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Asymmetric conjugate addition of thiols to (*E*)-3-crotonoyloxazolidin-2-one by iron or cobalt/pybox catalyst

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Abstract

The enantioselective conjugate addition of thiols to (*E*)-3-crotonoyloxazolidin-2-one was effectively catalyzed by the $Fe(BF_4)_2 \cdot 6H_2O$/(*S*,*S*)-*ip*-pybox catalyst, and the addition product was obtained with up to a 95% ee. Furthermore, the $Co(ClO_4)_2 \cdot 6H_2O$/(*S*,*S*)-*ip*-pybox catalyst also catalyzed the same reaction with a high enantioselectivity.

Keywords: Iron catalyst; Cobalt catalyst; Conjugate addition; Enantioselectivity; Thiol

1. Introduction

Conjugate addition is one of the most important bond forming reactions in synthetic organic chemistry, and several types of reactions including the asymmetric reaction of active methylene compounds have been attained using chiral Lewis acid catalysts or chiral organocatalysts.[1–3] On the other hand, the asymmetric conjugate addition of thiols to α,β-unsaturated substrates[4] is also a very useful reaction because it produces optically active compounds, such as pharmaceuticals.[5] However, even this type of reaction is a difficult process, and there are only limited examples of the transition metal-catalyzed enantioselective addition of thiols to (*E*)-3-crotonoyloxazolidin-2-one. The first example was reported by Kanemasa et al. in 1999; Ni/DBFOX catalyzed the highly enantioselective reactions of several thiols to (*E*)-3-crotonoyloxazolidin-2-one.[6] After their pioneering work, three groups independently demonstrated this kind of reaction using chiral Yb,[7] Hf,[8] and Sc[9] catalysts.

On the other hand, iron is one of the most abundant and environmentally friendly metals on the earth. During the past two decades, some efficient organic transformations, which were catalyzed by iron salts, were reported.[10] Most of these reports demonstrated carbon–carbon bond formations such as coupling, cycloaddition, or polymerization reactions. Our group also reported some iron-catalyzed reactions, i.e., cycloaddition reactions and Michael addition-type reactions in an organic or ionic liquid solvent system.[11] However, until recently, iron was relatively underrepresented in the field of asymmetric catalysts[12,13] compared to other transition metals for chiral complexes such as palladium, rhodium, ruthenium, etc. Therefore, we believe that the use of iron required for asymmetric organic syntheses and the enantioselective construction of the carbon–heteroatom bond is one of the most challenging topics in this field. From this perspective, the iron-catalyzed conjugate addition of thiols to α,β-unsaturated compounds still remains unresolved. Recently, we discovered that the iron/pybox catalyst exhibits a high enantioselectivity during the conjugate addition of thiols to the (*E*)-3-crotonoyloxazolidin-2-one.[14] During the course of this study, we found that a cobalt salt with a pybox ligand also catalyzes the same reaction with similar enantiomeric excesses. In this paper, we report the chiral iron and cobalt-catalyzed asymmetric conjugate addition of aromatic thiols to the (*E*)-3-crotonoyloxazolidin-2-one.

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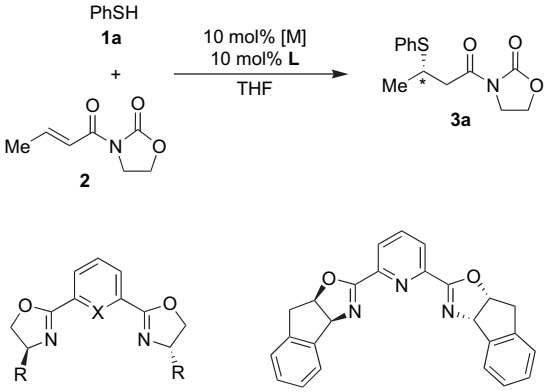
2. Results and discussion

