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Cationic iridium-catalyzed enantioselective activation of secondary sp^3 C–H bond adjacent to nitrogen atom

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ABSTRACT

A cationic Ir(I)–tolBINAP complex catalyzed an enantioselective C–C bond formation, which was initiated by secondary sp^3 C–H bond cleavage adjacent to nitrogen atom. A wide variety of 2-(alkylamino) pyridines and alkenes were selectively transformed into the corresponding chiral amines with moderate to almost perfect enantiomeric excesses. Alkynes were also investigated as coupling partners. The effect of alkyl structure in substrates and directing groups were studied. This transformation represents the first example of a highly enantioselective C–H bond activation of a methylene group, not at allylic or benzylic position.

1. Introduction

The efficient functionalization of C–H bonds has attracted much attention from both academia and industry, especially with regard to C–C bond formation based on transition-metal catalysis.[1] In last decade, various methods have been reported for the initiation of C–H bond cleavage, and many synthetically useful transformations have been disclosed.[2] Among the C–H bond functionalizations, activation of the sp^2 C–H bond, such as aromatic and vinylic C–H bonds, has been widely investigated. However, the examples of sp^3 C–H bond activation are relatively few.[3-5] In particular, those of secondary sp^3 C–H bond activation are scarce and limited to benzylic and allylic positions.[6] For example, Jun reported pioneering work of a Ru-catalyzed reaction of 2-(benzylamino)pyridine with alkenes, which was initiated by secondary sp^3 C–H bond cleavage at the benzylic position.[6b] Murai also reported a Ru-catalyzed reaction of 2-(*N*-pyrrolidinyl)pyridine with alkenes.[6c] In contrast to these achievements of secondary sp^3 C–H bond activation, enantioselective secondary sp^3 C–H bond activation still remains highly challenging.[7,8] Against these backgrounds, we realized an enantioselective cleavage of secondary sp^3 C–H bond adjacent to nitrogen of 2-(alkylamino)pyridine at relatively lower temperature by using a chiral Ir catalyst.[9]

In the precedent communication, we reported that a cationic Ir(I)–tolBINAP complex catalyzed an enantioselective secondary sp^3 C–H bond activation of 2-(ethylamino)pyridine with styrene derivatives in good yields with high enantiomeric excesses.[10] In this manuscript, we scrutinized the effect of alkyl group on the nitrogen atom of amino group and directing group other than pyridine. In the case of a longer alkyl group, higher reaction temperature was required, but the successful transformation was achieved. In contrast, the reaction of 2-(alkylamino)pyridine possessing a bulky alkyl group did not proceed. We screened various nitrogen-containing heterocycles as directing groups and found that pyridine and quinoline were the best directing groups. Then we further examined the scope of alkenes: the reaction with ethyl acrylate provided the corresponding amine with perfect enantiomeric excess. Vinylsilanes and allylsilanes also gave the desired products with moderate to good ee. Finally, alkynes were also used as coupling partners to 2-(alkylamino)pyridines in this transformation.

2. Results and discussion

2.1. Optimization of the reaction conditions

In previous report, we found that (*S*)-tolBINAP was the best chiral ligand for enantioselective secondary sp^3 C–H bond activation.[10] We further examined the counteranion of iridium complex, solvent and reaction temperature in this transformation (Table 1). As for counteranion, the results of PF_6, OTf, or BARF did not exceed those of BF_4 (entries 1–4).[11] We next examined various solvents other than chlorobenzene. Toluene

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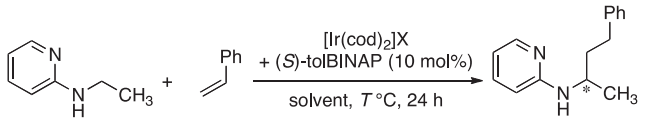
and 1,2-dichloroethane (DCE) were tested, but the results were not better than those of chlorobenzene (entries 5 and 6). In contrast, the best yield of 95% was achieved by using dioxane, yet along with significant decrease of ee (entry 7). At lower temperature, the reaction sluggishly proceeded, but the ee was significantly improved (entries 8 and 9). The mixed solvent of dioxane and chlorobenzene gave the desired product **3aa**, but the ee was less than 80% (entries 10–12). When 1,2-dimethoxylethane (DME) was used as a solvent, the reaction proceeded efficiently even at 75 °C and the enantioselectivity reached ca. 90% (entry 15). Three equivalent amounts of styrene were sufficient to achieve good yield and high ee at slightly higher reaction temperature (entry 16). We decided to use the reaction conditions of entry 15 for further investigation.

Table 1
Investigation of the best reaction conditions



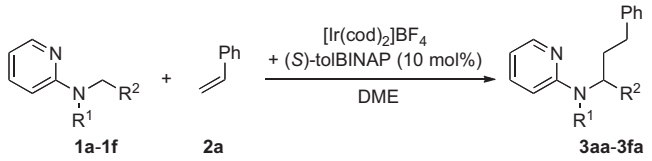
Entry[a]	X	Solvent	T (°C)[b]	Yield (%)	Ee (%)
1	BF_4	PhCl	135	62	80
2	PF_6	PhCl	135	24	74
3	OTf	PhCl	135	48	81
4	BARF[c]	PhCl	135	9	40
5	BF_4	$PhCH_3$	135	66	68
6	BF_4	DCE	135	43	76
7	BF_4	Dioxane	135	95	63
8	BF_4	Dioxane	95	49	80
9	BF_4	Dioxane	75	21	77
10	BF_4	Dioxane/PhCl (9:1)	135	95	52
11	BF_4	Dioxane/PhCl (1:1)	135	72	79
12	BF_4	Dioxane/PhCl (1:9)	135	47	79
13	BF_4	DME	95	62	82
14	BF_4	DME	75	40	87
15[d]	BF_4	DME	75	76	88
16[e]	BF_4	DME	85	75	86

[a] Conditions: **1a** (0.1 mmol), **2a** (0.8 mmol), solvent (0.2 mL), unless otherwise noted.
[b] Bath temperature.
[c] BARF: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate.
[d] The reaction time was 48 h.
[e] Styrene (0.3 mmol) was used, and the reaction time was 72 h.

