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Catalytic enantioselective Henry reaction of α-keto esters, 2-acylpyridines and 2-acylpyridine *N*-oxides†

Feilong He, ‡[a] Guanghui Chen,‡[a] Junxia Yang,[a] Guojuan Liang,[a] Ping Deng,[a] Yan Xiong [b] and Hui Zhou *[a]

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A pre-prepared Ni–PyBisulidine complex has been developed for the catalytic asymmetric Henry reaction of α-keto esters, 2-acylpyridines and 2-acylpyridine *N*-oxides. The corresponding β-nitro-α-hydroxy esters were obtained in good to excellent yields (up to 99%) with a high enantiomeric excess (ee) (up to 94%) with a catalyst loading of 1–2 mol%. The desired products of 2-acylpyridines and 2-acylpyridine *N*-oxides, which were simple methyl ketones, were obtained in medium to excellent yields (up to 94%) with medium to good ee (up to 86%) by using 2 mol% of catalyst.

Introduction

The Henry reaction is one of the important methods for C–C bond formation.[1] The resulting products, β-nitroalcohols, are key intermediates and building blocks for the synthesis of bioactive natural products and pharmaceutical agents.[1] Thus, increasing efforts have been directed towards developing a catalytic asymmetric Henry reaction.[2] Compared with the well developed asymmetric Henry reaction of aldehydes, the asymmetric Henry reaction of ketones with the formation of a quaternary stereogenic center is more challenging because it often suffers from low reactivity and poor stereoselectivity.[3] Although Tosaki *et al.* reported the kinetic resolution of racemic derivatives,[4] the catalytic asymmetric Henry reaction of simple ketones is rarely reported. At present, the study mainly focused on reactive substrates such as trifluoromethyl ketones,[5] α-keto esters,[6] α-keto amides,[7] α-keto-phosphonates,[8] and glyoxal hydrates.[9] Holmquist *et al.* expanded the scope of this reaction to 2-acylpyridine *N*-oxide, simple ketones, for the first time.[10] Although great progress has been achieved, several factors, including the relatively high catalyst loading (5–20 mol%) or catalyst preparation, limit the use of existing catalytic methods. At the same time, developing new catalysts for the enantioselective Henry reaction of ketones is still necessary. Recently a sulfonylated pyridine bisimidazolidine: nickel–pyridine bisulidine (Ni–PyBisulidine) complex was introduced for the asymmetric hydrophosphonylation of aldehydes.[11–13] In this paper, the use of pre-prepared Ni–PyBisulidine complexes for the asymmetric Henry reaction of α-keto esters, 2-acylpyridines and 2-acylpyridine *N*-oxides with low catalyst loading (down to 1 mol%) is reported.

Results and discussion

The initial studies of the catalytic asymmetric Henry reaction focused on the addition of nitromethane (CH_3NO_2) to methyl phenyloxoacetate in the presence of the complex of chiral PyBisulidine **L1** as ligand (Fig. 1). The complexes of nickel(II) acetate–**L1** [$Ni(OAc)_2$–**L1**], cobalt(II) acetate–**L1** [$Co(OAc)_2$–**L1**], zinc(II) acetate–**L1** [$Zn(OAc)_2$–**L1**] promoted the reaction in a 70–86% enantiomeric excess (ee) with low yields at room temperature (rt; Table 1, entries 1, 3 and 5). When nickel(II) acetylacetonate [$Ni(acac)_2$] and copper(II) acetate [$Cu(OAc)_2$] were used as the central metal, a low chiral induction was observed (Table 1, entries 2 and 4). When the complexes of iron(II) acetate–**L1** [$Fe(OAc)_2$–**L1**] and palladium(II) acetate–**L1** [$Pd(OAc)_2$–**L1**] were used as the catalysts, the corresponding products were not detected (Table 1, entries 6 and 7). Fortunately, the $Ni(OAc)_2$–**L1** complex could catalyze this reaction

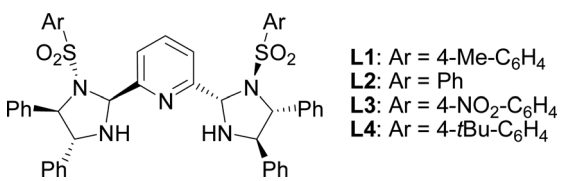

Fig. 1 Chiral PyBisulidine used as ligands for the asymmetric Henry reaction.

[a]School of Pharmaceutical Science, Chongqing Medical University, Chongqing 400016, PR China. E-mail: hzhou@cqmu.edu.cn

[b]School of Chemistry and Chemical Engineering, Chongqing University, Chongqing 401331, PR China

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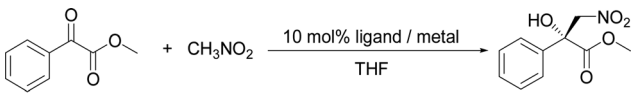
‡ These authors contributed equally.

Table 1 Screening of central metals, PyBisulidine ligands and temperature in the asymmetric Henry reaction of methyl phenyloxoacetate[a]



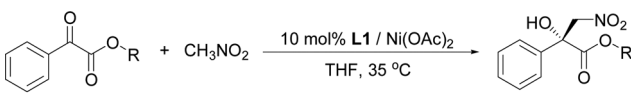
1aa 2aa

Entry	Metal	Ligand	T (°C)	Yield[b] (%)	ee[c] (%)
1	$Ni(OAc)_2$	**L1**	rt	16	86
2	$Ni(acac)_2$	**L1**	rt	76	8
3	$Co(OAc)_2$	**L1**	rt	37	75
4	$Cu(OAc)_2$	**L1**	rt	18	8
5	$Zn(OAc)_2$	**L1**	rt	19	70
6[d]	$Fe(OAc)_2$	**L1**	rt	ND[e]	—
7[d]	$Pd(OAc)_2$	**L1**	rt	ND[e]	—
8	$Ni(OAc)_2$	**L1**	35	85	83
9	$Ni(OAc)_2$	**L1**	50	84	80
10	$Ni(OAc)_2$	**L2**	35	84	69
11	$Ni(OAc)_2$	**L3**	35	82	88
12	$Ni(OAc)_2$	**L4**	35	62	72

[a] Reactions were carried out using methyl phenyloxoacetate (0.2 mmol) with CH_3NO_2 (0.2 mL) in THF (0.8 mL) in the presence of metal–PyBisulidines prepared *in situ* for 20 h. [b] Isolated yield. [c] Determined using HPLC analysis on a chiral stationary phase. [d] The reaction time was 65 h. [e] ND: not detected.

smoothly with 83% ee with a 85% yield when the reaction temperature rose to 35 °C (Table 1, entry 8). However, further increasing the reaction temperature did not improve the reactivity (Table 1, entry 9). After screening the benzenesulfonyl moiety of the ligands (Table 1, entries 8, 10–12), $Ni(OAc)_2$–**L1** was selected for further optimization which considered the reactivity and economy.