2.1. Iron/pybox-catalyzed reaction

The screening of an effective iron catalyst for the conjugate addition of benzenethiol (**1a**) to (*E*)-3-crotonoyloxazolidin-2-one (**2**) was performed using various iron salts ($FeCl_2$, $FeCl_3$, $Fe(BF_4)_2$, $Fe(ClO_4)_2$, $Fe(ClO_4)_3$, $Fe(OAc)_2$, $Fe(acac)_2$, etc.), chiral ligands (BINAP, MOP, phox, pybox, box, Jacobsen ligand, etc.[15]), and solvents (toluene, THF, diethyl ether, dioxane, dichloromethane, acetonitrile, dimethylforamide, etc.). We discovered that the iron(II) salt with the bisoxazoline-based chiral ligand in THF exhibited a better reactivity and enantioselectivity than the other iron catalysts and solvents (Scheme 1).[16] For example, iron(II) chloride with the chiral (*S*,*S*)-*ip*-pybox ligand (**L1**)[17] gave the addition product **3a** in 79% yield with 53% ee (entry 1 in Table 1). On the other hand, iron(III) chloride with **L1** gave the product **3a** with 17% ee (entry 2). Based on these results, it is obvious that the iron(II) salts are promising catalysts for the asymmetric conjugate addition of thiol **1a** to the α,β-unsaturated amide **2**. Therefore, we attempted to evaluate the iron(II) salts, switching the catalyst from $FeCl_2$ to $Fe(ClO_4)_2\cdot 6H_2O$ increased the chemical yield of **3a** up to 90%, while the enantioselectivity significantly decreased to 40% ee (entry 3). Optimization of the iron(II) salts concluded that combination of iron(II) tetrafluoroborate $Fe(BF_4)_2\cdot 6H_2O$ with the (*S*,*S*)-*ip*-pybox ligand (**L1**) was the best catalyst, and the desired addition product **3a** was obtained in 74% yield with 66% ee (entry 4). Interestingly, the reaction using other chiral bisoxazoline-based ligands, such as (*S*,*S*)-*phe*-pybox (**L2**) and (*S*,*S*)-*ip*-phebox (**L3**), showed no enantioselectivity (entries 5 and 6). These results suggest that both the isopropyl group[18] in the pybox ligand and pyridyl backbone are essential for realizing a highly enantioselective reaction. Based on these results, we concluded that the chiral iron catalyst with (*S*,*S*)-*ip*-pybox (**L1**) is the most effective Lewis acid iron catalyst for the asymmetric conjugate addition of benzenethiol **1a** to **2**. The higher enantioselectivity (86% ee) was attained at a lower temperature (−20 °C), while the reaction rate significantly decreased and it took 150 h to complete the reaction (entry 7).



Scheme 1.

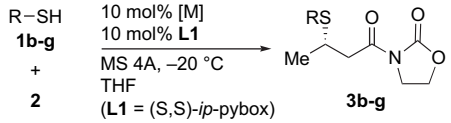
Table 1
Iron-catalyzed asymmetric conjugate addition of benzenethiol (**1a**) to (*E*)-3-crotonoyloxazolin-2-one (**2**)[a]

Entry	[Fe]	L	Additive	Temp/time (h)	Yield[b] (%)	ee[b,c] (%)
1	$FeCl_2$	**L1**	—	rt/24	79	53
2	$FeCl_3$	**L1**	—	rt/24	69	17
3	$Fe(ClO_4)_2\cdot 6H_2O$	**L1**	—	rt/24	90	40
4	$Fe(BF_4)_2\cdot 6H_2O$	**L1**	—	rt/24	74	66
5	$Fe(BF_4)_2\cdot 6H_2O$	**L2**	—	rt/24	92	0
6	$Fe(BF_4)_2\cdot 6H_2O$	**L3**	—	rt/24	95	0
7	$Fe(BF_4)_2\cdot 6H_2O$	**L1**	—	−20 °C/150	86	86
8	$Fe(BF_4)_2\cdot 6H_2O$	**L1**	MS 4 Å	−20 °C/24	86	90
9[d]	$Fe(BF_4)_2\cdot 6H_2O$	**L1**	MS 4 Å	−20 °C/72	93	90

[a] All reactions were carried out with **1a** (0.75 mmol), **2** (0. 50 mmol), 10 mol % iron salt, and 10 mol % chiral ligand in 0.8 mL of THF under nitrogen.
[b] Values for ee and yields are for pure, isolated compounds and are an average of two runs.
[c] Values of ee were determined by chiral HPLC using Daicel CHIRALPAK AD-H (hexane/2-propanol=5/1).
[d] [Fe] of 3 mol % and **L1** were used.