2.2. Effect of alkyl substituents on the nitrogen atom

We achieved the good enantioselectivity in the reaction of 2-(ethylamino)pyridine **1a** with styrene **2a**. The effect of alkyl substituents on the nitrogen atom of 2-aminopyridine was next investigated in the present reaction (Table 2). We first examined the effect of the length of alkyl chain. As a result, the products **3ba** and **3ca** were obtained with moderate yields at a slightly higher reaction temperature, and their enantiomeric excesses were still high (entries 2 and 3). In the reaction of aminopyridine **1d** possessing six-carbon alkyl chain, further high reaction temperature was required to give product **3da**, and the ee slightly decreased (entry 4). The steric effect of alkyl chain plays an important role in this reaction: aminopyridine **1e** with more bulky alkyl group, such as isobutyl, was completely unreactive at much higher reaction temperature (entry 5). When 2-(*N*-pyrrolidinyl)pyridine (**1f**) was submitted to the reaction, only a trace amount of the desired product was obtained (entry 6). This result indicated that cyclic aminopyridine, namely tertiary amine was an inappropriate substrate in the present catalysis.[12]

Table 2
Effect of alkyl substituents on the nitrogen atom



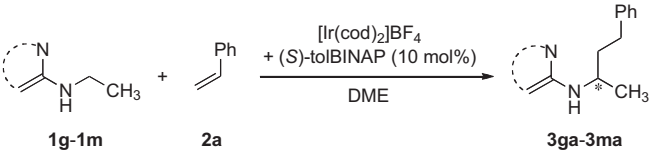
Entry[a]	R^1	R^2		Cond.[b]	Yield (%)	Ee (%)
1	H	CH_3	(**1a**)	75/2	76 (**3aa**)	88
2	H	CH_2CH_3	(**1b**)	85/4	69 (**3ba**)	83
3	H	$(CH_2)_2CH_3$	(**1c**)	85/7	58 (**3ca**)	86
4	H	$(CH_2)_4CH_3$	(**1d**)	95/4	60 (**3da**)	73
5[c]	H	$CH(CH_3)_2$	(**1e**)	135/3	— (**3ea**)	—
6[c]	$-(CH_2)_3-$		(**1f**)	135/2	Trace (**3fa**)	—

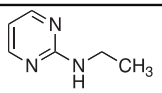
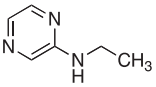
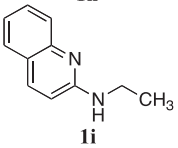
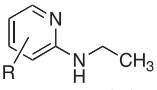
[a] Condition: **1** (0.1 mmol), **2a** (0.8 mmol), DME (0.2 mL), unless otherwise noted.
[b] Cond.: bath temperature/time=°C/day.
[c] Chlorobenzene (0.2 mL) was used as solvent.

2.3. Scope of nitrogen-containing heterocycles

We next investigated the scope of nitrogen-containing heterocycles bearing ethylamino substituent at 2-position (Table 3). Pyrimidine and pyrazine could not operate as efficient directing group in the secondary sp^3 C–H bond activation (entries 1 and 2). However, when quinoline was used as a directing group in present reaction, the desired product **3ia** was obtained with good yield, and its enantiomeric excess reached 98% (entry 3). Furthermore, dependent on the position of methyl group on the pyridine ring, the yield and ee were changed (entries 4–6): compared with pyridine

Table 3
Scope of nitrogen-containing heterocycles



Entry[a]	Substrate	Cond.[b]	Yield (%)	Ee (%)
1[c]	 **1g**	135/1	— (**3ga**)	—
2[c]	 **1h**	135/3	Trace (**3ha**)	—
3	 **1i**	85/1	72 (**3ia**)	98
4	 R = 3-Me (**1j**)	85/3	47 (**3ja**)	55
5	R=5-Me (**1k**)	85/2	76 (**3ka**)	65
6	R=6-Me (**1l**)	85/7	47 (**3la**)	77
7[c]	R=6-Cl (**1m**)	135/1	— (**3ma**)	—

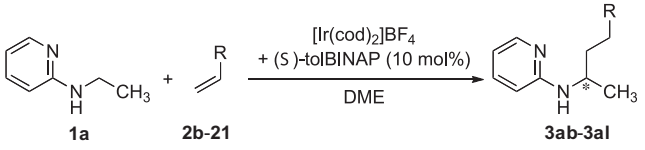
[a] Condition: **1** (0.1 mmol), **2a** (0.8 mmol), DME (0.2 mL), unless otherwise noted.
[b] Cond.: bath temperature/time=°C/day.
[c] Chlorobenzene (0.2 mL) was used as a solvent.

itself as directing group, the yields and enantiomeric excesses generally decreased. The coordination of the nitrogen in the pyridine ring to Ir would be crucial for the reaction efficiency and enantiomeric excess. Electronic effect on the backbone of pyridine ring also plays an important role in this reaction: pyridine bearing chloro group at 6-position rendered the reaction, and the desired alkylated product **3ma** could not be detected even at higher reaction temperature (entry 7).

2.4. Scope of alkenes

We further examined the scope of alkenes in the reaction with 2-(ethylamino)pyridine (Table 4). In previous report, we mainly used styrene derivatives: in the reaction of *p*-methoxystyrene, the absolute configuration of obtained pyridyl amine **3ab** was determined to be *S* by its derivation to a known chiral amine.[10] We next submitted a simple alkene to the reaction (entry 2). The reaction of 1-nonene gave the corresponding product **3ac** with low yield, but the ee was high. In the reaction with allylbenzene, higher reaction temperature was required, and the desired product **3ad** was obtained in moderate yield and ee (entry 3). 1,3-Diene was a favourable substrate, and high ee was achieved at higher reaction temperature (entry 4). The reaction with acrylate derivatives also proceeded to give γ-amino acid derivatives **3af** and **3ag** (entries 5 and 6). In particular, ethyl acrylate was the best coupling partner, and the enantiomeric excess reached 99%. Furthermore, vinylsilane derivatives also reacted with 2-(ethylamino)pyridine (**1a**). Regardless of the substituents on the silicon atom, the silylated amines were obtained in the almost same yields and ee (entries 7–9). In the case of allylsilane, the choice of substituents on silicon atom was important, and allyltriphenylsilane achieved high yield and ee (entries 10 and 11).