Table 2 Screening of the ester group R and catalyst preparation method[a]



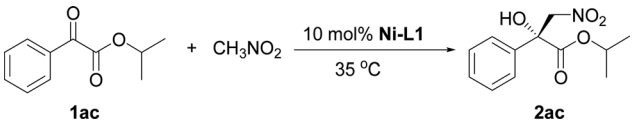
1aa: R = Me
1ab: R = Et
1ac: R = *i*Pr

2aa-2ac

Entry	R	Catalyst preparation method[b]	Yield[c] (%)	ee[d] (%)
1	Me	*In situ*	85 (**2aa**)	83
2	Et	*In situ*	62 (**2ab**)	86
3	i-Pr	*In situ*	83 (**2ac**)	88
4	i-Pr	Pre-prepared	85 (**2ac**)	91

[a] Reactions were carried out using an α-keto ester (0.2 mmol) in a mixture of THF (0.8 mL) and CH_3NO_2 (0.2 mL) for 20 h. [b] For details, see ref. 11. [c] Isolated yield. [d] Determined using HPLC analysis on a chiral stationary phase.

Table 3 Screening of the solvents used in the asymmetric Henry reaction of isopropyl phenyloxoacetate[a]



1ac 2ac

Entry	Solvent	Yield[b] (%)	ee[c] (%)
1	THF	85	91
2	$CHCl_3$	37	89
3	CH_3OH	56	43
4	Toluene	68	90
5	DME	Trace	—
6	Diglyme[d]	62	91

[a] Reactions were carried out on a 0.2 mmol scale of isopropyl phenyloxoacetate in the mixture of THF (0.8 mL) and CH_3NO_2 (0.2 mL) for 20 h. The catalyst was pre-prepared. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Diglyme = diethylene glycol dimethyl ether.

The influence of the ester group in the substrate was tested next (Table 2, entries 1–3). The best result in terms of the conversion and enantioselectivity was obtained with the isopropyl ester (Table 2, entry 3). The pre-prepared complex[14] gave better results than the complex prepared *in situ* (Table 2, compare entries 3 and 4).

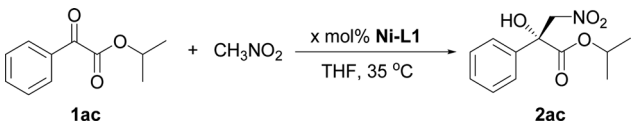
Encouraged by the initial results in the asymmetric Henry reaction, various solvents were screened in the presence of 10 mol% pre-prepared Ni–**L1** (Table 3). Whereas small or trace amounts of products were detected in chloroform ($CHCl_3$) or 1,2-dimethoxyethane (DME; Table 3, entries 2 and 5). Other solvents tested, such as methanol (CH_3OH, MeOH), toluene and diethylene glycol dimethyl ether, gave moderate yields (Table 3, entries 3, 4 and 6). Tetrahydrofuran (THF) exhibited the best performance (Table 3, entry 1).

When the catalyst loading was reduced, the reactivity decreased sharply with slightly increasing ee (Table 4, entries 1–4). To increase the reactivity, some additives were screened in this reaction (Table 4, entries 5–8). The yields of Henry products were improved when using a 4 Å molecular sieve (MS; Table 4, entries 7 and 11) and addition of *tert*-amines (Table 4, entries 5, 6, 9 and 10). However, some acidic additives, such as benzoic acid (PhCOOH), were harmful for the reaction (Table 4, entry 8).

When the catalyst loading was reduced to 2 mol%, *N*-methylmorpholine showed a better performance than iPr_2NEt in terms of enantioselectivity (Table 4, entries 9 and 10). The amount of 4 Å MS was screened together with 10 mol% *N*-methylmorpholine (Table 4, entries 12–14). Under the optimized conditions (at 35 °C, in the presence of 2 mol% Ni–**L1**, 10 mol% *N*-methylmorpholine, and 150 mg $mmol^{-1}$ 4 Å MS in THF), **2ac** was obtained with a 92% yield with 93% ee (Table 4, entry 13).

The current catalytic system was applied to various α-keto esters (Table 5). In all cases, the reactions were clean and proceeded and gave good to excellent yields with high

Table 4 Screening the effects of reducing the amount of catalyst loading, additive and base in the asymmetric Henry reaction of isopropyl phenyloxoacetate[a]



1ac 2ac

Entry	Catalyst loading	Base (mol%)	Additive	Yield[b] (%)	ee[c] (%)
1	10 mol%	None	None	85	91
2	5 mol%	None	None	80	92
3	2 mol%	None	None	49	93
4	1 mol%	None	None	28	94
5	10 mol%	iPr_2NEt[d] (10)	None	92	86
6	10 mol%	*N*-Methyl-morpholine (10)	None	90	89
7	10 mol%	None	4 Å MS[e] (38 mg)	95	86
8	10 mol%	None	PhCOOH (10 mol%)	46	90
9	2 mol%	iPr_2NEt (10)	None	69	88
10	2 mol%	*N*-Methyl-morpholine (10)	None	66	92
11	2 mol%	None	4 Å MS (38 mg)	56	93
12	2 mol%	*N*-Methyl-morpholine (10)	4 Å MS (20 mg)	80	93
13	2 mol%	*N*-Methyl-morpholine (10)	4 Å MS (30 mg)	92	93
14	2 mol%	*N*-Methyl-morpholine (10)	4 Å MS (50 mg)	90	93

[a] Reactions were carried out using scale of isopropyl phenyloxoacetate (0.2 mmol) in a mixture of THF (0.8 mL) and CH_3NO_2 (0.2 mL) for 20 h. The catalyst was pre-prepared. [b] Isolated yield. [c] Determined using HPLC analysis on a chiral stationary phase. [d] *N*,*N*-Diisopropylethylamine. [e] Molecular sieve.

enantioselectivities. Aromatic keto esters bearing the electron-donating groups gave smaller yields but the high enantioselectivities were maintained (72–83% yield, Table 5, **2bc–2dc**, and **2gc**). Aromatic keto esters bearing the electron-withdrawing group gave excellent yields (Table 5, **2ec**, and **2ic–2mc**) and the catalyst loading could be reduced to 1 mol% with high to excellent yields and high enantioselectivities (Table 5, **2ic–2mc**). The keto esters derived from the bulkier ketone, such as β-acetonaphthone, also gave an excellent yield and high enantioselectivity (Table 5, **2fc**). The heteroaromatic and alkyl keto esters gave smaller ee values (Table 5, **2hc** and **2nb**). The configuration of **2ac** was identified as *R* using single crystal diffraction analysis,[15] and the configuration of the other products were inferred to be analogous with that of **2ac**. It should be noted that the pre-prepared complex Ni–**L1** can be stored in air at 4 °C for at least three months without any loss of activity.[16]

The Ni–**L1** was also used in the asymmetric Henry reaction of 2-acylpyridine *N*-oxides (Table 6).[17] High yields and good ee were obtained with methyl ketones (Table 6, **4a–4d**, **4f**). Whereas low ee were obtained with ethyl ketones (Table 6, **4g**). The corresponding product of 3-methyl-2-acylpyridine *N*-oxide was not detected (Table 6, **4e**).

