 equiv) and diluted with H_2O. The organic layer was separated dried over anhydrous Na_2SO_4 concentrated, and the residue was purified by column chromatography on silica gel (1-2% EtOAc in hexane) to afford product **3m** (96 mg, 0.37 mmol, 84% yield) as colorless oil. Er: 83:17 (Chiralcel® OJ-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 6.4 min (major); t_1 = 6.1 min). $[\alpha]_D^{22}$ + 73.8° (*c* 1.25, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.43 (t, *J* = 7.8 Hz, 1H), 7.20-7.17 (m, 2H), 7.14-7.09 (m, 2H), 7.03-7.01 (m, 2H), 6.81 (dt, *J* = 7.5, 0.8 Hz, 1H), 3.05-2.96 (m, 2H), 2.95-2.90 (m, 1H), 1.82-1.74(m, 1H), 1.68-1.61(m, 1H), 1.22-1.12 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.6, 150.9, 140.4, 138.4, 129.1, 128.1, 125.8, 121.6, 49.4, 41.8, 36.7, 20.6, 14.0. HRMS (TOF MS EI) calcd for $C_{16}H_{18}ClN$ $[M]^+$ 259.1128, found 259.1127.

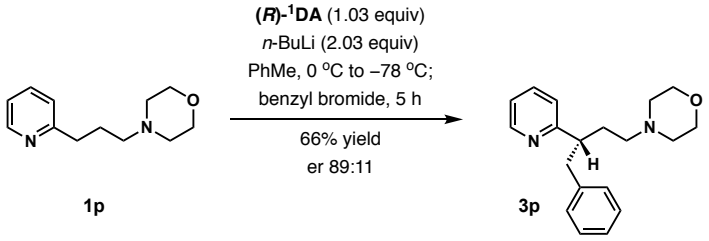


(*R*)-2-Fluoro-6-(1-phenylpentan-2-yl)pyridine (3n). *n*-BuLi (0.422 mL, 2.50 M in hexanes, 1.056 mmol, 2.4 equiv) was added dropwise to a solution of diisopropyl amine (0.062 mL, 0.44 mmol, 1 equiv), HMPA (0.688 mL, 0.639 M in toluene, 0.44 mmol, 1.0 equiv), and **(R)-^{1}DA** (0.161 g, 0.616 mmol, 1.4 equiv) in toluene (4.4 ml) at 0 °C and stirring was continued for 15 min. Then 2-butyl-6-fluoropyridine (**1n**) (67 mg, 0.44 mmol) was added and the resulting mixture was allowed to stir for 15 min. The reaction mixture was then cooled to –78 °C and stirred for an additional 10 min. Benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) was added to the reaction mixture dropwise. The resultant mixture was stirred for 2 h at –78 °C before quenching with MeOH (300 µL). After 10 min, the reaction mixture was diluted with water and ethyl acetate. The aqueous layer was separated and the organic layer was acidified with aq. HCl (0.125 mL, 6 M in H_2O, 1.7 equiv) and diluted with H_2O. The organic layer was separated dried over anhydrous Na_2SO_4 concentrated, and the residue was purified by column chromatography on silica gel (1-2% EtOAc in hexane) to afford product **3n** (86 mg, 0.35 mmol, 80% yield) as colorless oil. Er: 86:14 (Chiralcel® OJ-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 6.14 min (major); t_1 = 5.78 min). $[\alpha]_D^{24}$ + 75.6° (*c* 0.77, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.57-7.53 (m, 1H), 7.20-7.16 (m, 2H), 7.13-7.10 (m, 1H), 7.02-7.0 (m, 2H), 6.78-6.75 (m, 1H), 6.70-6.68 (m, 1H), 3.03-2.90 (m, 3H), 1.83-1.76 (m, 1H), 1.66-1.60 (m, 1H), 1.20-1.11 (m, 2H), 0.84 (t, *J* = 7.37

Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.4 (d, *J* = 238 Hz), 163.8 (d, *J* = 12), 140.7 (d, *J* = 7.7 Hz), 140.4, 129.0, 128.1, 125.8, 120.6 (d, *J* = 4.2 Hz), 106.7 (d, *J* = 38 Hz), 49.2, 41.8, 36.7, 20.6, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): -67.5 (d, J = 7.9 Hz). HRMS (TOF MS EI) calcd for $C_{16}H_{18}FN$ $[M]^+$ 243.1423, found 243.1420.

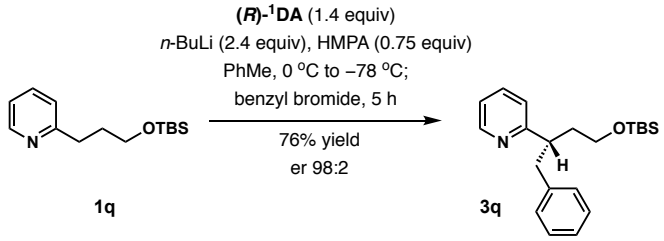


(*R*)-2-Methoxy-6-(1-phenylpentan-2-yl)pyridine (3o). The title compound was prepared according to **general procedure III** using 2-butyl-6-methoxypyridine (**1o**) (73 mg, 0.44 mmol), HMPA (0.52 mL, 0.638 M in toluene, 0.33 mmol, 0.75 equiv), **(*R*)-^{1}DA** (0.161 g, 0.457 mmol, 1.4 equiv), and *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3o** (53 mg, 0.213 mmol, 48% yield) was obtained after purification by column chromatography on silica gel (20% CH_2Cl_2 in hexane). Er: 98:2 (Chiralcel® OJ-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 5.55 min (major); t_1 = 5.07 min). $[\alpha]_D^{25}$ – 146° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.38 – 7.32 (m, 1H), 7.17 (t, *J* = 7.3 Hz, 2H), 7.14 – 7.08 (m, 1H), 7.02 (d, *J* = 6.9 Hz, 2H), 6.49 (dd, *J* = 9.6, 7.7 Hz, 2H), 3.94 (s, 3H), 3.10 – 3.01 (m, 1H), 2.93 – 2.83 (m, 2H), 1.85 – 1.72 (m, 1H), 1.65 – 1.55 (m, 1H), 1.22 – 1.11 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.68, 161.96, 141.15, 138.23, 129.07, 127.95, 125.58, 115.92, 107.40, 53.10, 49.15, 41.87, 36.91, 20.63, 14.16. HRMS (TOF MS EI) calcd for $C_{17}H_{21}NO$ $[M]^+$ 255.1623, found 255.1625.