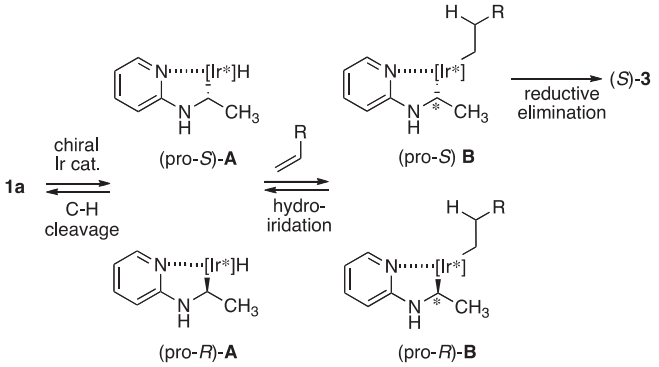
Table 4
Scope of alkenes



Entry[a]	R	Alkene	Cond.[b]	Yield (%)	Ee (%)
1	4-$MeOC_6H_4$	**2b**	75/2	76 (**3ab**)	87 (*S*)
2	*n*-C_7H_{15}	**2c**	85/5	27 (**3ac**)	78
3	CH_2Ph	**2d**	95/2	57 (**3ad**)	61
4	CH=CHPh	**2e**	95/2	84 (**3ae**)	87
5	COOEt	**2f**	85/3	75 (**3af**)	99
6	COO*t*-Bu	**2g**	85/3	52 (**3ag**)	89
7[c]	$SiMe_3$	**2h**	85/3	71 (**3ah**)	76
8	$SiEt_3$	**2i**	85/3	87 (**3ai**)	69
9	$SiPh_3$	**2j**	85/3	81 (**3aj**)	72
10	CH_2SiMe_3	**2k**	85/3	33 (**3ak**)	73
11	CH_2SiPh_3	**2l**	85/1	88 (**3al**)	87

[a] Condition: **1a** (0.1 mmol), **2** (0.8 mmol), DME (0.2 mL), unless otherwise noted.
[b] Cond.: bath temperature/time=°C/day.
[c] Vinyltrimethylsilane (16 equiv) was used.

We showed a possible mechanism in Scheme 1. Enantioselective cleavage of secondary sp^3 C–H bond adjacent to a nitrogen atom is an initiation step, and an asymmetric carbon atom is generated in the intermediate **A**. Subsequent hydroiridation to alkene provides intermediate **B**.[13] Finally, reductive elimination gives a chiral amine as an alkylated product. The enantioselectivities were significantly changed from 61 to 99% by the alkenes (Table 4). These results explained as follows: the chiral Ir catalyst affords (pro-*S*)-**A** or (pro-*R*)-**A** by C–H bond cleavage. The subsequent hydroiridation rate of (pro-*S*)-**A** and that of (pro-*R*)-**A** are not same because they are diastereomers. Therefore, the relative rates could be changed by alkenes, which induces different selectivity to the formation of (pro-*S*)-**B** and (pro-*R*)-**B**. Moreover, C–H bond cleavage and hydroiridation are reversible steps.

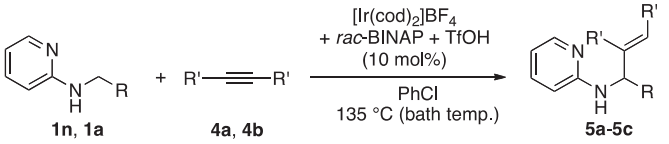


Scheme 1. Possible mechanism initiated by enantioselective cleavage of secondary sp^3 C–H bond.

2.5. Reaction of 2-(alkylamino)pyridine with alkynes

Finally, the reaction of 2-alkylaminopyridines with alkynes was examined (Table 5). The reaction of 2-(methylamino) pyridine (**1n**) with diphenylacetylene (**4a**) proceeded efficiently to give alkenylation product **5a** in high yield by adding a catalytic amount of trifluoromethanesulfonic acid (TfOH) (entry 1).[14] The present reaction proceeded without TfOH in moderate yield, but longer reaction time was required (entry 2). Simple alkyne, 5-decyne (**4b**), was also submitted to the reaction with 2-(methylamino)pyridine (**1n**): it required a long reaction time, but the desired product **5b** was obtained in acceptable yield. We further examined the reaction of 2-(ethylamino)pyridine (**1a**) with 5-decyne (**4b**): to our delight, secondary sp^3 C–H bond activation proceeded, and the alkenylation product **5c** with a chiral centre was obtained, albeit in low yield.[15]

Table 5
Reaction of 2-(alkylamino)pyridine with alkynes



Entry[a]	R	R′	Time (h)	Yield (%), ee (%)
1	H (**1n**)	Ph (**4a**)	8	82 (**5a**)
2[b]	H (**1n**)	Ph (**4a**)	24	59 (**5a**)
3	H (**1n**)	*n*-C_4H_9 (**4b**)	24	42 (**5b**)
4[b,c]	Me (**1a**)	*n*-C_4H_9 (**4b**)	18.5	32 (**5c**), 89%

[a] Condition: **1** (0.1 mmol), **4** (0.2 mmol), TfOH (0.01 mmol), PhCl (0.2 mL), unless otherwise noted.
[b] The reaction was examined without TfOH.
[c] (*S*)-tolBINAP was used as a chiral ligand.

3. Conclusions

In summary, we have developed the chiral Ir(I)-catalyzed enantioselective C–C bond formation initiated by secondary sp^3 C–H bond cleavage adjacent to nitrogen atom. Numerous 2-(alkylamino)pyridines and series of alkenes and alkynes were efficiently transformed into alkylated and alkenylated pyridylamines with moderate to almost perfect enantiomeric excesses. The structure of

alkyl chain in 2-alkylaminopyridine and the directing group play important roles in this transformation.

4. Experimental section

4.1. General

All reactions were examined under an argon atmosphere in oven-dried glassware with a magnetic stirring bar. The cationic iridium complexes $[Ir(cod)_2]X$ (X=BF_4, PF_6, OTf) were prepared from [IrCl(cod)] and AgX according to the literature procedure.[16] $[Ir(cod)_2]$BARF was purchased from Umicore. 2-Alkylaminopyridines **1a** and **1n** are commercially available. 2-Alkylaminopyridines **1b**–**1e** and **1h**–**1l** were prepared from 2-aminopyridine and the corresponding alkyl iodides (**1b**, **1e**, and **1h**–**1l**) or bromides (**1c** and **1d**) using *n*-BuLi as a base according to the literature procedure.[17] Aminopyridines **1f** and **1m** were prepared from 2-bromopyridine and the corresponding amines using CuI as a catalyst according to the literature procedure.[18] 2-Ethylaminopyrimidine (**1g**) was prepared by the literature procedure.[19] Dehydrated solvents were purchased from Kanto or Wako, and dried over activated molecular sieves 3A or 4A. Flash column chromatography was performed with silica gel (Kanto Chemical Co., Inc. 60N 40–50 μm). Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Merck 60 GF254) prepared in our laboratory. IR spectra were recorded with Horiba FT730 spectrophotometer. NMR spectra were measured with JEOL AL-400 (400 MHz) using TMS as an internal standard and $CDCl_3$ was used as a solvent. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-SX102A with FAB (Fast Atomic Bombardment) method or JMS-T100CS with ESI (Electro Spray Ionization) method. Optical rotations were measured with Jasco DIP-1000 polarimeter.