Inspired by the research of Tosaki *et al.*[4] and Holmquist *et al.*[10], the Henry reaction of 2-acylpyridines was also investigated (Table 7).[17] In most cases, 50–60% yields and 70–86% ee were obtained with methyl ketones. Racemic products were obtained for ethyl ketones (Table 7, **6g**). The Henry reaction of 3-methyl-2-acylpyridine did not take place at all. The results were similar to those obtained using 2-acylpyridine *N*-oxides, indicating that they had similar transition states.

The proposed structure of Ni–**L1** on the basis of the related structure of Fe–PyBisulidine complex,[12a] the geometry of **L1** optimized using Chem3D at the MM2 level (Fig. 2) and the electrospray ionization-high resolution mass spectrometry (ESI-HRMS) analysis of the complex has previously been reported.[11] To gain some insight into the active species, ESI-HRMS studies of the mixture of Ni–**L1** and **3a** were carried out. The spectrum displayed ions at *m*/*z* 1085.28625 and 1025.26555, which corresponded to **C-I** and **C-II** (Fig. 3). It was speculated that the complex **C-I** or **C-II** would be the active species. **TS1–TS6** are proposed to rationalize the asymmetric induction. As illustrated in Fig. 4, the keto functionality is coordinated to Ni(II) in the more Lewis acidic equatorial position for maximal activation,[18] whereas the nitronate generated by the amine is positioned by the hydrogen bonding.[13g,13h]

Conclusions

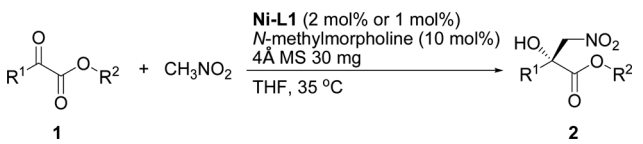
A catalytic asymmetric Henry reaction of α-keto esters, 2-acylpyridines and 2-acylpyridine *N*-oxides, was developed using a Ni–PyBisulidine complex with a low catalyst loading (1–2 mol%). This is the first example of the direct asymmetric synthesis of tertiary nitro alcohols derived from 2-acylpyridines, which were simple methyl ketones. The catalytic system is tolerant of air and moisture. Further investigations into other versions of asymmetric catalysis are in progress.

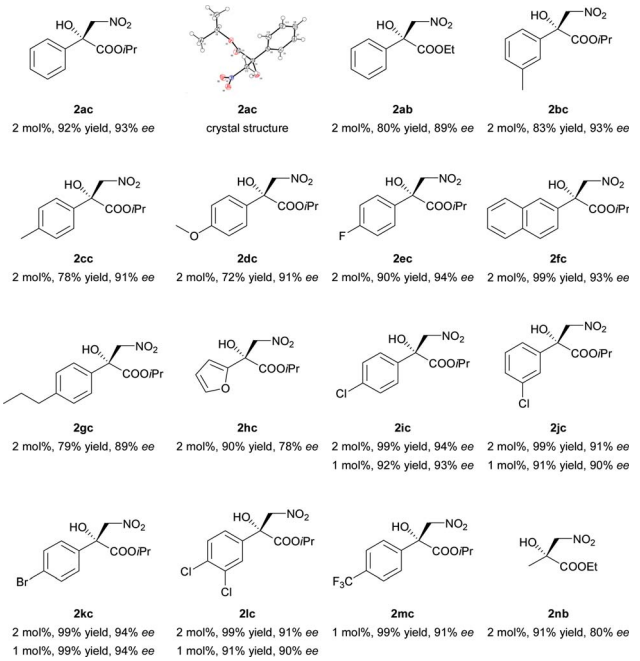
Experimental

General methods

Commercial reagents were used as purchased. High resolution mass spectra were recorded using a Bruker SolariX Fourier-

Table 5 Substrate scope of catalytic asymmetric Henry reaction of α-keto esters[a]





[a] Unless otherwise noted, all reactions were carried out with α-keto ester (0.2 mmol) with *N*-methylmorpholine (10 mol%) and 4 Å MS (30 mg) in a mixture of THF (0.8 mL) and CH_3NO_2 (0.2 mL) for 20 h. The catalyst was pre-prepared. The reaction time for **2dc**, **2gc**, and **2hc** was 36 h.

transform ion cyclotron mass spectrometry (FT-ICR-MS) system. Nuclear magnetic resonance (NMR) spectra were recorded in the deuterated solvents [deuterated chloroform ($CDCl_3$) or deuterated methanol (CD_3OD)] as stated, using residual non-deuterated solvent as internal standard. The enantiomeric excess (ee) was determined using high-performance liquid chromatography (HPLC) analysis using the corresponding commercial chiral column as stated in the experimental procedures at 23 °C with an ultraviolet detector at 220 nm or 215 nm or 254 nm. Optical rotations were measured on a commercial polarimeter and are reported as follows: $[\alpha]_D^T$ (c = g per 100 mL solvent).

General procedure for catalytic asymmetric reaction

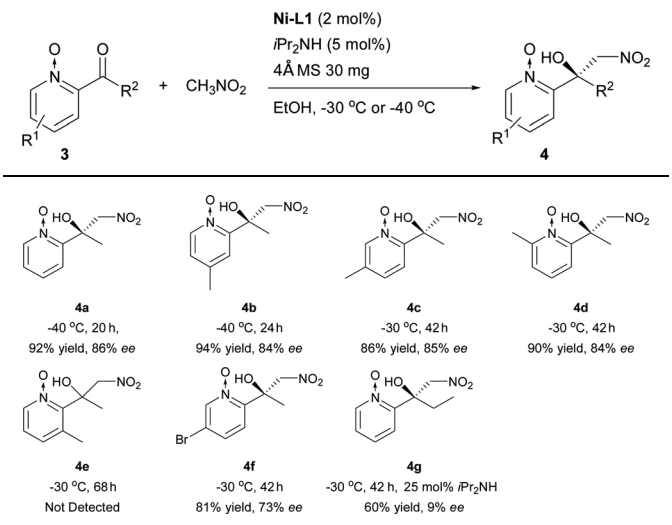
α-Keto esters. The mixture of CH_3NO_2 (0.2 mL), Ni–**L1** (2 mol% or 1 mol%), 4 Å MS (30 mg) and *N*-methylmorpholine (10 mol%) was stirred in THF (0.8 mL) under an air atmosphere at 35 °C for 10 min followed by the addition of the α-keto ester (0.2 mmol). The stirring was continued for the reaction time given in Table 5 at 35 °C. The residue was purified using silica gel flash column chromatography (petroleum ether/ethyl acetate (EtOAc), 60 : 1–15 : 1) to give the products. The absolute configuration of **2ac** was determined using X-ray crystallographic analysis. The absolute configuration of **2ab** was assigned by comparison with the sign of optical rotation value found in the literature.[6b] The absolute configuration of **2bc–2mc** and **2aa** was determined by analogy. The absolute configuration of **2nb** was assigned by comparison with the sign of optical rotation values found in the literature.[6a,6b,6e,6f,6i]

