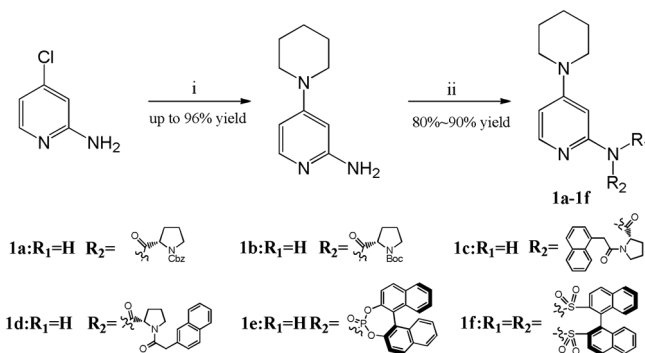


SIMPLE AND EFFECTIVE SYNTHETIC APPROACH TO CHIRAL 2-AMINO-4-PIPERIDINYL PYRIDINE DERIVATIVES

Hua Tian, Qing-Wen Liu, Hao Xu, Wen-Bo Huang, Jian Lin, and Suo-Qin Zhang

Department of Chemistry, Jilin University, Changchun, China

GRAPHICAL ABSTRACT



Abstract A facile way has been developed to provide a series of novel chiral *N*-(4-(piperidin-1-yl)pyridin-2-yl)amide derivatives as potential stereoselective catalysts. The key intermediate, 2-amino-4-piperidinyl pyridine, was obtained by nucleophilic substitution of 2-amino-4-chloropyridine with piperidine in good yields (up to 96%). The total control of enantioselectivity was obtained for the synthesis of *L*-proline and (*R*)-1,1'-bi(2-naphthol) derivatives.

Keywords 2-Amino-4-piperidinyl pyridine; chiral catalysts; DMAP; PPY

INTRODUCTION

In past decades, 4-dimethylaminopyridine (DMAP) and 4-pyrrolidinopyridine (PPY) have been extensively used as potential nucleophilic catalysts in acylation reactions and related transformations.^[1–6] Because chiral DMAP and PPY derivatives have been successfully employed as chiral nucleophilic catalysts in a wide range of asymmetric synthetic processes,^[7–14] various chiral 4-(*N,N*-disubstituted-amino) pyridine derivatives have been described over the years.^[15–20] Such compounds

Received December 16, 2010.

Address correspondence to Suo-Qin Zhang, Department of Chemistry, Jilin University, Changchun 130012, China. E-mail: suoqin@jlu.edu.cn

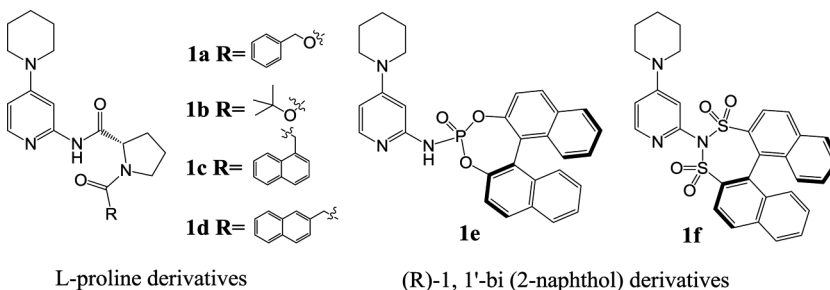


Figure 1. Structure of compounds **1a–1f**.

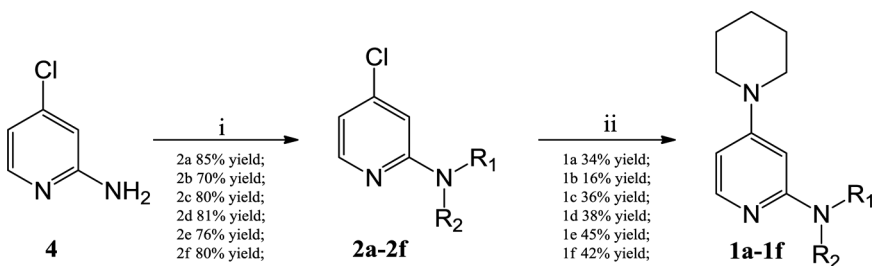
require the presence of a stereogenic center to induce stereoselectivity during the catalytic process.^[21–24] However, preparation of these new catalysts tends to involve complex routes of synthesis and does not generally allow facile structural modifications.