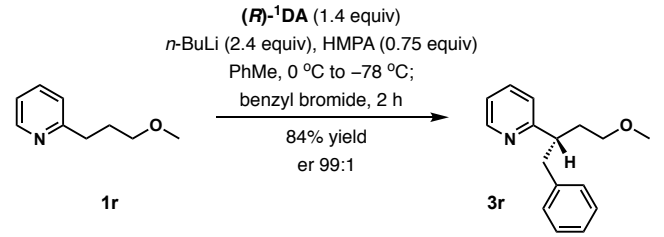


(*S*)-4-(4-Phenyl-3-(pyridin-2-yl)butyl)morpholine (3p). The title compound was prepared according to **general procedure III** using 4-(3-pyridin-2-ylpropyl)morpholine (**1p**) (92 mg, 0.44 mmol), **(*R*)-^{1}DA** (0.119 g, 0.456 mmol, 1.03 equiv), and *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.5 ml) followed by the addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3p** (87 mg, 0.293 mmol, 66% yield) was obtained after purification by column chromatography on silica gel (3% MeOH in CH_2Cl_2). Er: 89:11 (Chiralcel® AD-H; 1% *i*-PrOH in hexanes, 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 18.18 min (major); t_1 = 16.27 min). $[\alpha]_D^{22}$ – 26.2° (*c* 1.030, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (d, *J* = 4.2 Hz, 1H), 7.49 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18

(t, *J* = 7.3 Hz, 2H), 7.15 – 7.06 (m, 2H), 7.03 (d, *J* = 7.1 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 1H), 3.64 (t, *J* = 4.5 Hz, 4H), 3.13 – 3.01 (m, 2H), 2.97 – 2.89 (m, 1H), 2.44 – 2.16 (m, 5H), 2.13 – 2.05 (m, 1H), 2.05 – 1.97 (m, 1H), 1.94 – 1.82 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.11, 149.73, 140.70, 136.29, 129.40, 128.44, 126.19, 123.69, 121.64, 67.26, 57.21, 53.93, 48.18, 42.59, 31.52. HRMS (TOF MS ES) calcd for $C_{19}H_{24}N_2OH$ $[M+H]^+$ 297.1967, found 297.1980.

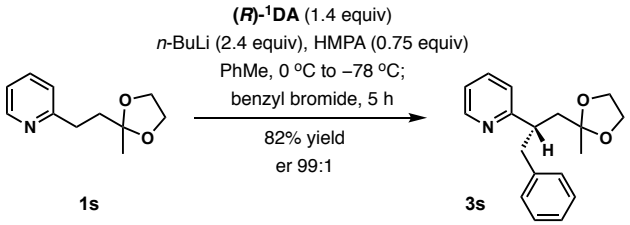


(*S*)-2-(4-((*Tert*-butyldimethylsilyl)oxy)-1-phenylbutan-2-yl)pyridine (3q). The title compound was prepared according to **general procedure III** using tert-butyl-dimethyl-(3-pyridin-2-ylpropoxy)silane (**1q**) (111 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), **(*R*)-^{1}DA** (0.161 g, 0.457 mmol, 1.4 equiv), and *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of benzyl bromide (63 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3q** (116 mg, 0.337 mmol, 76% yield) was obtained after purification by column chromatography on silica gel (2% EtOAc in hexane). Er: 98:2 (Chiralcel® OD-H; 2% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_2 = 18.1 min (major); t_1 = 14.9 min). $[\alpha]_D^{27}$ – 43.5° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.59 (ddd, *J* = 4.8,1.9, 0.9 Hz, 1H), 7.46 (td, *J* = 7.5, 1.9 Hz, 1H), 7.18-7.15 (m, 2H), 7.12-7.09 (m, 1H), 7.06 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.02-6.99 (m, 2H), 6.89 (dt, *J* = 7.8, 1.0 Hz,1H), 3.53-3.49 (m, 1H), 3.40-3.36 (m, 1H), 3.23-3.17 (m, 1H), 3.06-3.02 (m, 1H), 2.97-2.93 (m, 1H), 0.83 (s, 9H), -0.064 (s, 3H), -0.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.7, 149.4, 140.5, 135.8, 129.1, 128.0, 125.7, 123.8, 121.2, 61.0, 45.9, 42.1, 37.5, 25.9, 18.2, -5.4. HRMS (TOF MS EI) calcd for $C_{21}H_{31}NOSi$ $[M]^+$ 341.2175, found 341.2171.

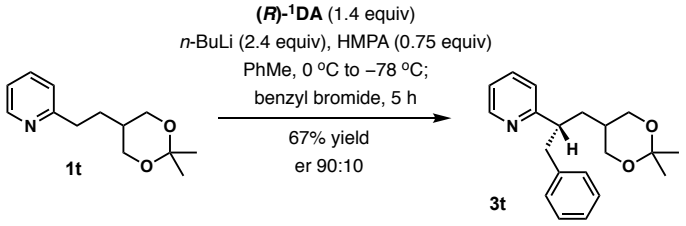


(*S*)-2-(4-Methoxy-1-phenylbutan-2-yl)pyridine (3r). The title compound was prepared according to **general procedure III** using 2-(3-methoxypropyl) pyridine (**1r**) (66 mg, 0.44 mmol), HMPA (0.52 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.42 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (4.6 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 2 h and product **3r** (90 mg, 0.373 mmol, 84%

yield) was obtained after purification by column chromatography on silica gel (3% EtOAc in hexane). Er: 99:1 (Chiralcel® AD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 8.14 min (major); t_1 = 7.23 min). $[\alpha]_D^{24}$ – 81.7° (*c* 1.15, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.59 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.48 (td, *J* = 7.6, 1.8 Hz, 1H), 7.19-7.15 (m, 2H), 7.12-7.10 (m, 1H), 7.09-7.06 (m, 1H), 7.02 (m, 2H), 6.92 (dt, *J* = 7.8, 1.0 Hz, 1H), 3.28-3.23(m, 1H), 3.20 (s, 3H), 3.20-3.16 (m, 1H), 3.15-3.10 (m, 1H), 3.07-3.04 (m, 1H), 2.97-2.93 (m, 1H), 2.11-1.97 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.5, 149.4, 140.3, 135.9, 129.1, 128.0, 125.8, 123.6, 121.3, 70.6, 58.4, 46.2, 42.1, 34.4. HRMS (TOF MS EI) calcd for $C_{16}H_{19}NO$ $[M]^+$ 241.1467, found 241.1464.

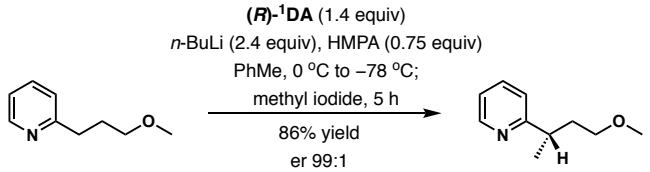


(*S*)-2-(1-(2-Methyl-1,3-dioxolan-2-yl)-3-phenylpropan-2-yl)pyridine (3s). The title compound was prepared according to **general procedure III** using 2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)pyridine (**1s**) (86 mg, 0.44 mmol), HMPA (0.52 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.47 mL, 2.29 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3s** (103 mg, 0.364 mmol, 82% yield) was obtained after purification by column chromatography on silica gel (30% EtOAc in hexane). Er: 99:1 (Chiralcel® AD-H; 1% *i*-PrOH in hexanes, 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 16.55 min (major); t_2 = 21.00 min). $[a]_D^{25}$ – 72.5° (*c* 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (d, *J* = 5.6 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.07 – 7.02 (m, 1H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 3.84 – 3.74 (m, 3H), 3.71 – 3.63 (m, 1H), 3.28 – 3.17 (m, 1H), 2.97 (d, *J* = 8.0 Hz, 2H), 2.45 (dd, *J* = 14.4, 9.2 Hz, 1H), 2.01 (dd, *J* = 14.4, 3.5 Hz, 1H), 1.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.50, 149.07, 140.26, 135.74, 129.10, 128.03, 125.80, 123.44, 121.03, 109.75, 64.20, 45.37, 43.27, 42.40, 24.42. HRMS (TOF MS EI) calcd for $C_{18}H_{21}NO_2$ $[M]^+$ 283.1572, found 283.1581.