Fortunately a significant acceleration was obtained when the reaction was conducted in the presence of molecular sieves 4 Å,[19] and the enantioselectivity also slightly increased up to 90% ee (entry 8). Furthermore, it was found that the reaction proceeded with an excellent enantioselectivity using only 3 mol % of the catalyst, though a longer reaction time was needed (entry 9).

Results of the asymmetric conjugate addition of various types of thiols by this iron/*ip*-pybox catalyst system (Scheme 2) are summarized in Table 2. All reactions were carried out in the presence of $Fe(BF_4)_2\cdot 6H_2O$ (10 mol %), *ip*-pybox (10 mol %), and MS 4 Å in THF at −20 °C. The reactions of the aromatic thiols exhibited both high yields and enantiomeric excesses (Table 2, entries 1–5). The highest enantioselectivity (95% ee) was obtained for the reaction of the sterically hindered 2-methylbenzenethiol (**1d**) (entry 3). This type of steric effect on enantioselectivity was previously reported by Tomioka et al.[4a,b] It should be emphasized that an excellent enantioselectivity was obtained even when the reaction was performed using 3 mol % of the chiral iron catalyst, though it required a longer reaction time to complete the reaction (entry 6). Unfortunately, it was found that our catalyst system was not effective for the reaction of an alkyl thiol, such as benzyl mercaptan (**1g**), and it produced **3g** with only a 24% ee (entry 7).[20]



1b: R = *p*-Methoxyphenyl
1c: R = *p*-Chlorophenyl
1d: R = *o*-Tolyl
1e: R = *p*-Tolyl
1f: R = 2-Naphthyl
1g: R = Benzyl

Scheme 2.

Table 2
$Fe(BF_4)_2$/*ip*-pybox-catalyzed asymmetric conjugate addition of thiols **1b–g** to **2**[a]

Entry	1	Temp (°C)/time (h)	Yield[b] (%)	ee[b,c] (%)
1	**1b**	−20/24	84	85
2	**1c**	−20/24	99	87
3	**1d**	−20/108	92	95
4	**1e**	−20/24	87	90
5	**1f**	−20/72	96	89
6[d]	**1f**	−20/168	72	91
7	**1g**	−20/48	53	24

[a] All reactions were carried out with **1** (0.75 mmol), **2** (0.50 mmol), 10 mol % iron salt, 10 mol % chiral ligand, and MS 4 Å (17 mg) in 0.8 mL of THF under nitrogen.
[b] Values for ee and yields are for pure, isolated compounds and are an average of two runs.
[c] Values of ee were determined by chiral HPLC.
[d] $Fe(BF_4)_2 \cdot 6H_2O$ of 3 mol % and (*S*,*S*)-*ip*-pybox (**L1**) were used.

2.2. Cobalt/pybox-catalyzed reaction

During the course of the iron/pybox-catalyzed reaction, we found that a cobalt salt with a chiral ligand also catalyzes the same reaction with high enantiomeric excesses. Based on the results of the iron/pybox-catalyzed reaction, we examined several cobalt/pybox catalysts for the conjugate addition of **1a** to **2** (Scheme 1). As shown in Table 3, the trend in the enantioselectivity was very similar to the results for the iron/pybox-catalyzed reaction. Some cobalt salts exhibited a good reactivity and produced the addition product **3** in good isolated yield. However, the enantiomeric excess was lower than 34% ee when $Co(acac)_3$, $Co(acac)_2$, or CoI_2 was used (Table 3, entries 1–3). A higher enantiomeric excess (62% ee) was observed for the reaction using $Co(OAc)_2$, but the isolated yield was slightly lower (67%) (entry 4). Finally, we found that $Co(ClO_4)_2 \cdot 6H_2O$ with (*S*,*S*)-*ip*-pybox is the best combination, and **3a** was obtained in 91% yield with 62% ee (entry 5). Again, the addition of molecular sieves 4 Å (MS 4 Å) effectively increased the enantioselectivity up to 78% ee (entry 6). For this $Co(ClO_4)_2 \cdot 6H_2O$ catalyzed reaction, other pybox type ligands did not show any enantioselectivities similar to the iron-catalyzed reaction (entries 7–9). These results strongly suggest that both the pyridyl backbone and isopropyl group on the oxazoline ring are essential for realizing a high enantioselective reaction. To attain a much higher enantioselectivity, the reaction was conducted at a lower temperature (−20 °C), but both the reaction rate and enantioselectivity decreased. Fortunately, the addition of MS 4 Å again increased both these factors, and thus we succeeded in obtaining the addition product in 88% yield with 91% ee (entry 11). It was further found that the reaction proceeded without losing any enantioselectivity when a 5 mol % cobalt catalyst was used, though a longer reaction time (168 h) was needed (entry 12).