This article describes a simple and effective synthetic approach to chiral 2-amino-4-piperidinyl pyridine derivatives (Fig. 1).

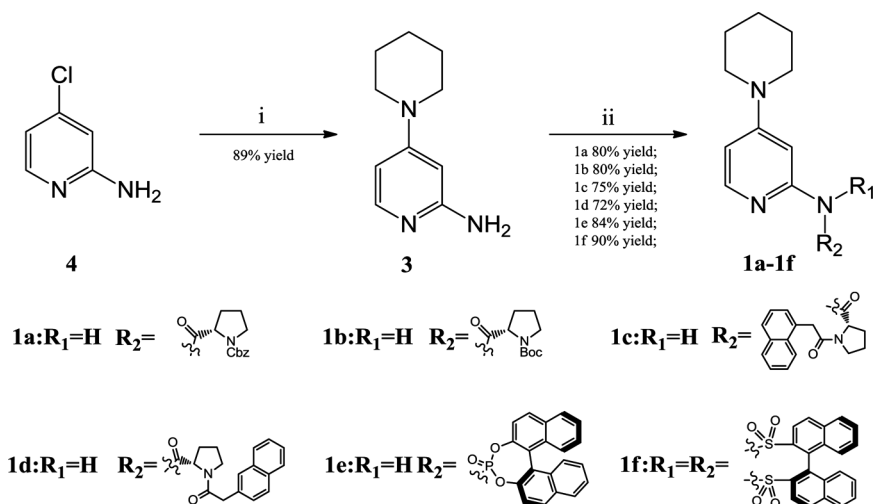
RESULTS AND DISCUSSION

Our approach is based on the design of a convenient synthetic way to chiral 2-amino-4-piperidinyl pyridine derivatives, which will allow rapid optimization. Furthermore, the stereogenic centers are positioned distant from the catalytic site (the nitrogen atom of the pyridinyl group) to avoid the reactivity problem. The general structure for this new family of N-(4-(piperidin-1-yl) pyridin-2-yl) amide derivatives **1** is represented in Scheme 1.

The synthesis of compound **4** (Scheme 1) has already been described in the literature.^[25] Initially, a synthetic route reported by Badawneh et al.^[26] was applied to synthesize target compounds (Scheme 1). Intermediates **2** were prepared through the acylation reaction of 2-amino-4-chloropyridine with corresponding acid chloride. Subsequent nucleophilic substitution of the 4-chlorosubstituent with excess piperidine afforded the target compounds **1**. Because of poor yields (total yield no more than 35%), an alternative strategy was applied to synthesize target molecules, which is shown in Scheme 2. Intermediate 2-amino-4-piperidinyl pyridine **3** was synthesized



Scheme 1. First synthetic route of compounds **1a–1f**. Reagents and conditions: (i) N-protected L-prolyl chloride/(R)-1,1'-binaphthyl-2,2'-diylphosphorochloridate/(R)-[1,1'-binaphthalene]-2,2-disulfonyl dichloride, N(Et)₃, DCM, 0–5 °C, rt, 6 h; (ii) piperidine, 160 °C, 24 h.



Scheme 2. Second synthetic route of compounds **1a–1f**. Reagents and conditions: (i) piperidine, autoclave, 250 °C, 48 h; (ii) N-protected L-prolyl chloride (R)-1,1'-binaphthyl-2,2'-diylphosphorochloridate/(R)-[1,1'-binaphthalene]-2,2-disulfonyl dichloride, N(Et)₃, DCM, 0–5 °C, rt, 15 h.

by nucleophilic substitution of 2-amino-4-chloropyridine with piperidine as structure backbone. Then, the desired compounds were obtained with excellent yield (total yield up to 80%).