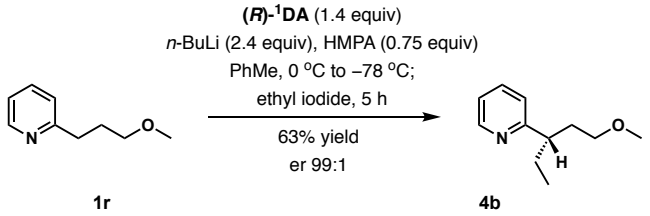
(*R*)-2-(1-(2,2-Dimethyl-1,3-dioxan-5-yl)-3-phenylpropan-2-yl)pyridine (3t). The title compound was prepared according to **general procedure III** using 2-(2-(2,2-dimethyl-1,3-dioxan-5-yl)ethyl)pyridine (**1s**) (98 mg, 0.44

mmol), HMPA (0.52 mL, 0.639 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of benzyl bromide (63 µL, 0.528 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **3t** (93 mg, 0.297 mmol, 67% yield) was obtained after purification by column chromatography on silica gel (30% EtOAc in hexane). Er: 90:10 (Chiralcel® AD-H; 1% *i*-PrOH in hexanes, 0.05% Et_3N; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 17.29 min (major); t_2 = 18.84 min). $[\alpha]_D^{24}$ – 37.2° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 6.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 2H), 7.15 – 7.07 (m, 2H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 1H), 3.81 (dd, *J* = 11.6, 4.6 Hz, 1H), 3.59 – 3.49 (m, 2H), 3.44 (dd, *J* = 11.6, 9.7 Hz, 1H), 3.06 – 2.95 (m, 2H), 2.94 – 2.84 (m, 1H), 1.82 – 1.73 (m, 1H), 1.70 – 1.61 (m, 1H), 1.61 – 1.48 (m, 1H), 1.37 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 163.34, 149.87, 140.28, 136.51, 129.29, 128.45, 126.25, 123.75, 121.88, 97.98, 65.46, 64.81, 47.30, 43.15, 33.72, 32.61, 28.00, 20.48. HRMS (TOF MS EI) calcd for $C_{20}H_{25}NO_2$ $[M]^+$ 311.1885, found 311.1879.

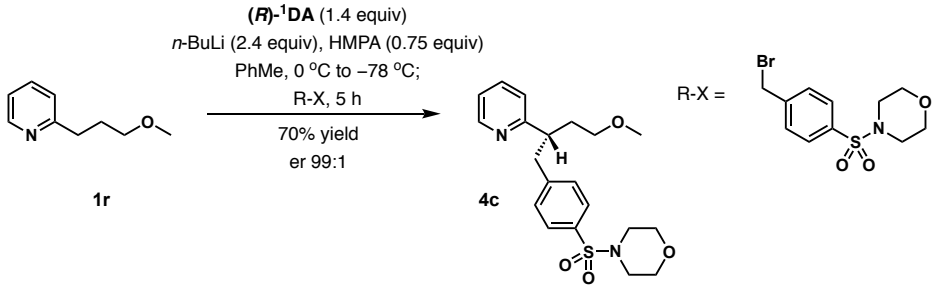


1r **4a**

(*S*)-2-(4-Methoxybutan-2-yl)pyridine (4a). The title compound was prepared according to **general procedure III** using 2-(3-methoxypropyl) pyridine (**1r**) (67 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of methyl iodide (33 µL, 0.532 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 h and product **4a** (63 mg, 0.377 mmol, 86% yield) was obtained after purification by column chromatography on silica gel (7% EtOAc in hexane). Er: 99:1 (Chiralcel® AD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 8.52 min (major); t_1 = 8.17 min). $[\alpha]_D^{23}$ + 24.6° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.55 (d, *J* = 4.7 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.10 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.35 – 3.29 (m, 1H), 3.27 (s, 3H), 3.26 – 3.21 (m, 1H), 3.10 – 2.98 (m, 1H), 2.09 – 1.97 (m, 1H), 1.95 – 1.82 (m, 1H), 1.30 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.82, 149.22, 136.27, 121.89, 121.11, 70.78, 58.48, 38.50, 36.55, 20.84. HRMS (TOF MS EI) calcd for $C_{10}H_{14}NO$ $[M-H]^+$ 164.1075, found 164.1078.

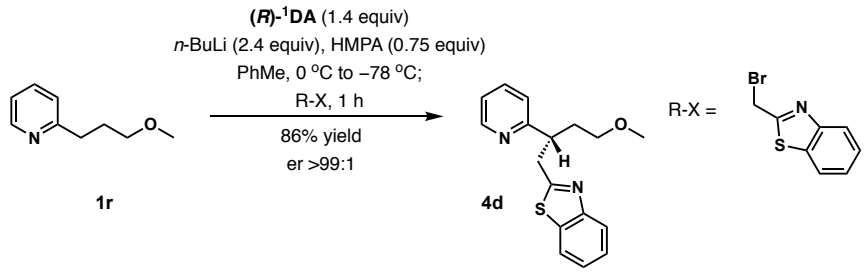


(*S*)-2-(1-Methoxypentan-3-yl)pyridine (4b). The title compound was prepared according to **general procedure III** using 2-(3-methoxypropyl) pyridine (**1r**) (67 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of ethyl iodide (40 µL, 0.488 mmol, 1.1 equiv) at –78 °C. The reaction was quenched after 5 h and product **4b** (50 mg, 0.279 mmol, 63% yield) was obtained after purification by column chromatography on silica gel (15% EtOAc in hexane). Er: 99:1 (Chiralcel® AD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 7.21 min (major); t_1 = 6.63 min). $[\alpha]_D^{27}$ + 13.9° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.56 (d, *J* = 5.7 Hz, 1H), 7.58 (t, *J* = 8.6 Hz, 1H), 7.16 – 7.05 (m, 2H), 3.28 – 3.21 (m, 4H), 3.20 – 3.12 (m, 1H), 2.84 – 2.74 (m, 1H), 2.01 – 1.93 (m, 2H), 1.80 – 1.66 (m, 2H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 164.45, 149.35, 135.97, 123.14, 121.09, 70.78, 58.45, 46.03, 35.01, 28.55, 11.99. HRMS (TOF MS EI) calcd for $C_{10}H_{14}NO$ $[M\text{-}CH_3]^+$ 164.1075, found 164.1080.

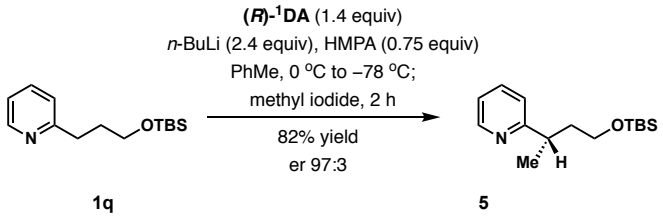


(*S*)-4-((4-(4-Methoxy-2-(pyridin-2-yl)butyl)phenyl)sulfonyl)morpholine (4c). The title compound was prepared according to **general procedure III** using 2-(3-methoxypropyl) pyridine (**1r**) (67 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of a solution of 4-(bromomethyl)benzene-1-sulfonylmorpholine[12] (156 mg, 0.488 mmol, 1.1 equiv) in toluene (1.5 mL) at –78 °C. The reaction was quenched after 5 h and product **4c** (0.121 g, 0.310 mmol, 70% yield) was obtained after purification by column chromatography on silica gel (80% EtOAc in hexane). Er: 99:1 (Chiralcel® OD-H; 10% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 33.54 min (major); t_1 = 30.38 min). $[\alpha]_D^{21}$ – 54.6° (*c* 1.88, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 5.5 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.48 (t, *J* = 9.0 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.13 – 7.06 (m, 1H), 6.86 (d, *J* = 7.4 Hz, 1H), 3.77 – 3.66 (m, 4H), 3.35 – 3.26 (m, 1H), 3.23 (s, 3H), 3.19 – 3.03 (m, 4H), 2.98 – 2.88 (m, 4H), 2.16 – 2.06 (m, 1H), 2.07 – 1.98 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 162.36, 149.55, 146.50, 136.07, 132.37, 129.72, 127.62,

123.75, 121.56, 70.23, 66.03, 58.53, 45.96, 41.68, 34.84. HRMS (TOF MS EI) calcd for $C_{20}H_{26}N_2O_4S$ $[M]^+$ 390.1613, found 390.1594.