4.2. Typical experimental procedure for 3

$[Ir(cod)_2]BF_4$ (0.01 mmol) and (*S*)-tolBINAP (0.01 mmol) were placed in a Schlenk tube, which was then evacuated and backfilled argon (×3). To the reaction vessel were added 2-(alkylamino)pyridine **1** (0.10 mmol), alkene **2** (0.80 mmol), and 1,2-dimethoxylethane (0.2 mL), unless otherwise noted. The sealed reaction vessel was immersed in a pre-heated oil bath. After the reaction was complete, the mixture of the reaction was cooled to room temperature and the solvent was removed under reduced pressure, and the crude products were purified by thin-layer chromatography to give desired product **3**.

*4.2.1. N-(4-Phenylbutan-2-yl)pyridin-2-amine (**3aa**).* Isolated by thin-layer chromatography (hexane/AcOEt=1/1, R_f=0.6). The title compound was obtained as colourless oil (76%). ^{1}H NMR δ 8.07 (dd, *J*=5.0, 0.8 Hz, 1H), 7.41–7.36 (m, 1H), 7.29–7.26 (m, 2H), 7.20–7.14 (m, 3H), 6.54 (dd, *J*=6.8, 5.0 Hz, 1H), 6.28 (d, *J*=8.4 Hz, 1H), 4.35 (d, *J*=8.4 Hz, 1H), 3.84–3.70 (m, 1H), 2.79–2.65 (m, 2H), 1.92–1.79 (m, 2H), 1.24 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 158.4, 148.4, 142.0, 137.5, 128.4, 128.3, 125.9, 112.6, 106.6, 46.7, 38.9, 32.4, 20.9. IR (neat) 3261, 2925, 1601, 1495, 1446, 769 cm^{-1}; HRMS(ESI) calcd for $C_{15}H_{19}N_2$ (M^++H): 227.1548; found: 227.1558. $[\alpha]_D^{26}$=−17.3 (*c* 0.61, $CHCl_3$, 88% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak AD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 2% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 17.1 min for minor isomer and 18.7 min for major isomer).

*4.2.2. N-(1-Phenylpentan-3-yl)pyridin-2-amine (**3ba**).* Isolated by thin-layer chromatography (hexane/AcOEt=3/1, R_f=0.6). The title compound was obtained as colourless oil (69%). ^{1}H NMR δ 8.06 (d, *J*=4.8 Hz, 1H), 7.40–7.35 (m, 1H), 7.28–7.25 (m, 2H), 7.19–7.15 (m, 3H), 6.54–6.51 (m, 1H), 6.28 (d, *J*=8.8 Hz, 1H), 4.39 (d, *J*=8.8 Hz, 1H), 3.66–3.59 (m, 1H), 2.77–2.63 (m, 2H), 1.95–1.86 (m, 1H), 1.80–1.71 (m, 1H), 1.70–1.61 (m, 1H), 1.58–1.48 (m, 1H), 0.94 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 158.9, 148.3, 142.2, 137.5, 128.5, 128.4, 125.8, 112.4, 106.4, 52.1, 36.4, 32.2, 27.7, 9.9. IR (neat) 3255, 2962, 1601, 1485, 769 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2$ (M^++H): 241.1705; found: 241.1696. $[\alpha]_D^{31}$=2.2 (*c* 0.81, $CHCl_3$, 83% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 1% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 20.2 min for major isomer and 22.3 min for minor isomer).

*4.2.3. N-(1-Phenylhexan-3-yl)pyridin-2-amine (**3ca**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.5). The title compound was obtained as colourless oil (58%). ^{1}H NMR δ 8.05 (d, *J*=4.8, 1.6 Hz, 1H), 7.39–7.34 (m, 1H), 7.28–7.24 (m, 2H), 7.18–7.14 (m, 3H), 6.51 (dd, *J*=6.4, 4.8 Hz, 1H), 6.26 (d, *J*=8.4 Hz, 1H), 4.35 (d, *J*=8.8 Hz, 1H), 3.73–3.65 (m, 1H), 2.77–2.63 (m, 2H), 1.95–1.86 (m, 1H), 1.80–1.71 (m, 1H), 1.63–1.54 (m, 1H), 1.52–1.33 (m, 3H), 0.91 (t, *J*=7.2 Hz, 3H); ^{13}C NMR δ 158.8, 148.3, 142.1, 137.4, 128.4, 128.3, 125.8, 112.3, 106.3, 50.8, 37.6, 37.1, 32.2, 19.1, 14.1. IR (neat) 3255, 2931, 1601, 1496, 1452, 1333, 1288, 769 cm^{-1}; HRMS(ESI) calcd for $C_{17}H_{23}N_2$ (M^++H): 255.1861; found: 255.1852. $[\alpha]_D^{32}$=3.1 (*c* 0.73, $CHCl_3$, 86% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6×250 mm, 254 nm UV detector, rt, eluent: 1% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 19.4 min for minor isomer and 21.0 min for major isomer).

*4.2.4. N-(1-Phenyloctan-3-yl)pyridin-2-amine (**3da**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.6). The title compound was obtained as pale yellow oil (60%). ^{1}H NMR δ 8.06 (d, *J*=5.2 Hz, 1H), 7.39–7.34 (m, 1H), 7.28–7.24 (m, 2H), 7.19–7.14 (m, 3H), 6.52 (t, *J*=6.0 Hz, 1H), 6.26 (d, *J*=8.4 Hz, 1H), 4.38 (d, *J*=9.6 Hz, 1H), 3.70–3.66 (m, 1H), 2.74–2.64 (m, 2H), 1.93–1.73 (m, 2H), 1.62–1.45 (m, 2H), 1.41–1.26 (m, 6H), 0.86 (t, *J*=6.0 Hz, 3H); ^{13}C NMR δ 157.4, 146.9, 140.8, 136.1, 127.1, 127.0, 124.4, 111.0, 104.9, 49.7, 35.7, 33.9, 30.9, 30.6, 24.1, 21.2, 12.7. IR (neat) 3255, 2929, 1604, 1496, 1454, 1333, 1153, 769, 700 cm^{-1}; HRMS(ESI) calcd for $C_{19}H_{27}N_2$ (M^++H): 283.2174; found: 283.2166. $[\alpha]^{33}_{435}$=−2.6 (*c* 0.58, $CHCl_3$, 73% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 14.6 min for minor isomer and 16.0 min for major isomer).