Apparently, the synthesis of compound **3** has become a key point in the whole synthetic route **2**. In the structure of compound **4**, an amino group is substituted at C-2 position of pyridine, which made the nucleophilic substitution at C-4 position much more difficult. Therefore, some optimization work has been done, which is summarized in Table 1.

As shown in Table 1, when the mixture of 2-amino-4-chloropyridine and piperidine was heated up to 105 °C for 24 h in the presence of a series of bases (entries 1–3), the reaction did not proceed. However, when the reaction mixture was taken into an autoclave and heated up to 200 °C for 24 h without any base, the product was obtained, in a yield of 43%. Through optimizing of process conditions, such as temperature and reaction time, the desired compound **3** was obtained, which

Table 1. Reaction of 2-amino-4-chloropyridine with piperidine

Entry	Base	Temp. (°C)	Time (h)	Yield (%)
1	K ₂ CO ₃	105	24	<1
2	NaOH	105	24	<1
3	Cs ₂ CO ₃	105	24	<1
4	None	200	24	43 ^{a,b}
5	None	250	24	60 ^{a,b}
6	None	250	48	89 ^{a,b}
7	None	300	48	86 ^{a,b}

^aIsolated yield after silica-gel column chromatography.

^bReacted in an autoclave.

was suitable for use in the next step without any further purification in a greatly increased yield of 96% (entry 6).

Then, compound **3** was coupled with corresponding acid chloride to yield chiral 2-amino-4-piperidinyl pyridine derivatives **1a–1f** in an enantiomerically pure form (ee = 100%). Our first attempt was to obtain N-protected derivatives of L-proline amide **1a**, **1b**, **1c**, and **1d**. The synthesis of **1a** was carried out as outlined in Scheme 2. Treatment of N-benzyloxycarbonyl-L-proline with thionyl chloride furnished the corresponding acid chloride, which was then coupled with **3** to afford amide **1a** in yields of 80%. In a similar fashion, **1b**, **1c**, and **1d** were obtained in yields of 80%, 75%, and 72% respectively. With a view toward maximizing both catalyst rigidity and potential for π – π interaction, (R)-1,1'-bi(2-naphthol)-derived structures (**1e** and **1f**) were synthesized in yields of 84% and 90% respectively.

CONCLUSION

In conclusion, the key intermediate 2-amino-4-piperidinyl pyridine **3** has been successfully synthesized with excellent yield. A simple and effective synthetic route for the preparation of a family of novel chiral N-(4-(piperidin-1-yl) pyridin-2-yl) amide derivatives **1** has been developed. These six compounds are closely related to DMAP but contain a stereogenic center. An investigation of the catalytic properties of these interesting molecules will be reported in due course.

EXPERIMENTAL

Infrared (IR; KBr pellets) spectra were recorded in the 350–4000 cm^{-1} range on a Perkin-Elmer spectrophotometer. Elemental analyses (C, H, and N) were performed on a Perkin-Elmer 2400 CHN elemental analyzer. All ^1H NMR spectra (300 MHz) were reported as chemical shifts downfield with tetramethylsilane (TMS) as internal standard (δ scale) and CDCl_3 as the solvent. All ^{13}C NMR spectra (75 MHz) were determined with complete proton decoupling and reported in δ . The enantiomeric excess was determined by chiral high-performance liquid chromatography (HPLC) with Daicel Chiralpak AD-H (4.6 mm \times 250 mm) column. All reagents and solvents for the reactions were of analytical grade and were dried and distilled if necessary.