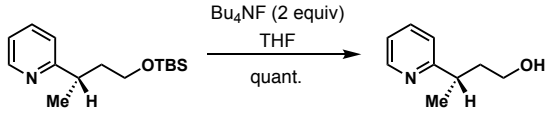


(*R*)-2-(4-Methoxy-2-(pyridin-2-yl)butyl)benzothiazole (4d). The title compound was prepared according to **general procedure III** using 2-(3-methoxypropyl) pyridine (**1r**) (67 mg, 0.44 mmol), HMPA (0.64 mL, 0.522 M in toluene, 0.33 mmol, 0.75 equiv), and **(*R*)-^{1}DA** (0.160 g, 0.616 mmol, 1.4 equiv), *n*-BuLi (0.43 mL, 2.5 M in hexanes, 1.065 mmol, 2.4 equiv) in toluene (5.0 ml) followed by addition of a solution of 2-(bromomethyl)-1,3-benzothiazole[17] (0.111 g, 0.488 mmol, 1.1 equiv) in toluene (0.3 mL) at –78 °C. The reaction was quenched after 1 h and product **4d** (0.113 g, 0.381 mmol, 86% yield) was obtained after purification by column chromatography on silica gel (30% EtOAc in hexane). Er: 99:1 (Chiralcel® OJ-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 24.76 min (major); t_2 = 29.97 min). $[\alpha]_D^{24}$ – 99.9° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.61 (d, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.30 (t, *J* = 7.0 Hz, 1H), 7.14 – 7.09 (m, 2H), 3.65 (dd, *J* = 13.8, 8.5 Hz, 1H), 3.58 (dt, *J* = 14.7, 7.0 Hz, 1H), 3.49 (dd, *J* = 13.8, 5.7 Hz, 1H), 3.34 – 3.26 (m, 1H), 3.23 (s, 3H), 3.19 (dt, *J* = 9.6, 7.0 Hz, 1H), 2.12 (q, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 170.11, 162.01, 153.00, 149.56, 136.23, 135.19, 125.69, 124.54, 123.87, 122.45, 121.74, 121.32, 70.07, 58.43, 44.41, 39.50, 34.94. HRMS (TOF MS EI) calcd for $C_{17}H_{18}N_2OS$ $[M]^+$ 298.1140, found 298.1140.



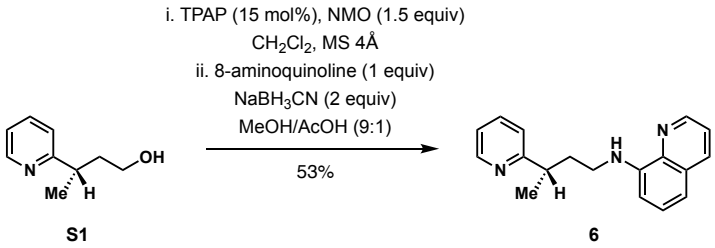
(*S*)-2-(4-((*Tert*-butyldimethylsilyl)oxy)butan-2-yl)pyridine (5). The title compound was prepared according to **general procedure III** using tert-butyl-dimethyl-(3-pyridin-2-ylpropoxy)silane (**1q**) (251 mg, 1.0 mmol), HMPA (0.13 mL, 0.75 mmol, 0.75 equiv), **(*R*)-^{1}DA** (0.364 g, 1.4 mmol, 1.4 equiv), and *n*-BuLi (0.96 mL, 2.5 M in hexanes, 2.4 mmol, 2.4 equiv) in toluene (12.5 ml) followed by addition of methyl iodide (74 µL, 1.2 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 2 h and product **5** (0.216 g, 0.82 mmol, 82% yield) was obtained after purification by column chromatography on silica gel (5% EtOAc in hexane). Er: 97:3.[21] $[\alpha]_D^{24}$ + 30.7° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.53 (d, *J* = 4.7 Hz, 1H), 7.57 (td, *J* = 7.7, 1.8 Hz,

1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.10 – 7.05 (m, 1H), 3.60 – 3.45 (m, 2H), 3.04 (h, *J* = 6.9 Hz, 1H), 2.04 – 1.93 (m, 1H), 1.86 – 1.74 (m, 1H), 1.28 (d, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), -0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 171.49, 154.56, 141.55, 127.32, 126.39, 66.57, 45.05, 43.62, 31.31, 26.28, 23.64, 0.00. HRMS (TOF MS EI) calcd for $C_{14}H_{24}NOSi$ $[M\text{-}CH_3]^+$ 250.1627, found 250.1635.



5 **S1**

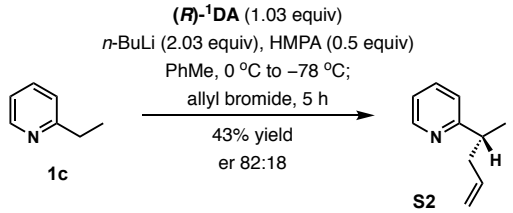
(*S*)-3-(Pyridin-2-yl)butan-1-ol (S1). 2-(4-((*Tert*-butyldimethylsilyl)oxy)butan-2-yl)pyridine (**5**) (215 mg, 0.80 mmol) was dissolved in THF (8 mL) and TBAF hydrate (0.511 g, 1.62 mmol, 2 equiv) was added. After stirring for 2 h the reaction was quenched with saturated aqueous ammonium chloride and transferred to a separatory funnel. The aqueous layer was made basic with 1M NaOH and extracted with EtOAc. Combined organics were dried over anhydrous Na_2SO_4, concentrated, and product **S1** (0.120 g, 0.80 mmol, 100% yield) was obtained after purification by column chromatography on silica gel (70% EtOAc in hexane). Er: 97:3 (Chiralcel® AD-H; 2% *i*-PrOH in hexanes; flow rate = 1 mL/min; detection at 254 nm; t_1 = 27.0 min (major); t_2 = 28.1 min). $[\alpha]_D^{22}$ + 22.0° (*c* 1.12, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.51 (d, *J* = 6.6 Hz, 1H), 7.64 (td, *J* = 7.7, 1.9 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.10 (m, 1H), 3.69 – 3.54 (m, 2H), 3.23 – 3.12 (m, 1H), 2.05 – 1.94 (m, 1H), 1.93 – 1.84 (m, 1H), 1.34 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 166.04, 148.99, 137.31, 122.04, 121.71, 60.59, 39.54, 39.09, 20.88. HRMS (TOF MS ES) calcd for $C_9H_{13}NONa$ $[M+Na]^+$ 174.0895, found 174.0889.