*4.2.5. N-(4-Phenylbutan-2-yl)quinolin-2-amine (**3ia**).* Isolated by thin-layer chromatography (hexane/AcOEt/Et_3N=6/1/1, R_f=0.6). The title compound was obtained as yellow oil (72%). ^{1}H NMR δ 7.79 (d, *J*=8.8 Hz, 1H), 7.65 (*J*=8.0 Hz, 1H), 7.56 (d, *J*=8.0 Hz, 1H), 7.53–7.49 (m, 1H), 7.29–7.24 (m, 2H), 7.21–7.18 (m, 4H), 6.54 (d, *J*=8.8 Hz, 1H), 4.60 (d, *J*=8.0 Hz, 1H), 4,17–4.11 (m, 1H), 2.75 (t, *J*=8.0 Hz, 2H), 1.97–1.82 (m, 2H), 1.29 (dd, *J*=6.4, 1.2 Hz, 3H); ^{13}C NMR δ 156.5, 148.2, 142.0, 137.3, 129.5, 128.4, 128.4, 127.4, 126.1, 125.8, 123.3, 121.9, 111.0, 46.5, 39.0, 32.5, 21.2. IR (neat) 3410, 2924, 1618, 1522, 1400, 1248, 1144, 818, 754, 700 cm^{-1}; HRMS(ESI) calcd for $C_{19}H_{21}N_2$ (M^++H): 277.1705; found: 277.1713. $[\alpha]_D^{30}$=34.4 (*c* 0.60, $CHCl_3$, 98% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 10% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 20.2 min for major isomer and 24.0 min for minor isomer).

*4.2.6. 3-Methyl-N-(4-phenylbutan-2-yl)pyridin-2-amine (**3ja**).* Isolated by thin-layer chromatography (hexane/AcOEt=3/1, R_f=0.6). The title compound was obtained as colourless oil (47%). ^{1}H NMR δ 8.01 (dd, *J*=4.8, 0.8 Hz, 1H), 7.28–7.24 (m, 2H), 7.19–7.15 (m, 4H),

6.48 (dd, *J*=7.2, 5.2 Hz, 1H), 4.37–4.28 (m, 1H), 3.87 (d, *J*=8.0 Hz, 1H), 2.73 (dt, *J*=7.6, 2.0 Hz, 2H), 2.00 (s, 3H), 1.93–1.86 (m, 2H), 1.28 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 156.4, 145.5, 142.4, 136.7, 128.3, 128.2, 125.7, 116.2, 112.1, 64.2, 39.1, 32.6, 21.4, 17.0. IR (neat) 3414, 2964, 2927, 1601, 1497, 1452, 1145, 773, 700 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2$ (M^++H): 241.1705; found: 241.1716. $[\alpha]_D^{34}$=11.6 (*c* 0.54, $CHCl_3$, 55% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 6.7 min for major isomer and 7.5 min for minor isomer).

*4.2.7. 5-Methyl-N-(4-phenylbutan-2-yl)pyridin-2-amine (**3ka**).* Isolated by thin-layer chromatography (hexane/AcOEt=4/1, R_f=0.5). The title compound was obtained as (pale) yellow oil (76%). ^{1}H NMR δ 7.89 (s, 1H), 7.28–7.16 (m, 6H), 6.22 (d, *J*=8.0 Hz, 1H), 4.22 (d, *J*=8.4 Hz, 1H), 3.76–3.69 (m, 1H), 2.74–2.69 (m, 2H), 2.16 (s, 3H), 1.88–1.77 (m, 2H), 1.22 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 156.6, 147.8, 142.0, 138.4, 128.4, 128.3, 125.8, 121.2, 106.3, 46.9, 39.0, 32.4, 21.0, 17.3. IR (neat) 3408, 2920, 1614, 1500, 1394, 1155, 814, 746, 698 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2$ (M^++H): 241.1705; found: 241.1708. $[\alpha]_D^{31}$=−9.6 (*c* 0.82, $CHCl_3$, 65% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak AD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 21.4 min for minor isomer and 24.8 min for major isomer).

*4.2.8. 6-Methyl-N-(4-phenylbutan-2-yl)pyridin-2-amine (**3la**).* Isolated by thin-layer chromatography (hexane/AcOEt=3/1, R_f=0.6). The title compound was obtained as colourless oil (47%). ^{1}H NMR δ 7.33–7.26 (m, 3H), 7.20–7.16 (m, 3H), 6.42 (d, *J*=6.8 Hz, 1H), 6.09 (d, *J*=8.8 Hz, 1H), 4.42 (d, *J*=8.4 Hz, 1H), 3.69–3.59 (m, 1H), 2.73 (dt, *J*=8.0, 2.4 Hz, 2H), 2.36 (s, 3H), 1.91–1.79 (m, 2H), 1.23 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 157.9, 157.1, 141.9, 137.9, 128.4, 128.3, 125.8, 111.9, 102.5, 46.8, 38.9, 32.4, 24.3, 20.9. IR (neat) 3404, 3280, 2924, 1597, 1496, 1415, 1331, 1155, 777, 700 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2$ (M^++H): 241.1705; found: 241.1716. $[\alpha]_D^{33}$=−33.6 (*c* 0.33, $CHCl_3$, 77% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 6.4 min for major isomer and 7.2 min for minor isomer.