2-Acylpyridine *N*-oxides. The mixture of CH_3NO_2 (0.2 mL), Ni–**L1** (2 mol%), 4 Å MS (30 mg), 2-acylpyridine *N*-oxides (0.2 mmol) and iPr_2NH (5 mol%) was stirred in EtOH (0.8 mL) at the temperature specified in Table 6 (−30 °C or −40 °C) under an air atmosphere for the reaction time identified in Table 6. The residue was purified using silica gel flash column chromatography (petroleum ether/EtOAc, 10 : 1) to give the products. The absolute configuration of **4a–4d** and **4f** was assigned by comparison with the sign of optical rotation value found in the literature.[10]

2-Acylpyridines. The mixture of CH_3NO_2 (0.2 mL), Ni–**L1** (2 mol%), 4 Å MS (40 mg), 2-acylpyridine (0.2 mmol) and iPr_2-NEt (10 mol%) was stirred in THF (0.8 mL) at the temperature specified in Table 7 (−10 °C or −20 °C) under an air atmosphere for the reaction time indicated in Table 7. The residue was purified using silica gel flash column chromatography (petroleum ether/EtOAc, 10 : 1) to give the products. The absolute configuration of **6a** was assigned by comparison with the sign of optical rotation value of its reduced product (7) found in the literature.[10] The absolute configuration of **6b–6d** and **6f** was determined by analogy.

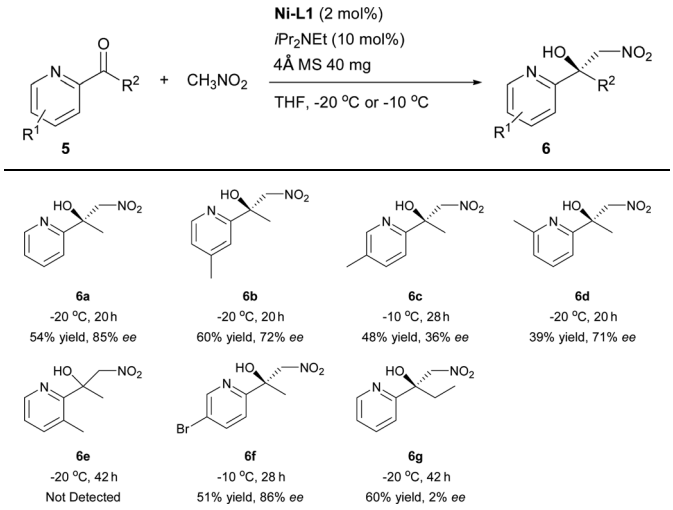
Methyl 2-hydroxy-3-nitro-2-phenyl propanoate (2aa). Colorless oil, 38.3 mg, 85% yield, 83% ee; ^{1}H-NMR (600 MHz, $CDCl_3$)

Table 6 Catalytic asymmetric Henry reaction of 2-acylpyridine *N*-oxides[a]



[a] Reactions were carried out with 2-acylpyridine *N*-oxides (0.2 mmol) with diisopropylamine (iPr_2NH; 5 mol%) and 4 Å MS (30 mg) in a mixture of EtOH (0.8 mL) and CH_3NO_2 (0.2 mL) for 20–42 h. The catalyst was pre-prepared. EtOH: ethanol.

Table 7 Catalytic asymmetric Henry reaction of 2-acylpyridine[a]



[a] Reactions were carried out with 2-acylpyridine (0.2 mmol) with iPr_2NEt (10 mol%) and 4 Å MS (40 mg) in a mixture of THF (0.8 mL) and CH_3NO_2 (0.2 mL) for 20–42 h. The catalyst was pre-prepared.

δ 7.59 (d, 2H, $J = 7.1$), 7.43–7.36 (m, 3H), 5.26 (d, 1H, $J = 14.2$), 4.68 (d, 1H, $J = 14.2$), 4.25 (s, 1H), 3.91 (s, 3H); $[\alpha]_D^{25} = -4.8$ [c 0.56, dichloromethane (CH_2Cl_2)] [lit.[6i] $[\alpha]_D^{25} = -15.6$ (c 0.54, CH_2Cl_2) in 70% ee]; HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 85/15, flow rate = 1.0 mL min^{-1}, detection at 220 nm), retention time = 11.9 min (major) and = 9.1 min (minor).

Ethyl 2-hydroxy-3-nitro-2-phenyl propanoate (2ab). Colorless oil, 38.2 mg, 80% yield, 89% ee; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.61 (d, 2H, $J = 7.2$), 7.42–7.36 (m, 3H), 5.26 (d, 1H, $J = 14.2$), 4.68 (d, 1H, $J = 14.2$), 4.42–4.31 (m, 2H), 4.26 (s, 1H), 1.34 (t, 3H, $J = 7.1$); $[\alpha]_D^{25} = -10.2$ (c 0.54, CH_2Cl_2) [lit.[6b] $[\alpha]_D^{23} = -16.2$ (c 1.13, CH_2Cl_2) in 86% ee]; HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), t_r = 12.9 min (major) and = 10.1 min (minor).

Isopropyl 2-hydroxy-3-nitro-2-phenyl propanoate (2ac).[6i] White solid, 46.5 mg, 92% yield, 93% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.61 (d, 2H, $J = 7.4$), 7.42–7.35 (m, 3H), 5.24 (d, 1H, $J = 14.2$), 5.22–5.15 (m, 1H), 4.67 (d, 1H, $J = 14.2$), 4.23 (s, 1H), 1.35 (d, 3H, $J = 6.3$), 1.29 (d, 3H, $J = 6.3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.2, 136.7, 129.1, 128.9, 125.3, 80.8, 76.0, 72.0, 21.6, 21.5. $[\alpha]_D^{25} = -4.2$ (c 0.70, CH_2Cl_2) [lit.[6i] $[\alpha]_D^{25} = -2.3$ (c 1.07, CH_2Cl_2) in 62% ee]; HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), t_r = 9.9 min (major) and = 8.0 min (minor).