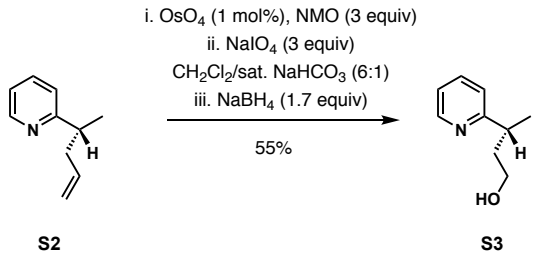
S1 **6**

(*S*)-*N*-(3-(Pyridin-2-yl)butyl)quinolin-8-amine (6). Solid TPAP (20 mg, 0.056 mmol, 0.15 equiv) was added in one portion to a stirred solution of 3-(pyridin-2-yl)butan-1-ol (**S1**) (57 mg, 0.376 mmol), NMO (66 mg, 0.564 mmol, 1.5 equiv), and ground 4Å molecular sieves (188 mg) in CH_2Cl_2 (3.7 mL) under Ar. After stirring for 4 h the solution is passed through a plug of silica (100% EtOAc) and organics are evaporated. The crude mixture is dissolved in a 9:1 mixture of methanol/acetic acid (3.76 mL) and 8-aminoquinoline (54 mg, 0.376 mmol, 1.0 equiv) is added followed by $NaBH_3CN$ (47 mg, 0.752, 2 equiv). After stirring for 12 h, the solvent is evaporated and organics are dissolved in EtOAc, washed with a dilute solution of $NaHCO_3$, rinsed with brine, dried over anhydrous Na_2SO_4, concentrated, and product **6** (55 mg, 0.201 mmol, 53% yield) was obtained after purification by column chromatography on silica gel (10% EtOAc in hexane). Er: 97:3 (Chiralcel® OJ-H;

2% *i*-PrOH in hexanes; flow rate = 0.5 mL/min; detection at 254 nm; t_2 = 36.30 min (major); t_1 = 32.22 min). $[\alpha]_D^{19}$ + 43.5° (*c* 0.900, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (d, *J* = 4.9 Hz, 1H), 8.04 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.17 – 7.10 (m, 1H), 7.00 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 3.30 – 3.20 (m, 2H), 3.20 – 3.10 (m, 1H), 2.33 – 2.22 (m, 1H), 2.16 – 2.04 (m, 1H), 1.39 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 165.59, 149.32, 146.68, 144.83, 138.19, 136.44, 135.91, 128.65, 127.79, 121.83, 121.28, 113.49, 104.46, 41.53, 39.81, 36.22, 21.14. HRMS (TOF MS EI) calcd for $C_{18}H_{19}N_3$ $[M]^+$ 277.1579, found 277.1584.

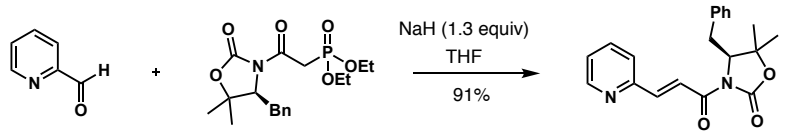


(*R*)-2-(Pent-4-en-2-yl)pyridine (S2). The title compound was prepared according to **general procedure III** using 2-ethylpyridine (48 mg, 0.44 mmol), HMPA (0.425 mL, 0.522 M in toluene, 0.22 mmol, 0.5 equiv), **(*R*)-^{1}DA** (0.119 g, 0.457 mmol, 1.03 equiv), and *n*-BuLi (0.36 mL, 2.5 M in hexanes, 0.901 mmol, 2.03 equiv) in toluene (5.1 ml) followed by addition of allyl bromide (46 µL, 0.535 mmol, 1.2 equiv) at –78 °C. The reaction was quenched after 5 hours and product **S2** (28 mg, 0.191 mmol, 43% yield) was obtained after purification by column chromatography on silica gel (3% EtOac in hexane). Er: 82:18[20] $[\alpha]_D^{25}$ – 3.7° (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.55 (d, *J* = 5.6 Hz, 1H), 7.59 (td, *J* = 7.7, 1.8 Hz, 1H), 7.16 – 7.07 (m, 2H), 5.73 (ddt, *J* = 17.4, 10.2, 7.1 Hz, 1H), 5.07 – 4.90 (m, 2H), 2.98 (p, *J* = 7.0 Hz, 1H), 2.53 (dt, *J* = 13.6, 6.8 Hz, 1H), 2.34 (dt, *J* = 14.9, 7.4 Hz, 1H), 1.30 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.65, 149.10, 136.79, 136.20, 121.54, 121.08, 116.04, 41.67, 41.22, 20.06. HRMS (TOF MS EI) calcd for $C_{10}H_{13}N$ $[M]^+$ 147.1048, found 147.1042.



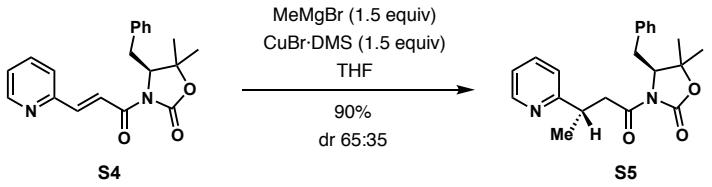
(*R*)-3-(Pyridin-2-yl)butan-1-ol (S3). Osmium tetroxide (38 µL, 0.0019 mmol, 0.05 M in ^{t}BuOH, 0.01 equiv) was added to a solution of 2-(pent-4-en-2-yl)pyridine (**S2**) (28 mg, 0.190 mmol) and NMO (67 mg, 0.57 mmol, 3.0 equiv) in CH_2Cl_2 (3 mL). The solution was stirred for 12 h, after which a solution of saturated $Na_2S_2O_3$ (5 mL) was added and the solution was allowed to stir for 10 min. Organic layers were separated, and the aqueous solution was extracted with CH_2Cl_2. Combined organic layers were evaporated, and the crude material was dissolved in a mixture of CH_2Cl_2 (3 mL) and sat. $NaHCO_3$ (0.5 mL). Sodium metaperiodate (0.121 g, 0.57

mmol, 3.0 equiv) was added in one portion and the mixture was stirred vigorously for 3 h. The solution was then filtered, concentrated, dissolved in methanol (3 mL), and cooled to 0 °C. Sodium borohydride (12 mg, 0.323 mmol, 1.7 equiv) was added in a single portion, and the reaction was stirred for 30 min. The reaction was quenched with sat. NH_4Cl and extracted with Et_2O. Organics were dried over anhydrous $MgSO_4$, concentrated, and the crude residue was purified by column chromatography on silica gel (70% EtOAc in hexane) affording **S3** as a clear oil (16 mg, 0.104 mmol, 55%). Er: 82:18 (Chiralcel® AD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_2 = 26.5 min (major); t_1 = 24.8 min). $[\alpha]_D^{22}$ – 16.7° (*c* 0.77, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.51 (d, *J* = 6.6 Hz, 1H), 7.64 (td, *J* = 7.7, 1.9 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.10 (m, 1H), 3.69 – 3.54 (m, 2H), 3.23 – 3.12 (m, 1H), 2.05 – 1.94 (m, 1H), 1.93 – 1.84 (m, 1H), 1.34 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 166.04, 148.99, 137.31, 122.04, 121.71, 60.59, 39.54, 39.09, 20.88. HRMS (TOF MS ES) calcd for $C_9H_{13}NONa$ $[M+Na]^+$ 174.0895, found 174.0889.