Table 3
Cobalt-catalyzed asymmetric conjugate addition of benzenethiol (**1a**) to (*E*)-3-crotonoyloxazolin-2-one (**2**)[a]

Entry	[Co]	L	Additive	Temp (°C)/time (h)	Yield[b] (%)	ee[c] (%)
1	$Co(acac)_3$	**L1**	None	25/24	64	28
2	$Co(acac)_2$	**L1**	None	25/24	68	34
3	CoI_2	**L1**	None	25/24	85	34
4	$Co(OAc)_2$	**L1**	None	25/24	67	62
5	$Co(ClO_4)_2 \cdot 6H_2O$	**L1**	None	25/24	91	66
6	$Co(ClO_4)_2 \cdot 6H_2O$	**L1**	MS 4 Å	25/24	97	78
7	$Co(ClO_4)_2 \cdot 6H_2O$	**L2**	None	25/24	74	0
8	$Co(ClO_4)_2 \cdot 6H_2O$	**L3**	None	25/24	96	0
9	$Co(ClO_4)_2 \cdot 6H_2O$	**L4**	None	25/24	71	0
10	$Co(ClO_4)_2 \cdot 6H_2O$	**L1**	None	−20/150	70	47
11	$Co(ClO_4)_2 \cdot 6H_2O$	**L1**	MS 4 Å	−20/72	88	91
12[d]	$Co(ClO_4)_2 \cdot 6H_2O$	**L1**	MS 4 Å	−20/168	86	90

[a] All reactions were carried out with **1a** (0.75 mmol), **2** (0.50 mmol), 10 mol % cobalt salt, and 10 mol % chiral ligand in 0.8 mL of THF under nitrogen unless otherwise noted.
[b] Isolated yield by silica gel column chromatography.
[c] Values of ee were determined by chiral HPLC using Daicel CHIRALPAK AD-H (hexane/2-propanol=5/1).
[d] $Co(ClO_4)_2 \cdot 6H_2O$ of 5 mol % and **L1** were used.

We also examined the reaction with various types of thiols using this cobalt/*ip*-pybox catalyst system (Scheme 2), and these results are summarized in Table 4. All reactions were carried out with a 10 mol % catalyst at −20 °C, and the reaction was monitored by TLC. The reactions of several aromatic thiols smoothly proceeded, and the addition products were obtained with over 85% yields (Table 4, entries 1–5). However, we found that the enantioselectivity was strongly affected by the electronic effects of the substituent on the aromatic ring. The reaction with 4-methoxybenzenethiol (**1b**) gave a result similar to the reaction with **1a**, but the enantioselectivity for the reaction with 4-chlorophenylbenzenethiol (**1c**) decreased to 40% ee (entries 1 and 2). Other aromatic thiols, such as 2-naphthylthiol (**1f**) and 4-methylbenzenethiol (**1e**), also exhibited both high yields and enantiomeric excesses (entries 3 and 4). The highest enantioselectivity (95% ee) was obtained for the reaction of the sterically hindered 2-methylbenzenethiol (**1d**), though it required a longer reaction time (144 h) to complete the reaction (entry 5). Unfortunately, it was found that this cobalt catalyst system was not effective for the reaction of an alkyl thiol, such as benzyl mercaptan (**1g**), and it produced only a 39% product with 0% ee (entries 6 and 7).