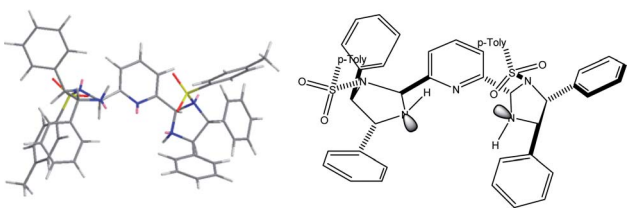


Fig. 2 The geometry of L1 optimized using Chem3D (8.0) at the MM2 level.

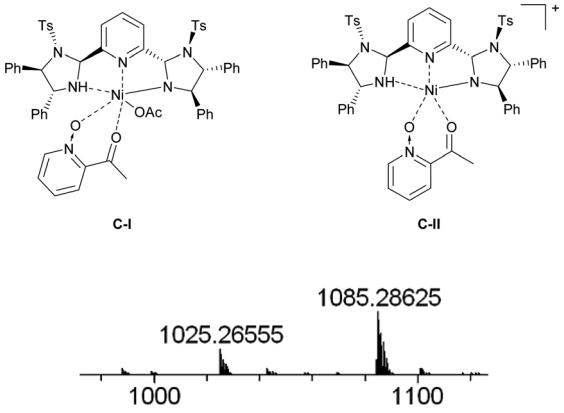


Fig. 3 ESI-HRMS for C-I: m/z calc'd for $C_{58}H_{55}N_6NiO_8S_2^+$ [$Ni(OAc)_2$ + M_{L1} + M_{3a} − HOAc + H]$^+$: 1085.28708, found: 1085.28625; ESI-HRMS for C-II: m/z calc'd for $C_{56}H_{51}N_6NiO_6S_2^+$ [$Ni(OAc)_2$ + M_{L1} + M_{3a} − HOAC − OAc]$^+$: 1025.26595, found: 1025.26555.

Isopropyl 2-hydroxy-2-(3-methyphenyl)-3-nitro propanoate (2bc). Light yellow oil, 44.3 mg, 83% yield, 93% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.4 (s, 1H), 7.29 (d, 1H, $J = 7.9$), 7.20 (t, 1H, $J = 7.7$), 7.09 (d, 1H, $J = 7.5$), 5.15 (d, 1H, $J = 14.2$), 5.14–5.08 (m, 1H), 4.57 (d, 1H, $J = 14.2$), 4.16 (s, 1H), 2.29 (s, 3H), 1.27 (d, 3H, $J = 6.3$), 1.22 (d, 3H, $J = 6.3$); $[\alpha]_D^{25} = -4.8$ (c 0.88, CH_2Cl_2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.2, 137.7, 135.5, 128.8, 127.7, 124.9, 121.2, 79.8, 74.9, 70.8, 20.52, 20.46, 20.39. HRMS (ESI): m/z calc'd for $C_{13}H_{17}NNaO_5^+$ [M + Na]$^+$: 290.0999, found: 290.0997. HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), t_r = 8.2 min (major) and = 6.5 min (minor).

Isopropyl 2-hydroxy-2-(4-methyphenyl)-3-nitro propanoate (2cc). Light yellow oil, 41.4 mg, 78% yield, 91% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.48 (d, 2H, $J = 8.2$), 7.20 (d, 2H, $J = 8.1$), 5.24–5.14 (m, 2H), 4.64 (d, 1H, $J = 14.2$), 4.22 (s, 1H), 2.35 (s, 3H), 1.34 (d, 3H, $J = 6.2$), 1.29 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$)

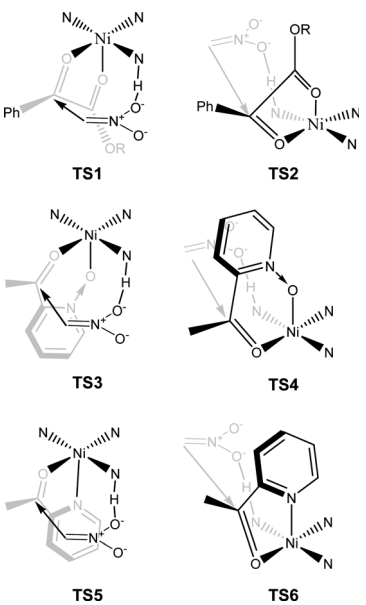


Fig. 4 The proposed working model.

δ 170.3, 138.0, 132.7, 128.5, 124.1, 79.8, 74.8, 70.8, 20.5, 20.4, 20.0. HRMS (ESI): *m*/*z* calc'd for $C_{13}H_{17}NNaO_5^+$ [M + Na]$^+$: 290.0999, found: 290.1000. $[\alpha]_D^{25} = -6.4$ (*c* 0.82, CH_2Cl_2); HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 9.2$ min (major) and = 6.9 min (minor).

Isopropyl 2-hydroxy-2-(4-methoxyphenyl)-3-nitro propanoate (2dc). White solid, 40.8 mg, 72% yield, 91% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.51 (d, 2H, $J = 8.8$), 6.91 (d, 2H, $J = 8.8$), 5.22–5.15 (m, 2H), 4.63 (d, 1H, $J = 14.2$), 4.20 (s, 1H), 3.81 (s, 3H), 1.34 (d, 3H, $J = 6.3$), 1.29 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.3, 159.0, 127.5, 125.6, 113.1, 79.8, 74.6, 70.8, 54.3, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{13}H_{17}NNaO_6^+$ [M + Na]$^+$: 306.0948, found: 306.0945. $[\alpha]_D^{25} = -11.4$ (*c* 0.65, CH_2Cl_2); HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 12.6$ min (major) and $t_r = 11.6$ min (minor).

Isopropyl 2-(4-flurophenyl)-2-hydroxy-3-nitro propanoate (2ec). Colorless oil, 48.5 mg, 90% yield, 94% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.62–7.58 (m, 2H), 7.08 (t, 2H, $J = 8.6$), 5.22–5.16 (m, 2H), 4.63 (d, 1H, $J = 14.1$), 4.27 (s, 1H), 1.34 (d, 3H, $J = 6.3$), 1.29 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.9, 163.0 and 161.1 ($^2J_{CF} = 225.0$, 1C), 131.3, 126.3, 126.2, 114.9, 114.7, 79.7, 74.5, 71.1, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{12}H_{14}FNNaO_5^+$ [M + Na]$^+$: 294.0748, found: 294.0748. $[\alpha]_D^{25} = -4.2$ (*c* 0.6, CH_2Cl_2); HPLC (CHIRALPAK IA column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 9.5$ min (major) and $t_r = 8.8$ min (minor).