2-Amino-4-piperidinyl Pyridine (**3**)

An autoclave was charged with 2-amino-4-chloropyridine (2.7 g, 21.0 mmol) and piperidine (30.0 mL, 0.28 mol). The reaction mixture was placed in a 250 °C preheated oven for 48 h, and then cooled to ambient temperature. The residue piperidine was removed by rotary evaporation and gentle heating. Purification of the residue by flash column chromatography with DCM/MeOH (10:1) gave 3.3 g (89%) 2-amino-4-piperidinyl pyridine as a yellow oil. IR (KBr): ν 3450, 3171, 3154 cm^{-1} . ^1H NMR (300 MHz, CDCl_3), δ : 7.56 (d, J = 9.0 Hz, 1H), 6.20–6.17 (m, 1H), 5.95–5.87 (m, 1H), 5.49 (br s, 2H), 3.36–3.31 (m, 4H), 1.65–1.59 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3), δ : 156.6, 156.5, 140.0, 100.7, 89.9, 47.3, 25.4, 24.0. (EI) m/z 178 (relintensity) ($\text{M}^+ + 1$) Analysis calculated for $\text{C}_{10}\text{H}_{15}\text{N}_3$: C, 67.76, H, 8.53; N, 23.71. Found: C, 67.80; H, 8.54; N, 23.69.

General Procedure for Preparing of Compounds 1a–1d

A mixture of N-protected L-proline (6.0 mmol) and thionyl chloride (10 mL) was refluxed for 3 h. Thionyl chloride was removed by rotary evaporation and gentle heating. The resulting residue was taken into dichloromethane (DCM) (5 mL) and then cooled to 0 °C, and a solution of 2-amino-4-piperidinylpyridine (5.0 mmol) and triethylamine (TEA) (6.0 mmol) in dichloromethane was added dropwise over 30 min. The solution was allowed to warm to room temperature and stirred for an additional 15 h. The organic layer was washed with brine (2 × 20 mL) and dried over anhydrous Na₂SO₄. After the removal of solvent under reduced pressure, the residue was purified through column chromatography on silica gel (DCM/MeOH 10:1) to give **1a–1d** as a white solid.

(S)-Benzyl-2-((4-(piperidin-1-yl)pyridin-2-yl)carbamoyl)pyrrolidine-1-carboxylate (1a)

White solid, mp. 124.2–126.0 °C. $[\alpha]_{\text{D}}^{20} = -109$ (c = 0.5, CHCl₃). IR (KBr): ν 3276, 2936, 2855, 1694 cm⁻¹. ¹H NMR (300 MHz, CDCl₃), δ : 9.02 (br s, 1H), 7.92 (d, *J* = 6.0 Hz, 1H), 7.72 (s, 1H), 7.37–7.19 (m, 5H), 6.43 (d, *J* = 3.0 Hz, 1H), 5.27–5.09 (m, 2H), 4.50–4.33 (m, 1H), 3.57–3.43 (m, 2H), 3.39–3.34 (m, 4H), 2.36–2.17 (m, 1H), 2.07–1.89 (m, 3H), 1.68–1.59 (m, 6H). ¹³C NMR (75 MHz, CDCl₃), δ : 170.6, 156.5, 152.3, 152.2, 147.7, 136.2, 128.2, 128.0, 127.8, 104.9, 97.6, 67.2, 61.3, 47.2, 46.9, 29.0, 25.0, 24.4, 24.2. (EI) *m/z* 409 (rel. intensity) (*M*⁺ + 1). Analysis calculated for C₂₃H₂₈N₄O₃: C, 67.63; H, 6.91; N, 13.72; O, 11.75. Found: C, 67.70; H, 6.80; N, 13.69; O, 11.80.