*4.2.9. N-(4-(4-Methoxyphenyl)butan-2-yl)pyridin-2-amine (**3ab**).* Isolated by thin-layer chromatography (hexane/AcOEt=1/1, R_f=0.5). The title compound was obtained as white solid (76%). Mp: 135 °C. ^{1}H NMR δ 8.07 (dd, *J*=5.0, 1.2 Hz, 1H), 7.44–7.32 (m, 1H), 7.08 (d, *J*=8.6 Hz, 2H), 6.82 (d, *J*=8.6 Hz, 2H), 6.53 (dd, *J*=6.8, 5.0 Hz, 1H), 6.28 (d, *J*=8.4 Hz, 1H), 4.37 (d, *J*=8.4 Hz, 1H), 3.85–3.68 (m, 4H), 2.73–2.59 (m, 2H), 1.88–1.72 (m, 2H), 1.23 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 158.4, 157.8, 148.4, 137.4, 134.0, 129.3, 113.8, 112.5, 106.6, 55.2, 46.6, 39.1, 31.4, 20.9. IR (CH_2Cl_2) 3418, 2965, 1601, 1512, 1270, 1036, 756, 698 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2O$ (M^++H): 257.1654; found: 257.1641. $[\alpha]_D^{27}$=−20.4 (*c* 0.83, $CHCl_3$, 87% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 2% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 22.1 min for major isomer and 25.0 min for minor isomer).

*4.2.10. N-(Undecan-2-yl)pyridin-2-amine (**3ac**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.4). The title compound was obtained as pale yellow oil (27%). ^{1}H NMR δ 8.06–8.05 (m, 1H), 7.41–7.37 (m, 1H), 6.52 (dd, *J*=6.4, 5.2 Hz, 1H), 6.34 (d, *J*=8.8 Hz, 1H), 4.32 (d, *J*=7.6 Hz, 1H), 3.75–3.68 (m, 1H), 1.57–1.25 (m, 16H), 1.19 (d, *J*=6.8 Hz, 3H), 0.88 (*J*=7.0 Hz, 3H); ^{13}C NMR δ 158.4, 148.3, 137.3, 112.3, 106.5, 47.2, 37.2, 31.9, 29.6, 29.6, 29.5, 29.3, 26.0, 22.7, 20.9, 14.1. IR (neat) 3263, 2925, 1603, 1485, 1446, 1331, 1151, 769 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{29}N_2$ (M^++H): 249.2331; found: 249.2322. $[\alpha]_D^{30}$=−8.3 (*c* 0.26, $CHCl_3$, 78% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 11.4 min for major isomer and 18.1 min for minor isomer).

*4.2.11. N-(5-Phenylpentan-2-yl)pyridin-2-amine (**3ad**).* Isolated by thin-layer chromatography (hexane/AcOEt=1/1, R_f=0.6). The title compound was obtained as colourless oil (57%). ^{1}H NMR δ 8.06 (d, *J*=4.8 Hz, 1H), 7.40–7.36 (m, 1H), 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 6.52 (t, *J*=6.0 Hz, 1H), 6.31 (d, *J*=8.2 Hz, 1H), 4.28 (d, *J*=8.2 Hz, 1H), 3.81–3.75 (m, 1H), 2.63 (t, *J*=7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.65–1.48 (m, 2H), 1.19 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 158.4, 148.4, 142.3, 137.4, 128.4, 128.3, 125.8, 112.4, 106.7, 46.9, 36.7, 35.8, 27.8, 20.9. IR (neat) 3268, 2963, 1603, 1496, 1447, 1330, 1285, 1152, 770, 699 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{21}N_2$ (M^++H): 241.1705; found: 241.1706. $[\alpha]_D^{30}$=−9.5 (*c* 0.35, $CHCl_3$, 61% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 2% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 17.2 min for major isomer and 18.6 min for minor isomer).

*4.2.12. N-(6-Phenylhex-5-en-2-yl)pyridin-2-amine (**3ae**).* Isolated by thin-layer chromatography (hexane/AcOEt=1/1, R_f=0.6). The title compound was obtained as colourless oil (84%, *E*/*Z*>20:1). ^{1}H NMR δ 8.07 (d, *J*=4.8 Hz, 1H), 7.41–7.37 (m, 1H), 7.33–7.25 (m, 4H), 7.21–7.17 (m, 1H), 6.55–6.52 (m, 1H), 6.40–6.33 (m, 2H), 6.25–6.18 (m, 1H), 4.35 (d, *J*=8.8 Hz, 1H), 3.88–3.78 (m, 1H), 2.35–2.29 (m, 2H), 1.77–1.63 (m, 2H), 1.24 (d, *J*=6.4 Hz, 3H); ^{13}C NMR δ 158.4, 148.4, 137.7, 137.4, 130.3, 130.1, 128.5, 126.9, 126.0, 112.5, 106.7, 46.6, 36.7, 29.5, 20.9. IR (neat) 3257, 2964, 1601, 1572, 1495, 1446, 769 cm^{-1}; HRMS(ESI) calcd for $C_{17}H_{21}N_2$ (M^++H): 253.1705; found: 253.1694. $[\alpha]_D^{25}$=−28.1 (*c* 1.08, $CHCl_3$, 87% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 31.1 min for major isomer and 37.8 min for minor isomer).

*4.2.13. Ethyl 4-(pyridin-2-ylamino)pentanoate (**3af**).* Isolated by thin-layer chromatography (hexane/AcOEt=1.5/1, R_f=0.6). The title compound was obtained as pale yellow oil (75%). ^{1}H NMR δ 8.05 (d, *J*=5.0 Hz, 1H), 7.40–7.36 (m, 1H), 6.53 (dd, *J*=5.0, 6.4 Hz, 1H), 6.36 (d, *J*=8.8 Hz, 1H), 4.31 (d, *J*=8.0 Hz, 1H), 4.11 (q, *J*=7.2 Hz, 2H), 3.99–3.84 (m, 1H), 2.41 (t, *J*=7.2 Hz, 2H), 1.89–1.84 (m, 2H), 1.22 (t, *J*=7.2 Hz, 3H), 1.22 (d, *J*=7.2 Hz, 3H); ^{13}C NMR δ 173.7, 158.2, 148.2, 137.3, 112.6, 107.0, 60.4, 46.6, 32.0, 31.1, 21.0, 14.2. IR (neat) 3388, 2976, 1731, 1602, 1485, 1448, 1228, 1180, 771 cm^{-1}; HRMS(ESI) calcd for $C_{12}H_{19}N_2O_2$ (M^++H): 223.1447; found: 223.1461. $[\alpha]_D^{27}$=−11.3 (*c* 0.22, $CHCl_3$, 99% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 10% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 13.3 min for major isomer and 15.0 min for minor isomer).