Isopropyl 2-hydroxy-2-(2-naphthyl)-3-nitro propanoate (2fc). White solid, 60.6 mg, 99% yield, 93% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.89–7.84 (m, 3H), 7.67 (d, 1H, $J = 8.7$), 7.55–7.52 (m, 2H), 5.37 (d, 1H, $J = 14.2$), 5.26–5.17 (m, 1H), 4.75 (d, 1H, $J = 14.2$), 4.36 (brs, 1H), 1.37 (d, 3H, $J = 6.3$), 1.31 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.1, 131.8, 131.3, 131.0, 126.7, 126.5, 125.6, 125.0, 124.8, 123.1, 120.4, 78.8, 74.1, 70.1, 19.6, 19.5. HRMS (ESI): *m*/*z* calc'd for $C_{16}H_{17}NNaO_5^+$ [M + Na]$^+$: 326.0999, found: 326.1000. $[\alpha]_D^{25} = -34.9$ (*c* 0.53, CH_2Cl_2); HPLC (CHIRALPAK AS-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 9.5$ min (major) and $t_r = 8.8$ min (minor).

Isopropyl 2-hydroxy-3-nitro-2-(4-propylphenyl) propanoate (2gc). Light yellow oil, 46.7 mg, 79% yield, 89% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.49 (d, 2H, $J = 8.2$), 7.20 (d, 2H, $J = 8.1$), 5.22 (d, 1H, $J = 14.2$), 5.20–5.14 (m, 1H), 4.65 (d, 1H, $J = 14.2$), 4.20 (brs, 1H), 2.58 (t, 2H, $J = 7.6$), 1.68–1.59 (m, 2H), 1.34 (d, 3H, $J = 6.3$), 1.29 (d, 3H, $J = 6.3$), 0.93 (t, 3H, $J = 7.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.3, 142.7, 132.9, 127.9, 124.1, 79.8, 74.8, 70.8, 36.5, 23.3, 20.5, 20.4, 12.8. HRMS (ESI): *m*/*z* calc'd for $C_{15}H_{21}NNaO_5^+$ [M + Na]$^+$: 318.1312, found: 318.1311. $[\alpha]_D^{25} = -7.8$ (*c* 0.71, CH_2Cl_2); HPLC (CHIRALPAK IA column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 10.0$ min (major) and $t_r = 8.1$ min (minor).

Isopropyl 2-(2-furyl)-2-hydroxy-3-nitropropanoate (2hc). Light yellow oil, 45 mg, 90% yield, 78% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.41 (d, 1H, $J = 0.6$), 6.41–6.38 (m, 2H), 5.26–5.17 (m, 2H), 4.91 (d, 1H, $J = 14.2$), 4.21 (brs, 1H), 1.33 (d, 3H, $J = 6.3$), 1.27 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 168.4, 148.3, 142.5, 109.8, 107.4, 77.2, 71.9, 71.2, 20.5, 20.3. HRMS (ESI): *m*/*z* calc'd for $C_{10}H_{13}NNaO_6^+$ [M + Na]$^+$: 266.0635, found: 266.0634. $[\alpha]_D^{25} = +3.1$ (*c* 0.9, CH_2Cl_2); HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 8.0$ min (major) and $t_r = 7.4$ min (minor).

Isopropyl 2-(4-chlorophenyl)-2-hydroxy-3-nitro propanoate (2ic). Light yellow oil, 57.4 mg, 99% yield, 94% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.55 (d, 2H, $J = 8.6$), 7.36 (d, 2H, $J = 8.6$), 5.22–5.13 (m, 2H), 4.63 (d, 1H, $J = 14.1$), 4.30 (brs, 1H), 1.34 (d, 3H, $J = 6.3$), 1.28 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.8, 134.2, 134.1, 128.0, 125.8, 79.5, 74.6, 71.2, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{12}H_{14}ClNNaO_5^+$ [M + Na]$^+$: 310.0453, found: 310.0449. $[\alpha]_D^{25} = -8.7$ (*c* 1.4, CH_2Cl_2); HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 9.2$ min (major) and $t_r = 7.7$ min (minor).

Isopropyl 2-(3-chlorophenyl)-2-hydroxy-3-nitro propanoate (2jc). Light yellow oil, 57.4 mg, 99% yield, 91% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.50–7.49 (m, 1H), 7.37–7.26 (m, 2H), 5.23–5.18 (m, 2H), 4.64 (d, 1H, $J = 14.2$), 4.27 (s, 1H), 1.35 (d, 3H, $J = 6.3$), 1.31 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.6, 137.5, 134.0, 129.1, 128.3, 124.8, 122.4, 79.5, 74.5, 71.4, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{12}H_{14}ClNNaO_5^+$ [M + Na]$^+$: 310.0453, found: 310.0451. $[\alpha]_D^{25} = -8.3$ (*c* 1.8, CH_2Cl_2); HPLC (CHIRALPAK IA column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 8.5$ min (major) and $t_r = 8.0$ min (minor).

Isopropyl 2-(4-bromophenyl)-2-hydroxy-3-nitro propanoate (2kc). Colorless oil, 57.2 mg, 99% yield, 94% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.51 (q, 4H, $J = 8.9$), 5.21–5.13 (m, 2H), 4.63 (d, 1H, $J = 14.1$), 4.28 (brs, 1H), 1.34 (d, 3H, $J = 6.3$), 1.28 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.7, 134.6, 131.0, 126.1, 122.5, 79.5, 74.6, 71.3, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{12}H_{14}BrNNaO_5^+$ [M + Na]$^+$: 353.9948, found: 353.9945. $[\alpha]_D^{25} = -8.1$ (*c* 2.3, CH_2Cl_2); HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 12.7$ min (major) and $t_r = 9.0$ min (minor).

Isopropyl 2-(3,4-dichlorophenyl)-2-hydroxy-3-nitro propanoate (2lc). Light yellow oil, 64.2 mg, 99% yield, 91% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.49–7.44 (m, 2H), 5.22–5.15 (m, 2H), 4.62 (d, 1H, $J = 14.2$), 4.32 (s, 1H), 1.35 (d, 3H, $J = 6.3$), 1.31 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.3, 135.6, 132.6, 132.3, 129.8, 126.7, 123.7, 79.4, 74.2, 71.6, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{12}H_{13}Cl_2NNaO_5^+$ [M + Na]$^+$: 344.0063, found: 344.0066. $[\alpha]_D^{25} = -12.5$ (*c* 0.21, CH_2Cl_2); HPLC (CHIRALPAK IA column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), $t_r = 8.6$ min (major) and $t_r = 7.7$ min (minor).