(S)-tert-Butyl-2-((4-(piperidin-1-yl)pyridin-2-yl)carbamoyl)-pyrrolidine-1-carboxylate (1b)

White solid, mp 45–47 °C. $[\alpha]_{\text{D}}^{20} = -62$ (c = 0.5, CHCl₃). IR (KBr): ν 3252, 2940, 2864, 1699, 1300 cm⁻¹. ¹H NMR (300 MHz, CDCl₃), δ : 9.06 (br s, 1H), 7.89 (d, *J* = 6.0 Hz, 1H), 7.75 (d, *J* = 3.0 Hz, 1H), 6.43–6.41 (m, 1H), 4.46–4.22 (m, 1H), 3.53–3.36 (m, 6H), 2.25–2.11 (m, 1H), 1.96–1.86 (m, 3H), 1.68–1.60 (m, 6H), 1.45 (s, 9H). ¹³C NMR (75 MHz, CDCl₃), δ : 170.1, 156.3, 153.6, 152.2, 147.5, 104.6, 97.0, 80.0, 61.3, 56.5, 47.0, 29.4, 28.1, 24.8, 24.2, 24.0. (EI) *m/z* 375 (rel. intensity) (*M*⁺ + 1). Analysis calculated for C₂₀H₃₀N₄O₃: C, 64.15; H, 8.07; N, 14.96; O, 12.82. Found: C, 64.23; H, 8.00; N, 14.69; O, 12.80.

(S)-1-(2-(Naphthalen-1-yl)acetyl)-N-(4-(piperidin-1-yl)pyridin-2-yl)pyrrolidine-2-carboxamide (1c)

White solid, mp 169.7–171.0 °C. $[\alpha]_{\text{D}}^{20} = -82$ (c = 0.5, CHCl₃). IR (KBr): ν 3202, 2938, 2879, 1697, 1656, 783 cm⁻¹. ¹H NMR (300 MHz, CDCl₃), δ : 9.34 (br s, 1H), 8.02–7.99 (m, 1H), 7.92 (d, *J* = 6.0 Hz, 1H), 7.87–7.83 (m, 1H), 7.78–7.75 (m, 1H), 7.67 (d, *J* = 3.0 Hz, 1H), 7.52–7.47 (m, 2H), 7.41 (d, *J* = 3.0 Hz, 1H), 7.39 (s, 1H), 6.42–6.39 (m, 1H), 4.76–4.73 (m, 1H), 4.17 (d, *J* = 1.5 Hz, 2H), 3.53–3.48 (m, 1H), 3.40–3.30 (m, 5H), 2.37–2.31 (m, 1H), 2.09–1.92 (m, 3H), 1.68–1.60 (m, 6H).

^{13}C NMR (75 MHz, CDCl_3), δ : 170.9, 170.2, 156.5, 152.4, 147.7, 133.7, 132.1, 130.6, 128.5, 127.6, 126.7, 126.2, 125.6, 125.4, 123.6, 104.8, 97.7, 61.1, 47.7, 47.3, 39.5, 28.1, 25.1, 24.9, 24.2. (EI) m/z 443 (rel. intensity) ($\text{M}^+ + 1$). Analysis calculated for $\text{C}_{27}\text{H}_{30}\text{N}_4\text{O}_2$: C, 73.28; H, 6.83; N, 12.66; O, 7.23. Found: C, 72.3; H, 6.80; N, 12.69; O, 7.25.

(S)-1-(2-(Naphthalen-2-yl)acetyl)-N-(4-(piperidin-1-yl)pyridin-2-yl)pyrrolidine-2-carboxamide (1d)

White solid, mp 86–88 °C. $[\alpha]_{\text{D}}^{20} = -122$ ($c = 0.5$, CHCl_3). IR (KBr): ν 3215, 2958, 2880, 1696, 1664, 785 cm^{-1} . ^1H NMR (300 MHz, CDCl_3), δ : 9.38 (br s, 1H), 7.92 (d, $J = 6.0$ Hz, 1H), 7.80–7.67 (m, 5H), 7.46–7.42 (m, 3H), 6.42–6.39 (m, 1H), 4.75–4.72 (m, 1H), 3.92 (s, 2H), 3.72–3.64 (m, 1H), 3.55–3.47 (m, 1H), 3.40–3.30 (m, 4H), 2.38–2.31 (m, 1H), 2.14–1.88 (m, 3H), 1.68–1.59 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3), δ : 171.1, 169.9, 156.6, 152.4, 148.0, 133.4, 132.3, 131.6, 128.3, 127.6, 127.5, 127.4, 127.2, 125.9, 125.6, 104.9, 97.6, 61.0, 47.6, 47.3, 42.1, 27.8, 25.1, 24.9, 24.3. (EI) m/z 443 (rel. intensity) ($\text{M}^+ + 1$). Analysis calculated for $\text{C}_{27}\text{H}_{30}\text{N}_4\text{O}_2$: C, 73.28; H, 6.83; N, 12.66; O, 7.23. Found: C, 72.32; H, 6.84; N, 12.60; O, 7.30.