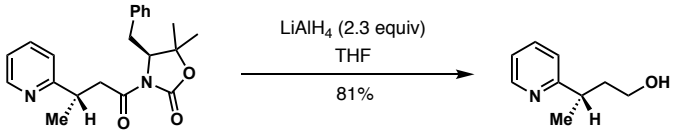
S4

(S,*E*)-4-Benzyl-5,5-dimethyl-3-(3-(pyridin-2-yl)acryloyl)oxazolidin-2-one (S4). [2-((*S*)-4-Benzyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl)-2-oxoethyl]phosphonic acid diethyl ester[20] (1.00 g, 2.61 mmol, 1.4 equiv) was dissolved in THF (6 mL) and added dropwise to a suspension of NaH (97 mg, 2.43 mmol, 1.3 equiv, 60% in mineral oil) in THF (12 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min, then at room temperature for 30 min, after which it was transferred to a solution of pyridine-2-carbaldehyde (0.200 g, 1.86 mmol) in THF (19 mL) at –78 °C by canula. The resultant mixture was stirred at this temperature for 30 min, then at room temperature for 2 h. The solution was quenched with sat. NH_4Cl and the layers were separated. The aqueous portion was extracted with EtOAc, and combined organics were rinsed with brine, dried over anhydrous Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (30% EtOAc in hexane) afforded **S4** as a white solid (0.571 g, 1.69 mmol, 91%). $[\alpha]_D^{25}$ – 60.0° (*c* 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.68 (d, *J* = 5.6 Hz, 1H), 8.27 (d, *J* = 15.5 Hz, 1H), 7.82 (d, *J* = 15.5 Hz, 1H), 7.72 (td, *J* = 7.7, 1.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 4.5 Hz, 1H), 7.30 – 7.21 (m, 5H), 4.63 (dd, *J* = 9.7, 3.7 Hz, 1H), 3.28 (dd, *J* = 14.4, 3.7 Hz, 1H), 2.93 (dd, *J* = 14.4, 9.7 Hz, 1H), 1.40 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm): 165.23, 153.14, 152.50, 150.21, 144.74, 136.95, 136.62, 129.06, 128.67, 126.78, 124.32, 124.06, 121.59, 82.34, 63.83, 35.22, 28.52, 22.33. HRMS (TOF MS ES) calcd for $C_{20}H_{20}N_2O_3Na$ $[M+Na]^+$ 359.1372, found 359.1364.



S4 **S5**

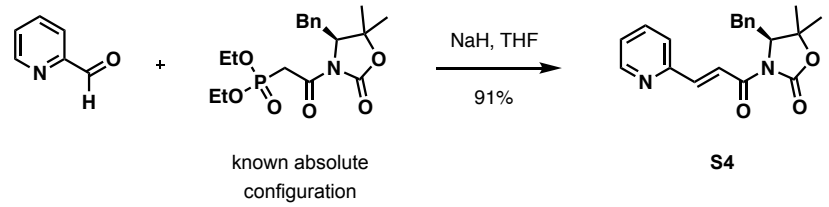
(*S*)-4-Benzyl-5,5-dimethyl-3-((*S*)-3-(pyridin-2-yl)butanoyl)oxazolidin-2-one (S5). Methyl magnesium bromide (0.22 mL, 0.667 mmol, 3.0 M in Et_2O, 1.5 equiv) was added to a solution of CuBr•DMS (137 mg, 0.667 mmol, 1.5 equiv) in THF (15 mL) and DMS (2.5 mL) at 0 °C. After stirring for 30 min, a solution of (*S*,*E*)-4-benzyl-5,5-dimethyl-3-(3-(pyridin-2-yl)acryloyl)oxazolidin-2-one (**S4**) (150 mg, 0.445 mmol) in THF (5 mL) was added dropwise, and the resultant mixture was stirred at 0 °C for 30 min, then room temperature for 12 h. The solution was quenched with sat. NH_4Cl and the layers were separated. The aqueous portion was extracted with EtOAc, and combined organics were rinsed with brine, dried over anhydrous Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (30% EtOAc in hexane) afforded **S5** as a white solid (0.140 g, 0.400 mmol, 90%, 65:35 d.r.). Recrystallization from pentane/ethanol afforded 33 mg of **S5** as a single diastereomer. $[\alpha]_D^{24}$ – 9.7° (*c* 1.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.48 (d, *J* = 5.8 Hz, 1H), 7.59 (td, *J* = 7.7, 1.9 Hz, 1H), 7.31 – 7.19 (m, 6H), 7.08 (dd, *J* = 8.0, 5.4 Hz, 1H), 4.43 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.65 (dd, *J* = 16.9, 8.4 Hz, 1H), 3.55 – 3.47 (m, 1H), 3.10 (ddd, *J* = 16.9, 11.0, 4.8 Hz, 2H), 2.86 (dd, *J* = 14.4, 9.6 Hz, 1H), 1.36 – 1.28 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 172.48, 164.63, 152.78, 149.17, 137.19, 136.48, 129.23, 128.70, 126.81, 122.08, 121.39, 82.26, 77.45, 77.19, 76.93, 63.47, 41.62, 37.68, 35.46, 28.45, 22.35, 21.19. HRMS (TOF MS ES) calcd for $C_{21}H_{24}N_2O_3H$ $[M+H]^+$ 353.1865, found 353.1873.