Isopropyl 2-hydroxy-3-nitro-2-(4-trifluoromethyl-phenyl) propanoate (2mc). Light yellow solid, 70.4 mg, 99% yield, 91% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.77 (d, 2H, $J = 8.2$), 7.67 (d, 2H, $J = 8.3$), 5.26–5.16 (m, 2H), 4.65 (d, 1H, $J = 14.2$), 4.34 (brs, 1H), 1.36 (d, 3H, $J = 6.3$), 1.30 (d, 3H, $J = 6.3$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 169.5, 139.5, 130.5, 130.3, 124.9, 124.9–124.7 (q, $^4J_{CF} = 3.8$, 1C), 79.5, 74.7, 71.5, 20.5, 20.4. HRMS (ESI): *m*/*z* calc'd for $C_{13}H_{14}F_3NNaO_5^+$ [M + Na]$^+$: 344.0716, found: 344.0715. $[\alpha]_D^{25} = -4.1$ (*c* 0.97, CH_2Cl_2); HPLC (CHIRALPAK IA column, hexane/2-

propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 220 nm), t_r = 10.6 min (major) and t_r = 9.8 min (minor).

Ethyl 2-hydroxy-2-methyl-3-nitropropanoate (2nb). Light yellow oil, 32.2 mg, 91% yield, 80% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.83 (d, 1H, J = 13.8), 4.55 (d, 1H, J = 13.8), 4.36–4.28 (m, 2H), 3.81 (s, 1H), 1.44 (s, 3H), 1.31 (t, 3H, J = 6.8). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.6, 79.1, 70.6, 61.2, 22.0, 12.1. $[\alpha]_D^{25}$ = +9.2 (*c* 0.6, CH_2Cl_2) [lit.[6b] $[\alpha]_D^{23}$ = +10.2 (*c* 1.19, CH_2Cl_2) in 92% ee]; HPLC (CHIRALPAK AS-H column, hexane/2-propanol = 95/5, flow rate = 1.0 mL min^{-1}, detection at 215 nm), t_r = 21.3 min (major) and t_r = 17.7 min (minor).

1-Methyl-2-nitro-1-(1-oxido-2-pyridinyl) ethanol (4a). Brown oil, 36.4 mg, 92% yield, 86% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.23 (d, 1H, J = 6.3), 7.78 (s, 1H), 7.46–7.39 (m, 2H), 7.36–7.32 (m, 1H), 5.30 (d, 1H, J = 11.1), 4.85 (d, 1H, J = 11.1), 1.77 (s, 3H); $[\alpha]_D^{20}$ = +41.3 (*c* 0.45, MeOH) [lit.[10] $[\alpha]_D^{20}$ = +48 (*c* 0.9, MeOH) in 86% ee]; HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 75/25, flow rate = 1.0 mL min^{-1}, detection at 220 nm), t_r = 10.5 min (major) and t_r = 25.0 min (minor).

1-Methyl-2-nitro-1-(4-methyl-1-oxido-2-pyridinyl) ethanol (4b). Brown solid, 39.9 mg, 94% yield, 84% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.14 (d, 1H, J = 6.6), 7.20–7.15 (m, 2H), 5.43 (d, 1H, J = 11.0), 4.74 (d, 1H, J = 11.0), 2.40 (s, 3H), 1.79 (s, 3H); $[\alpha]_D^{20}$ = +34.0 (*c* 0.61, MeOH) [lit.[10] $[\alpha]_D^{20}$ = +41 (*c* 0.9, MeOH) in 84% ee]; HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 75/25, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 7.2 min (major) and t_r = 25.8 min (minor).

1-Methyl-2-nitro-1-(5-methyl-1-oxido-2-pyridinyl) ethanol (4c). Brown oil, 36.6 mg, 86% yield, 85% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.00 (s, 1H), 7.29 (d, 1H, J = 8.2), 7.26–7.23 (m, 1H), 5.40 (d, 1H, J = 11.0), 4.73 (d, 1H, J = 11.0), 2.35 (s, 3H), 1.78 (s, 3H); $[\alpha]_D^{20}$ = +56.7 (*c* 0.52, MeOH) [lit.[10] $[\alpha]_D^{20}$ = +60 (*c* 0.6, MeOH) in 81% ee]; HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 75/25, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 12.5 min (major) and t_r = 18.1 min (minor).

1-Methyl-2-nitro-1-(6-methyl-1-oxido-2-pyridinyl) ethanol (4d). White solid, 38.2 mg, 90% yield, 84% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.36–7.27 (m, 3H), 5.39 (d, 1H, J = 10.9), 4.74 (d, 1H, J = 10.9), 2.54 (s, 3H), 1.79 (s, 3H); $[\alpha]_D^{20}$ = +70.0 (*c* 0.56, MeOH) [lit.[10] $[\alpha]_D^{20}$ = +109 (*c* 0.9, MeOH) in 55% ee]; HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 80/20, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 8.2 min (major) and t_r = 11.8 min (minor).

1-Methyl-2-nitro-1-(5-bromo-1-oxido-2-pyridinyl) ethanol (4f). White solid, 44.9 mg, 81% yield, 73% ee; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.41 (d, 1H, J = 1.9), 7.56 (dd, 1H, J = 8.7, 1.7), 7.31 (d, 1H, J = 10.8), 7.19 (s, 1H), 5.38 (d, 1H, J = 14.3), 4.79 (d, 1H, J = 14.3), 1.79 (s, 3H); $[\alpha]_D^{20}$ = +59.0 (*c* 0.6, MeOH) [lit.[10] $[\alpha]_D^{20}$ = +74 (*c* 0.9, MeOH) in 89% ee]; HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 80/20, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 9.9 min (major) and t_r = 11.1 min (minor).

1-Nitromethyl-1-(1-oxido-2-pyridinyl)propan-1-ol (4g). Brown oil, 25.7 mg, 61% yield, 9% ee; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, 1H, J = 6.4), 7.58 (s, 1H), 7.44–7.39 (m, 2H), 7.36–7.31 (m, 1H), 5.25 (d, 1H, J = 11.4), 5.02 (d, 1H, J = 11.4), 2.31–2.21 (m, 1H), 2.11–2.03 (m, 1H), 1.05 (t, 3H, J = 7.3).