(4R)-4-((4-(Piperidin-1-yl)pyridin-2-yl)amino)dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphine-4-oxide (1e)

1,1'-Binaphthyl-2,2'-diylphosphorochloridate (2.3 g, 6.0 mmol) was added to a stirred solution of 2-amino-4-piperidinyl pyridine (0.88 g, 5.0 mmol) and TEA (0.8 mL, 6.0 mmol) in DCM (10 mL) at room temperature and stirred for an additional 15 h. The organic layer was washed with brine (2×20 mL) and dried over anhydrous Na_2SO_4 . After the removal of the solvent under reduced pressure, the residue was purified through column chromatography on silica gel (DCM/MeOH 10:1) to give **1e** as a white solid (2.1 g, 84%). White solid, mp 228.2–229.3 °C. $[\alpha]_{\text{D}}^{20} = -370$ ($c = 0.2$, CHCl_3). IR (KBr): ν 3374, 3065, 2935, 2853, 1634, 1224, 750 cm^{-1} . ^1H NMR (300 MHz, CDCl_3), δ : 8.03 (d, $J = 9.0$ Hz, 1H), 7.95–7.88 (m, 2H), 7.80 (d, $J = 9.0$ Hz, 1H), 7.68 (d, $J = 9.0$ Hz, 1H), 7.57 (d, $J = 9.0$ Hz, 1H), 7.47–7.41 (m, 3H), 7.38–7.21 (m, 3H), 6.75 (d, $J = 6.0$ Hz, 1H), 6.37 (s, 1H), 5.24–5.22 (m, 1H), 3.45 (br s, 1H), 3.01–2.86 (m, 4H), 1.52–1.37 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3), δ : 157.0, 156.6, 149.1, 147.7, 147.6, 135.7, 132.4, 131.4, 131.2, 130.6, 130.3, 128.4, 128.3, 127.0, 126.8, 126.2, 125.9, 125.1, 124.5, 122.1, 121.9, 121.8, 121.6, 98.4, 95.5, 46.7, 25.0, 23.8. (EI) m/z 508 (rel. intensity) ($\text{M}^+ + 1$). Analysis calculated for $\text{C}_{30}\text{H}_{26}\text{N}_3\text{O}_3\text{P}$: C, 71.00; H, 5.16; N, 8.28; O, 9.46; P, 6.10. Found: C, 69.70; H, 5.08; N, 8.29; O, 9.50; P, 6.15.

(R)-4-(4-(Piperidin-1-yl)pyridin-2-yl)dinaphtho[2,1-d:1',2'-f][1,3,2]-dithiazepine-3,3,5,5-tetraoxide (1f)

(R)-[1,1'-Binaphthalene]-2,2'-disulfonyl dichloride (2.7 g, 6.0 mmol) was added to a stirred solution of 2-amino-4-piperidinyl pyridine (0.88 g, 5.0 mmol) and TEA (0.8 mL, 6.0 mmol) in DCM (10 mL) at room temperature and stirred for an