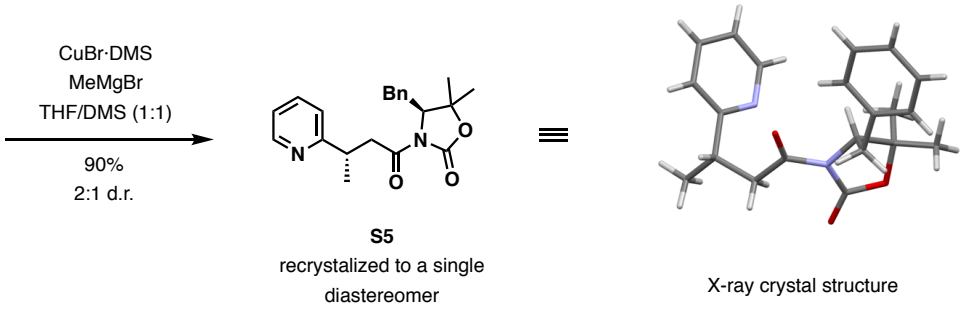


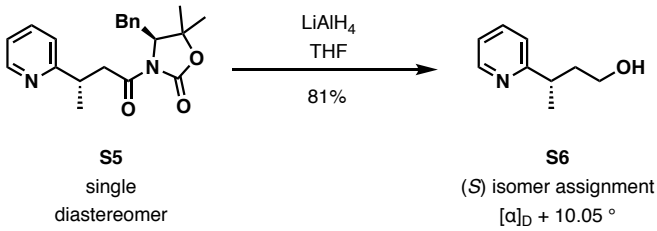
S5 **S6**

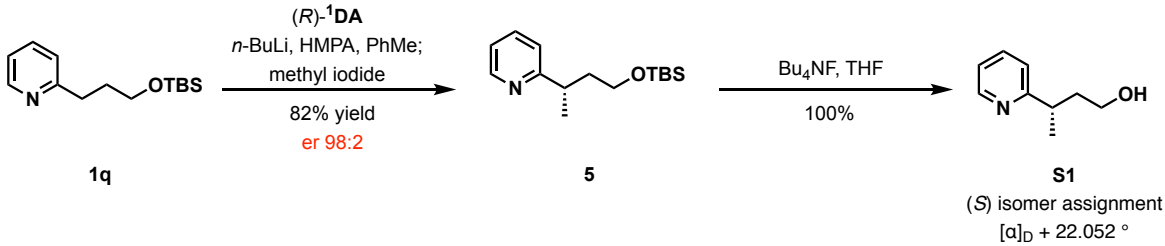
(*S*)-3-(Pyridin-2-yl)butan-1-ol (S6). (*S*)-4-Benzyl-5,5-dimethyl-3-((*S*)-3-(pyridin-2-yl)butanoyl)oxazolidin-2-one (**S5**) (4 mg, 0.011 mmol) was added to a solution of $LiAlH_4$ (1 mg, 0.026 mmol) in THF (1 mL). After stirring at room temperature for 1 h, a Fieser work up was performed and the crude residue was purified by column chromatography on silica gel (50% EtOAc in hexane) affording **S6** as a clear oil (1.3 mg, 8.9 μmmol, 81%). E.r.= 99:1 (Chiralcel® AD-H; 2% *i*-PrOH in hexanes; flow rate = 1.0 mL/min; detection at 254 nm; t_1 = 26.1 min (major); t_2 = 27.3 min). $[\alpha]_D^{19}$ + 10.1° (*c* 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.51 (d, *J* = 6.6 Hz, 1H), 7.64 (td, *J* = 7.7, 1.9 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.10 (m, 1H), 3.69 – 3.54 (m, 2H), 3.23 – 3.12 (m, 1H), 2.05 – 1.94 (m, 1H), 1.93 – 1.84 (m, 1H), 1.34 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 166.04, 148.99, 137.31, 122.04, 121.71, 60.59, 39.54, 39.09, 20.88. HRMS (TOF MS ES) calcd for $C_9H_{13}NONa$ $[M+Na]^+$ 174.0895, found 174.0889.

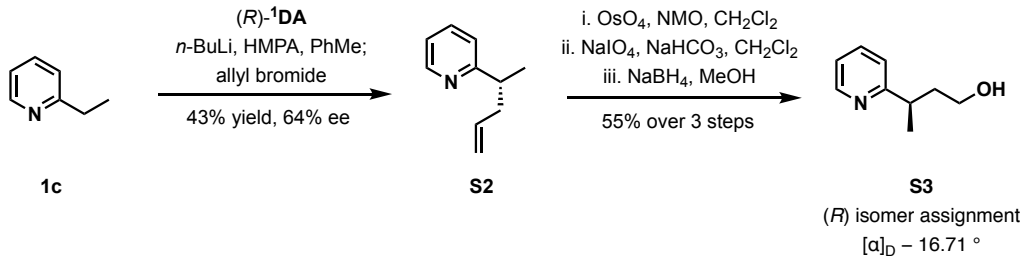
Stereochemical Assignment









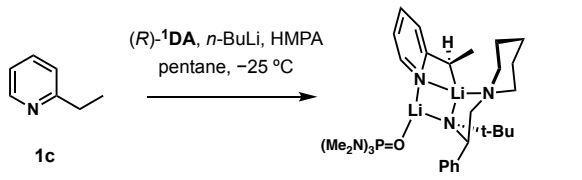


Comments: Preparation of **S4** from [2-((*S*)-4-Benzyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl)-2-oxoethyl]phosphonic acid diethyl ester and pyridine-2-carbaldehyde provided a compound of known absolute configuration. Cuprate addition provided **S5**, which was recrystallized to a single diastereomer. The relative configuration of

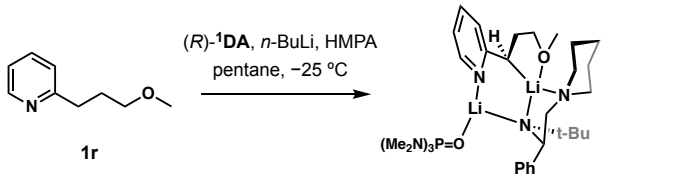
S5 was determined by X-ray crystallography, and the absolute configuration was determined by comparison to the known configuration of the oxazolidinone. Reductive cleavage of the oxazolidinone provided alcohol **S6** with (*S*) configuration. Asymmetric alkylation of **1q** with methyl iodide followed by desilylation provided the chiral alcohol **S1**. The absolute configuration of **S1** was assigned as (*S*) by comparison of HPLC and optical rotation data to that of **S6**.

Having discovered significant differences in the aggregate structures of **1c** and **1r**, a simple experiment was conducted to confirm that both structures acted in accordance with our hypothesis of stereochemical control arising from organolithium aggregation. The substrate **1c** was asymmetrically alkylated with allyl bromide, followed by dihydroxylation, diol cleavage, and reduction to afford the chiral alcohol **S3**. Both HPLC analysis and optical rotation data are in agreement that the (*R*) isomer was obtained.

Synthesis and Characterization of Organolithium Aggregate Structures



Aggregate CH_3(2-Py)CHLi•(*R*)-Li[1]DA•HMPA: 2-Ethylpyridine (50 mg, 0.467 mmol), (*R*)-[1]**DA** (0.122 g, 0.468 mmol, 1 equiv), and HMPA (41 μL, 0.236 mmol, 0.5 equiv) were added to a 25 mL round bottom flask and dissolved in pentane (5 mL) in an N_2-filled glovebox. After stirring for 10 min at 25 °C, the mixture was placed in a –25 °C freezer for 1 h. *n*-Butyllithium (0.38 mL, 0.95 mmol, 2.03 equiv, 2.5 M hexanes) was added dropwise to the cooled solution, and the bright orange solution was stirred at –25 °C for 10 min, at which point the reaction mixture was filtered through Celite supported on glass wool (0.5 x 1 cm). The Celite pad was then washed with pentane (2 mL). The washings were added to the filtrate. The orange filtrate was then concentrated to 3 mL *in vacuo* and stored at –25 °C for 72 h. This resulted in the deposition of orange crystals, which were isolated by decanting the supernatant.



Aggregate $CH_3O(CH_2)_2$(2-Py)CHLi•(*R*)-Li[1]DA•HMPA: 2-(3-methoxy-1-propyl)pyridine (50 mg, 0.333 mmol), (*R*)-[1]**DA** (0.121 g, 0.465 mmol, 1.4 equiv), and HMPA (43 μL, 0.247 mmol, 0.75 equiv) were added to a 25 mL round bottom flask and dissolved in pentane (1 mL) in an N_2-filled glovebox. After stirring for 10 min at 25 °C, the mixture was placed in a –25 °C freezer for 1 h. *n*-Butyllithium (0.32 mL, 0.8 mmol, 2.4 equiv, 2.5 M hexanes) was added dropwise to the cooled solution, and the bright orange solution was stirred at –25 °C for 10 min, at which point the solvent was removed *in vacuo* to give an orange oil. The oil was dissolved in PhMe (1 mL) and filtered through a Celite column supported on glass wool (0.5 x 1 cm). The Celite pad was then washed with PhMe (1 mL). The washings were added to the filtrate. The orange filtrate was layered with pentane (8 mL) and stored at –25 °C for 72 h. This resulted in the deposition of orange crystals, which were isolated by decanting off the supernatant.