*4.2.14. tert-Butyl 4-(pyridin-2-ylamino)pentanoate (**3ag**).* Isolated by thin-layer chromatography (hexane/AcOEt=2/1, R_f=0.6). The title compound was obtained as pale yellow oil (52%). ^{1}H NMR δ 8.06–8.05 (m, 1H), 7.40–7.36 (m, 1H), 6.53–6.51 (m, 1H), 6.35 (d, *J*=8.4 Hz, 1H), 4.33 (d, *J*=8.4 Hz, 1H), 3.88–3.81 (m, 1H), 2.33 (t, *J*=7.2 Hz, 2H), 1.81 (d, *J*=7.2 Hz, 2H), 1.43 (s, 9H), 1.21 (d, *J*=6.8 Hz, 3H); ^{13}C NMR δ 173.1, 158.3, 148.2, 137.3, 112.5, 106.9, 80.3, 46.7, 32.3, 32.0, 28.1, 21.1. IR (neat) 3392, 2976, 1726, 1601, 1485, 1448, 1255, 1153, 847, 771 cm^{-1}; HRMS(ESI) calcd for $C_{14}H_{23}N_2O_2$ (M^++H): 251.1760; found: 251.1763. $[\alpha]_D^{28}$=−12.6 (*c* 0.13, $CHCl_3$, 89% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent:

5% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 7.0 min for major isomer and 9.8 min for minor isomer).

*4.2.15. N-(4-(Trimethylsilyl)butan-2-yl)pyridin-2-amine (**3ah**).* Isolated by thin-layer chromatography (hexane/AcOEt=7/1, R_f=0.4). The title compound was obtained as yellow oil (71%). ^{1}H NMR δ 8.08–8.06 (m, 1H), 7.44–7.38 (m, 1H), 6.56–6.52 (m, 1H), 6.36 (d, J=8.4 Hz, 1H), 4.38 (d, J=8.0 Hz, 1H), 3.71–3.61 (m, 1H), 1.59–1.44 (m, 2H), 1.21 (d, J=6.4 Hz, 3H), 0.65–0.49 (m, 2H), 0.00 (s, 9H); ^{13}C NMR δ 158.4, 148.3, 137.4, 112.3, 106.4, 49.6, 31.1, 20.3, 12.5, -1.8. IR (neat) 3265, 2954, 1603, 1485, 1331, 1248, 1186, 862, 769 cm^{-1}; HRMS(ESI) calcd for $C_{12}H_{23}N_2Si$ (M^++H): 223.1631; found: 223.1623. $[\alpha]_D^{29}$=4.2 (*c* 0.45, $CHCl_3$, 76% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 1% isopropanol in hexane, flow rate: 3.0 mL/min, retention time: 31.5 min for minor isomer and 34.9 min for major isomer).

*4.2.16. N-(4-(Triethylsilyl)butan-2-yl)pyridin-2-amine (**3ai**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.6). The title compound was obtained as pale yellow oil (87%). ^{1}H NMR δ 8.06–8.05 (m, 1H), 7.41–7.37 (m, 1H), 6.53–6.50 (m,1H), 6.34 (d, J=8.4 Hz, 1H), 4.36 (d, J=7.0 Hz, 1H), 3.67–3.60 (m, 1H), 1.56–1.44 (m, 2H), 1.19 (d, J=5.9 Hz, 3H), 0.911 (t, J=8.0 Hz, 9H), 0.53–0.47 (m, 8H); ^{13}C NMR δ 158.1, 148.3, 137.3, 112.3, 106.5, 49.8, 30.9, 25.3, 7.4, 7.0, 3.1. IR (neat) 3259, 2952, 1601, 1485, 1448, 1238, 1186, 1014, 733 cm^{-1}; HRMS(ESI) calcd for $C_{15}H_{29}N_2Si$ (M^++H): 265.2100; found: 265.2088. $[\alpha]_D^{27}$=3.1 (*c* 0.83, $CHCl_3$, 69% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 4.3 min for minor isomer and 5.2 min for major isomer).

*4.2.17. N-(4-(Triphenylsilyl)butan-2-yl)pyridin-2-amine (**3aj**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.4). The title compound was obtained as pale yellow oil (81%). ^{1}H NMR δ 8.05–8.03 (m, 1H), 7.50–7.48 (m, 6H), 7.41–7.32 (m, 10H), 6.53–6.50 (m, 1H), 6.26 (d, J=8.5 Hz, 1H), 4.32 (d, J=8.5 Hz, 1H), 3.76–3.69 (m, 1H), 1.73–1.66 (m, 2H), 1.52–1.36 (m, 2H), 1.18 (d, J=6.3 Hz, 3H); ^{13}C NMR δ 158.3, 148.3, 137.3, 135.6, 134.8, 129.4, 127.9, 112.4, 106.7, 49.5, 30.7, 20.3, 9.0. IR (neat) 3338, 2968, 1603, 1485, 1429, 1290, 1111, 953, 702, 513 cm^{-1}; HRMS(ESI) calcd for $C_{27}H_{29}N_2Si$ (M^++H): 409.2100; found: 409.2106. $[\alpha]_D^{28}$=9.0 (*c* 1.01, $CHCl_3$, 72% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 10% isopropanol in hexane, flow rate: 1.0 mL/min, retention time: 5.7 min for minor isomer and 7.1 min for major isomer).

*4.2.18. N-(5-(Trimethylsilyl)pentan-2-yl)pyridin-2-amine (**3ak**).* Isolated by thin-layer chromatography (hexane/AcOEt=5/1, R_f=0.5). The title compound was obtained as pale yellow oil (33%). ^{1}H NMR δ 8.10–8.09 (m, 1H), 7.45–7.41, (m, 1H), 6.57–6.54 (m, 1H), 6.38 (d, J=8.0 Hz, 1H), 4.36 (d, J=7.6 Hz, 1H), 3.78–3.75 (m, 1H), 1.62–1.40 (m, 4H), 1.22 (d, J=6.4 Hz, 3H), 0.54 (t, J=8.4 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR δ 158.4, 148.3, 137.3, 112.3, 106.5, 46.9, 41.2, 20.8, 20.5, 16.6, −1.7. IR (neat) 3267, 2954, 1603, 1485, 1248, 837, 769 cm^{-1}; HRMS(ESI) calcd for $C_{13}H_{25}N_2Si$ (M^++H): 237.1787; found: 237.1781. $[\alpha]_D^{28}$=−27.1 (*c* 0.23, $CHCl_3$, 73% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 10.1 min for major isomer and 11.5 min for minor isomer).