additional 15 h. The organic layer was washed with brine (2×20 mL) and dried over anhydrous Na_2SO_4 . After the removal of solvent under reduced pressure, the residue was purified through column chromatography on silica gel (DCM/MeOH 10:1) to give **1f** as white solid (2.5 g, 90%). White solid, mp 205.2–207.0 °C. $[\alpha]_{\text{D}}^{20} = +181$ ($c = 0.2$, CHCl_3). IR (KBr): ν 3042, 2985, 1654, 754 cm^{-1} . ^1H NMR (300 MHz, CDCl_3), δ : 8.29–8.19 (m, 5H), 8.08 (d, $J = 9.0$ Hz, 2H), 7.70–7.65 (m, 2H), 7.45–7.39 (m, 4H), 6.70–6.66 (m, 2H), 3.40–3.30 (m, 4H), 1.69–1.59 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3), δ : 156.7, 149.9, 147.5, 135.6, 135.1, 131.6, 130.8, 129.3, 128.7, 128.2, 128.1, 123.1, 109.7, 108.8, 47.0, 25.0, 24.0. (EI) m/z 556 (rel. intensity) ($\text{M}^+ + 1$). Analysis calculated for $\text{C}_{30}\text{H}_{25}\text{N}_3\text{O}_4\text{S}_2$: C, 64.84; H, 4.53; N, 7.56; O, 11.52; S, 11.54. Found: C, 64.70; H, 4.48; N, 7.49; O, 11.50; S, 11.45.

ACKNOWLEDGMENTS

The authors thank the sophisticated instrumentation faculty at the department of analytical chemistry in Jilin University, Xu-Yang Luo for recording ^1H and ^{13}C NMR spectra, and Qin-Wen Liu for recording the mass spectra.

REFERENCES

1. Steglich, W.; Höfle, G. Über eine einfache darstellung von acyl-oxazolinonen-(5) aus 5-acyloxy-oxazolen II: Mitteilung über hypernucleophile acylierungskatalysatoren. *Tetrahedron Lett.* **1970**, *11*, 4727–4730.
2. Vorbrüggen, H. Simple new synthesis of N^6 -substituted adenosines and 2-aminoadenosines. *Angew. Chem. Int. Ed.* **1972**, *11*, 304–305.
3. Höfle, G.; Steglich, W.; Vorbrüggen, H. 4-Dialkylaminopyridines as highly active acylation catalysts. *Angew. Chem. Int. Ed.* **1978**, *17*, 569–583.
4. Hassner, A.; Krespi, L. R.; Alexanian, V. Aminopyridines as acylation catalysts for tertiary alcohols. *Tetrahedron* **1978**, *34*, 2069–2076.
5. Scriven, E. F. 4-Dialkylaminopyridines: Superacylation and alkylation catalysts. *Chem. Soc. Rev.* **1983**, *12*, 129–161.
6. Ragnarsson, U.; Grehn, L. Novel amine chemistry based on DMAP-catalyzed acylation. *Acc. Chem. Res.* **1998**, *31*, 494–501.
7. Kawabata, T.; Yamamoto, K.; Momose, Y.; Yoshida, H.; Nagaoka, Y.; Fuji, K. Kinetic resolution of amino alcohol derivatives with a chiral nucleophilic catalyst: Access to enantiopure cyclic *cis*-amino alcohols. *Chem. Commun.* **2001**, *0*, 2700–2701.
8. Yamada, S.; Misono, T.; Tsuzuki, S. Cation- π interactions of a thiocarbonyl group and a carbonyl group with a pyridinium nucleus. *J. Am. Chem. Soc.* **2004**, *126*, 9862–9872.
9. O'Dalaigh, C.; Connon, S. J. Nonenzymatic acylative kinetic resolution of Baylis–Hillman adducts. *J. Org. Chem.* **2007**, *72*, 7066–7069.
10. Dalaigh, C. O.; Hynes, S. J.; O'Brien, J. E.; McCabe, T.; Maher, D. J.; Watson, G. W.; Connon, S. J. Asymmetric acyl-transfer promoted by readily assembled chiral 4- N,N -dialkylaminopyridine derivatives. *Org. Biomol. Chem.* **2006**, *4*, 2785–2793.
11. Fu, G. C. Asymmetric catalysis with “planar-chiral” derivatives of 4-(dimethylamino)-pyridine. *Acc. Chem. Res.* **2004**, *37*, 542–547.
12. Kawabata, T.; Stragies, R.; Fukaya, T.; Nagaoka, Y.; Schedel, H.; Fuji, K. Preparation and properties of chiral 4-pyrrolidinopyridine (PPY) analogues with dual functional side chains. *Tetrahedron Lett.* **2003**, *44*, 1545–1548.