X-ray Crystallography. Data for **1c-Li** and **1r-Li** were collected on a Bruker KAPPA APEX II diffractometer equipped with an APEX II CCD detector using a TRIUMPH monochromater with a MoKα X-ray source (α = 0.71073 Å). Crystals were mounted on a cryoloop under Paratone-N oil, and all data were collected at 110(2) K for complex **1c-Li** and 105(2) K for complex **1r-Li** using an Oxford nitrogen gas cryostream system. X-ray data for **1c-Li** and **1r-Li** were collected utilizing frame exposures of 40 s. Data collection and cell parameter determination were conducted using the SMART program.[23] Integration of the data frames and final cell parameter refinement were performed using SAINT software.[24] Absorption correction of the data was carried out using the multi-scan method SADABS.[25] Subsequent calculations were carried out using SHELXTL.[26] Structure determination was done using direct methods and difference Fourier techniques. All hydrogen atom positions were idealized, and rode on the atom of attachment, unless otherwise stated. Structure solution, refinement, graphics, and creation of publication materials were performed using SHELXTL.[26]

Complex **1c-Li** contains minor positional disorder of the Li atoms, which was addressed using the EADP command to constrain their anisotropic temperature factors. Additionally, one carbon atom (C9) in the *tert*-butyl moiety was significantly disordered and its position relative to the other carbon atoms in the *tert*-butyl moiety was constrained using the SADI command. The hydrogen atoms that rode on C9 were manually generated and their positions and temperature factors were constrained using the SADI and EADP commands, respectively.

Complex **1r-Li** also contains minor positional disorder of the Li atoms, which was similarly addressed using the EADP command. Unresolved positional disorder for the carbon and nitrogen atoms within one HMPA moiety (N4-N6; C27-C32), one pyridine ring (N1; C1-C5), one piperidyl ring (N2; C22-C26), one *tert*-butyl moiety (C10-C13), as well as N2, C8, C15, C18, and C21 were resolved using the EADP command.

Further crystallographic details can be found in Table S4.

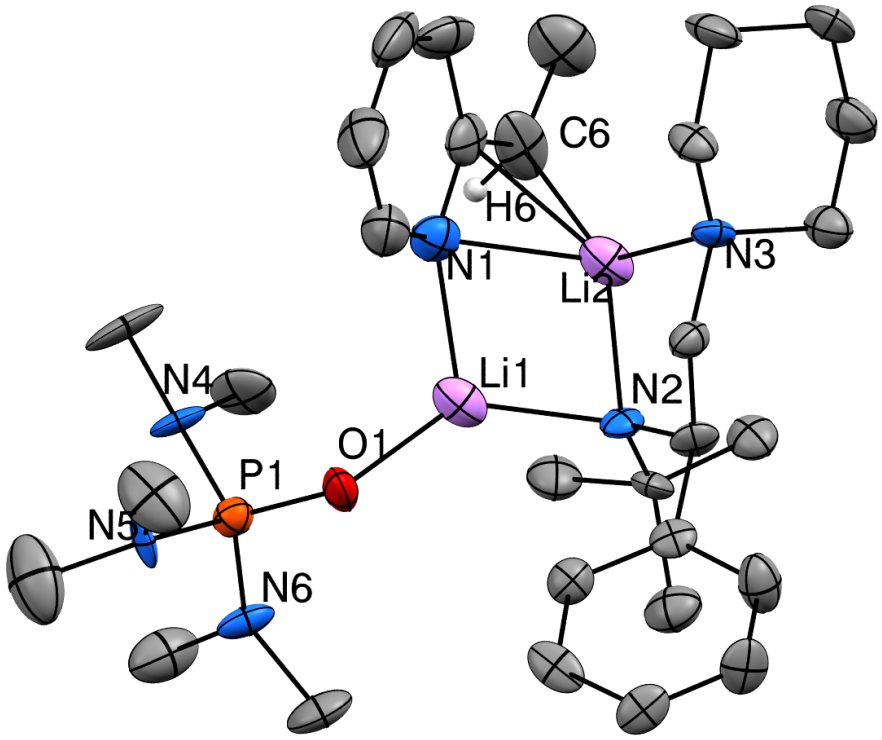


Figure S1. ORTEP diagram for **CH_3(2-Py)CHLi•(*R*)-Li[1]DA•HMPA (1c-Li)** shown with 50% probability ellipsoids.

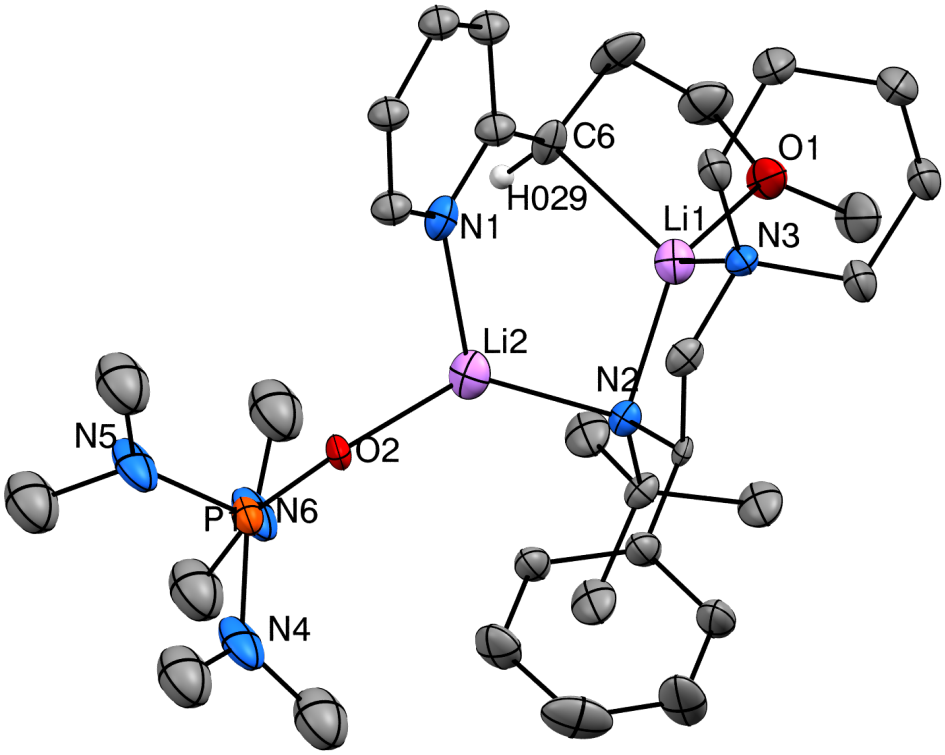


Figure S2. ORTEP diagram for **$CH_3O(CH_2)_2$(2-Py)CHLi•(*R*)-Li[1]DA•HMPA (1r-Li)** shown with 50% probability ellipsoids.

Table S4. X-ray Crystallographic Data for **1c-Li** and **1r-Li**.

	1c-Li	**1r-Li**
empirical formula	$C_{30}H_{53}Li_2N_6OP$	$C_{64}H_{114}Li_4N_{12}O_4P_2$
crystal habit, color	plate, orange	block, orange
crystal size (mm)	0.3 × 0.3 × 0.05	0.2 × 0.15 × 0.08
crystal system	orthorhombic	orthorhombic
space group	$P2_12_12_1$	$P2_12_12_1$
volume (Å^3)	3426(3)	7129(5)
a (Å)	10.770(6)	14.958(6)
b (Å)	10.980(6)	15.579(7)
c (Å)	28.973(17)	30.593(10)
α (deg)	90	90
β (deg)	90	90
γ (deg)	90	90
Z	4	4
formula weight (g/mol)	558.63	1205.37
density (calculated) (Mg/m^3)	1.083	1.123
absorption coefficient (mm^{-1})	0.110	0.112
F_{000}	1216	2624
total no. reflections	5228	9954
unique reflections	2314	6264
final R indices [I>2σ(I)]	R_1 = 0.0886	R_1 = 0.0863
	wR_2 = 0.1725	wR_2 = 0.1561
largest diff. peak and hole (e$^-$A^{-3})	0.314 and -0.359	0.461 and -0.568
GOF	1.095	1.452

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