*4.2.19. N-(5-(Triphenylsilyl)pentan-2-yl)pyridin-2-amine (**3al**).* Isolated by thin-layer chromatography (hexane/AcOEt=4/1, R_f=0.3). The title compound was obtained as colourless oil (88%). ^{1}H NMR δ 8.05 (d, J=5.2, 1H), 7.50–7.48 (m, 6H), 7.40–7.23 (m, 10H), 6.52–6.49 (m, 1H), 6.28 (d, J=7.6 Hz, 1H), 4.22 (d, J=7.2 Hz, 1H), 3.81–3.75 (m, 1H), 1.63–1.52 (m, 4H), 1.43–1.33 (m, 2H), 1.12 (dd, J=6.4, 1.2 Hz, 3H); ^{13}C NMR δ 158.3, 148.2, 137.2, 135.6, 135.0, 129.3, 127.8, 112.3, 106.7, 46.3, 41.1, 20.9, 20.5, 13.0. IR (neat) 3269, 3068, 2927, 1601, 1502, 1485, 1427, 1288, 1111, 771, 702, 515 cm^{-1}; HRMS(ESI) calcd for $C_{28}H_{31}N_2Si$ (M^++H): 423.2257; found: 423.2263. $[\alpha]_D^{30}$=−9.9 (*c* 1.69, $CHCl_3$, 87% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 5% isopropanol in hexane, flow rate: 0.5 mL/min, retention time: 32.3 min for minor isomer and 38.0 min for major isomer).

4.3. Typical experimental procedure for 5

$[Ir(cod)_2]BF_4$ (0.01 mmol) and *rac*-BINAP (0.01 mmol) were placed in a Schlenk tube, which was then evacuated and back-filled argon (×3). To the reaction vessel were added 2-alkylaminopyridine **1** (0.10 mmol), alkyne **4** (0.20 mmol), TfOH (0.01 mmol) and PhCl (0.2 mL), unless otherwise noted. The sealed reaction vessel was immersed in a pre-heated oil bath. After the reaction was complete, the mixture of the reaction was cooled to room temperature and NEt_3 (0.1 mmol) were added, then the solvent was removed under reduced pressure, and the crude products were purified by thin-layer chromatography to give desired product **5**.

*4.3.1. (E)-N-(2,3-Diphenylprop-2-enyl)pyridin-2-amine (**5a**).* Isolated by thin-layer chromatography (hexane/AcOEt=4/1, R_f=0.4). The title compound was obtained as pale yellow solid (82%). Mp: 118–120 °C; ^{1}H NMR δ 8.10 (dd, J=5.2, 1.2 Hz, 1H), 7.45–7.40 (m, 1H), 7.34–7.28 (m, 3H), 7.23–7.21 (m, 2H), 7.10–7.07 (m, 3H), 6.96–6.94 (m, 2H), 6.66 (s, 1H), 6.59 (ddd, J=7.2, 4.8, 0.8 Hz, 1H), 6.43 (d, J=8.4 Hz, 1H), 4.85 (dd, J=6.0, 5.6 Hz, 1H), 4.27 (dd, J=6.0, 1.2 Hz, 2H); ^{13}C NMR δ 158.5, 148.1, 139.2, 138.9, 137.6, 136.5, 129.2, 128.8, 128.6, 127.9, 127.5, 127.0, 126.7, 113.2, 106.6, 50.2. IR (CH_2Cl_2) 3423, 3255, 3022, 1601, 1493, 1323, 1290, 1153, 771, 698 cm^{-1}; HRMS(ESI) calcd for $C_{20}H_{19}N_2$ (M^++H): 287.1548; found: 287.1541.

*4.3.2. (E)-N-(2-Butylhept-2-enyl)pyridin-2-amine (**5b**).* Isolated by thin-layer chromatography (hexane/AcOEt=6/1, R_f=0.6). The title compound was obtained as brown oil (42%). ^{1}H NMR δ 8.06 (dd, J=4.8, 0.8 Hz, 1H), 7.43–7.39 (m, 1H), 6.55 (ddd, J=7.2, 5.2, 0.8 Hz, 1H), 6.36 (d, J=8.4 Hz, 1H), 5.39 (t, J=7.2 Hz, 1H), 4.70 (s, 1H), 3.79 (d, J=5.2 Hz, 2H), 2.09–2.01 (m, 4H), 1.42–1.25 (m, 8H), 0.93–0.88 (m, 6H); ^{13}C NMR δ 159.0, 147.9, 137.5, 136.0, 127.0, 112.7, 106.4, 48.0, 32.0, 30.8, 28.6, 27.3, 22.8, 22.4, 14.0, 12.2. IR (neat) 3257, 2956, 2858, 1603, 1512, 1458, 1325, 1290, 769, 733 cm^{-1}; HRMS(ESI) calcd for $C_{16}H_{27}N_2$ (M^++H): 247.2174; found: 247.2185.

*4.3.3. (E)-N-(3-Butyloct-3-en-2-yl)pyridin-2-amine (**5c**).* Isolated by thin-layer chromatography (hexane/AcOEt=7/1, R_f=0.4). The title compound was obtained as brown oil (32%). ^{1}H NMR δ 8.05–8.04 (m, 1H), 7.41–7.36 (m, 1H), 6.53 (dd, J=7.2, 5.2 Hz, 1H), 6.30 (d, J=8.8 Hz, 1H), 5.39 (dd, J=7.2, 6.8 Hz, 1H), 4.63 (d, J=7.2 Hz, 1H), 4.05–3.98 (m, 1H), 2.05–1.99 (m, 4H), 1.38–1.25 (m, 11H), 0.91–0.86 (m, 6H); ^{13}C NMR δ 158.4, 148.1, 140.5, 137.3, 125.6, 112.5, 106.4, 53.0, 32.0, 31.7, 28.1, 27.3, 23.2, 22.3, 21.4, 14.0, 13.9. IR (neat) 3257, 2956, 2858, 1601, 1506, 1444, 1153, 769 cm^{-1}; HRMS(ESI) calcd for $C_{17}H_{29}N_2$ (M^++H): 261.2331; found: 261.2334. $[\alpha]_D^{32}$=18.8 (*c* 0.22, $CHCl_3$, 89% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralcel OD: 4.6×250 mm, 254 nm UV detector, rt, eluent: 10% isopropanol in hexane, flow rate: 1.0 mL/

min, retention time: 3.4 min for major isomer and 4.1 min for minor isomer).

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