13. Priem, G.; Pelotier, B.; Macdonald, S. J. F.; Anson, M. S.; Campbell, I. B. The design of novel N-4-pyridinyl- α -methyl proline derivatives as potent catalysts for the kinetic resolution of alcohols. *J. Org. Chem.* **2003**, *68*, 3844–3848.
14. Spivey, A. C.; Charbonneau, P.; Fekner, T.; Hochmuth, D. H.; Maddaford, A.; Malardier-Jugroot, C.; Redgrave, A. J.; Whitehead, M. A. Energy barriers to rotation in axially chiral analogues of 4-(dimethylamino)pyridine. *J. Org. Chem.* **2001**, *66*, 7394–7401.
15. Vedejs, E.; Daugulis, O. 2-Aryl-4,4,8-trimethyl-2-phosphabicyclo[3.3.0]octanes: Reactive chiral phosphine catalysts for enantioselective acylation. *J. Am. Chem. Soc.* **1999**, *121*, 5813–5814.
16. Lee, E. C.; McCauley, K. M.; Fu, G. C. Catalytic asymmetric synthesis of tertiary alkyl chlorides. *Angew. Chem. Int. Ed.* **2007**, *46*, 977–979.
17. France, S.; Guerin, D. J.; Miller, S. J.; Lectka, T. Nucleophilic chiral amines as catalysts in asymmetric synthesis. *Chem. Rev.* **2003**, *103*, 2985–3012.
18. Fu, G. C. Enantioselective nucleophilic catalysis with “planar-chiral” heterocycles. *Acc. Chem. Res.* **2000**, *33*, 412–420.
19. Connon, S. J. Catalytic asymmetric acyl-transfer mediated by chiral pyridine derivatives. *Lett. Org. Chem.* **2006**, *3*, 333–338.
20. Wurz, R. P. Chiral dialkylaminopyridine catalysts in asymmetric synthesis. *Chem. Rev.* **2007**, *107*, 5570–5595.
21. Vedejs, E.; Chen, X. H. Parallel kinetic resolution. *J. Am. Chem. Soc.* **1997**, *119*, 2584–2585.
22. Vedejs, E.; MacKay, J. A. Kinetic resolution of allylic alcohols using a chiral phosphine catalyst. *Org. Lett.* **2001**, *3*, 535–536.
23. Tao, B. T.; Ruble, J. C.; Hoic, D. A.; Fu, G. C. Nonenzymatic kinetic resolution of propargylic alcohols by a planar-chiral DMAP derivative: Crystallographic characterization of the acylated catalyst. *J. Am. Chem. Soc.* **1999**, *121*, 5091–5092.
24. Spivey, A. C.; Maddaford, A.; Leese, D. P.; Redgrave, A. J. Atropisomeric α -methyl substituted analogues of 4-(dimethylamino)pyridine: synthesis and evaluation as acyl transfer catalysts. *J. Chem. Soc., Perkin Trans.* **2001**, *1*, 1785–1794.
25. Meigh, J. P.; Alvarez, M.; Joule, J. A. Cyclic ureas as ortho directing substituents. *J. Chem. Soc., Perkins Trans.* **2001**, *1*, 2012–2021.
26. Badawneh, M.; Manera, C.; Mori, C.; Saccomanni, G.; Ferrarini, P. L. Synthesis of variously substituted 1,8-naphthyridine derivatives and evaluation of their antimycobacterial activity. *Farmaco* **2002**, *57*, 631–639.

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