1-Nitro-2-(pyridin-2-yl)propan-2-ol (6a). Brown oil, 19.6 mg, 54% yield, 85% ee; $[\alpha]_D^{20}$ = +35.2 (*c* 0.35, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.51 (d, 1H, J = 4.5), 7.76 (t, 1H, J = 7.1), 7.54 (d, 1H, J = 8.0), 7.26–7.23 (m, 1H), 4.99 (s, 1H), 4.95 (d, 1H, J = 12.3), 4.70 (d, 1H, J = 12.3), 1.62 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.9(C), 148.2(CH), 137.4(CH), 122.9(CH), 119.4(CH), 83.7(CH_2), 73.6(C), 26.6(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_8H_{10}N_2NaO_3^+$ $[M + Na]^+$: 205.0584, found: 205.0588. HPLC (CHIRALPAK IA column, hexane/2-propanol = 90/10, flow rate = 0.8 mL min^{-1}, detection at 254 nm), t_r = 12.1 min (major) and t_r = 13.5 min (minor).

1-Methyl-2-nitro-1-(4-methyl-2-pyridinyl)ethanol (6b). Brown oil, 23.7 mg, 60% yield, 72% ee; $[\alpha]_D^{20}$ = +28.2 (*c* 0.33, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.35 (d, 1H, J = 5.0), 7.34 (s, 1H), 7.05 (d, 1H, J = 4.9), 5.07 (s, 1H), 4.91 (d, 1H, J = 12.2), 4.69 (d, 1H, J = 12.2), 2.38 (s, 3H), 1.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.7(C), 148.8(CH), 147.8(C), 123.9(CH), 120.1(CH), 83.8(CH_2), 73.5(C), 26.5(CH_3), 21.2(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_9H_{13}N_2O_3^+$ $[M + H]^+$: 197.0921, found: 197.0925. HPLC (CHIRALPAK AS-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 14.9 min (major) and t_r = 12.7 min (minor).

1-Methyl-2-nitro-1-(5-methyl-2-pyridinyl)ethanol (6c). Brown oil, 18.8 mg, 48% yield, 36% ee; $[\alpha]_D^{20}$ = −10.6 (*c* 0.16, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.55 (d, 1H, J = 8.0), 7.41 (d, 1H, J = 8.1), 5.08 (s, 1H), 4.89 (d, 1H, J = 12.1), 4.68 (d, 1H, J = 12.1), 2.32 (s, 3H), 1.59 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.9(C), 148.4(CH), 137.9(CH), 132.5(C), 118.9(CH), 83.9(CH_2), 73.4(C), 26.5(CH_3), 18.0(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_9H_{13}N_2O_3^+$ $[M + H]^+$: 197.0921, found: 197.0926. HPLC (CHIRALPAK AS-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 16.7 min (major) and t_r = 14.8 min (minor).

1-Methyl-2-nitro-1-(6-methyl-2-pyridinyl)ethanol (6d). Brown oil, 15.3 mg, 39% yield, 71% ee; $[\alpha]_D^{20}$ = −30.4 (*c* 0.24, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62 (t, 1H, J = 7.7), 7.26 (d, 1H, J = 7.9), 7.08 (d, 1H, J = 7.6), 5.41 (s, 1H), 4.83 (d, 1H, J = 11.8), 4.66 (d, 1H, J = 11.8), 2.51 (s, 3H), 1.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.6(C), 157.1(C), 137.6(CH), 122.5(CH), 116.2(CH), 84.2(CH_2), 73.1(C), 26.4(CH_3), 24.2(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_9H_{12}N_2NaO_3^+$ $[M + Na]^+$: 219.0740, found: 219.0744. HPLC (CHIRALPAK AD-H column, hexane/2-propanol = 95/05, flow rate = 0.8 mL min^{-1}, detection at 254 nm), t_r = 10.5 min (major) and t_r = 11.2 min (minor).

1-Methyl-2-nitro-1-(5-bromo-2-pyridinyl)ethanol (6f). Brown oil, 26.6 mg, 51% yield, 86% ee; $[\alpha]_D^{20}$ = −37.3 (*c* 0.45, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.55 (d, 1H, J = 1.8), 7.87 (dd, 1H, J = 8.5, 2.2), 7.51 (d, 1H, J = 8.4), 5.01 (d, 1H, J = 12.8), 4.70 (d, 1H, J = 12.8), 4.56 (s, 1H), 1.57 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.1(C), 149.4(CH), 139.9(CH), 121.0(CH), 119.9(C), 83.0(CH_2), 73.9(C), 26.8(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_8H_9BrN_2NaO_3^+$ $[M + Na]^+$: 282.9689, found: 282.9697. HPLC (CHIRALPAK AS-H column, hexane/2-propanol = 90/10, flow rate = 1.0 mL min^{-1}, detection at 254 nm), t_r = 14.8 min (major) and t_r = 13.1 min (minor).

1-Nitromethyl-1-(2-pyridinyl)propan-1-ol (6g). Brown oil, 25.5 mg, 60% yield, 2% ee; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.49 (d, 1H, $J = 4.6$), 7.73 (t, 1H, $J = 7.7$), 7.47 (d, 1H, $J = 8.0$), 7.24–7.20 (m, 1H), 5.14 (s, 1H), 4.94 (d, 1H, $J = 12.2$), 4.71 (d, 1H, $J = 12.2$), 1.94–1.87 (m, 2H), 0.74 (t, 3H, $J = 7.4$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.4(C), 148.0(CH), 137.2(CH), 122.8(CH), 120.0(CH), 83.3(CH_2), 76.0(C), 32.1(CH_2), 7.1(CH_3). HRMS (ESI): *m*/*z* calc'd for $C_9H_{13}N_2O_3^+$ $[M + H]^+$: 197.0921, found: 197.0925.

1-Amino-2-(pyridin-2-yl) propan-2-ol (7). To a solution of **6a** (18.2 mg, 0.10 mmol) in MeOH (10 mL) was added 5% palladium/carbon (20 mg) and the mixture was stirred vigorously at rt under an hydrogen atmosphere for 16 h. The catalyst was removed using filtration through a short pad of Celite, the filtrate was purified using silica gel flash column chromatography (EtOAc/MeOH, 6 : 1) to give 12.3 mg (81%) of compound **7**. $[\alpha]_D^{20} = +26.7$ (*c* 0.21, MeOH) [lit.[10] $[\alpha]_D^{20} = +33$ (*c* 0.8, MeOH) in 86% ee]; ^{1}H-NMR (400 MHz, CD_3OD) δ 8.50 (d, 1H, $J = 4.4$), 7.81 (td, 1H, $J = 7.7, 1.4$), 7.68 (d, 1H, $J = 8.0$), 7.28–7.24 (m, 1H), 3.07 (d, 1H, $J = 13.2$), 2.89 (d, 1H, $J = 13.2$), 1.48 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 164.5(C), 147.9(CH), 137.1(CH), 121.9(CH), 120.0(CH), 74.6(C), 51.2(CH_2), 25.5(CH_3).

Conflicts of interest

There are no conflicts to declare.

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