Table 4
Cobalt/pybox-catalyzed asymmetric conjugate addition of thiols **1b–g** to **2**[a]

Entry	1	Temp (°C)/time (h)	Yield[b] (%)	ee[c] (%)
1	**1b**	−20/96	85	91
2	**1c**	−20/72	90	40
3	**1f**	−20/120	88	87
4	**1e**	−20/96	87	88
5	**1d**	−20/144	85	95
6	**1g**	−20/48	0	—
7	**1g**	25/24	39	0

[a] All reactions were carried out with **1** (0.75 mmol), **2** (0.50 mmol), $Co(ClO_4)_2 \cdot 6H_2O$ (0.05 mmol), (*S*,*S*)-*ip*-pybox (0.05 mmol), and MS 4 Å (19 mg) in 0.8 mL of THF under nitrogen.
[b] Isolated yield by silica gel column chromatography.
[c] Values of ee were determined by chiral HPLC: Daicel CHIRALCEL OD-H (hexane/2-propanol=19/1) for **3b** and **3d–g**; Daicel CHIRALPAK AD-H (hexane/2-propanol=5/1) for **3c**.

3. Conclusion

In conclusion, we succeeded in demonstrating the iron or cobalt salt-catalyzed asymmetric conjugate addition of thiols

with α,β-unsaturated amide; both the iron and cobalt catalysts, which were prepared from $Fe(BF_4)_2 \cdot 6H_2O$ or $Co(ClO_4)_2 \cdot 6H_2O$ with the (*S*,*S*)-*ip*-pybox ligand, respectively, exhibited excellent enantioselectivities and the desired addition products were obtained in good yields.

4. Experimental section

4.1. General methods

All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5. NMR spectra were recorded on a JEOL JNM MH400 spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C) or JNM MH 500 spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. All iron salts and chiral ligands include $Fe(BF_4)_2 \cdot 6H_2O$, $Co(ClO_4)_2 \cdot 6H_2O$, 2,6-bis[(4*S*)-(−)-isopropyl-2-oxazolin-2-yl]pyridine {(*S*,*S*)-*ip*-pybox, **L1**}, 2,6-bis[(4*S*)-(−)-phenyl-2-oxazolin-2-yl]pyridine {(*S*,*S*)-*phe*-pybox, **L2**}, and (−)-2,6-bis[2-{3a*S*-(2(3′a*R**,8′a*S**),3aa,8aa)-3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole}]pyridine {*inda*-pybox (**L4**)} were purchased from Aldrich, and used without further purification. The following thiols are commercially available: thiophenol; *o*-tolylthiol; *p*-tolylthiol; *p*-methoxythiophenol; *p*-chlorothiophenol; 2-naphthylthiol; benzylthiol. (*E*)-3-Crotonoyloxazolin-2-one (**2**)[21] and 1,3-bis[(4*S*)-isopropyl-2-oxazolin-2-yl]benzene {(*S*,*S*)-*ip*-phebox (**L3**)}[22] were prepared according to the literatures. Other reagents and solvents were purchased from common commercial sources and were used as received or purified by distillation from appropriate drying agents.

4.2. General procedure of iron-catalyzed conjugate addition of thiols to (E)-3-crotonoyloxazolin-2-one (entry 8 in Table 1)

The reaction conditions and results are shown in Tables 1 and 2. A typical procedure is given for the reaction of (−)-(*S*)-3-(3-phenylthiobutanoyl)-2-oxazolidinone (**3a**) (Table 1, entry 8). To a solution of $Fe(BF_4)_2 \cdot 6H_2O$ (16.9 mg, 0.05 mmol), (*S*,*S*)-*ip*-pybox (15.1 mg, 0.05 mmol), (*E*)-3-crotonoyl-2-oxazolidinone (**2**) (77.6 mg, 0.50 mmol), and MS 4 Å (17 mg) in THF (0.8 mL) was added benzenethiol (**1a**) (78 mg, 0.75 mmol), then stirred at −20 °C for 24 h. The reaction mixture was quenched with satd NH_4Cl, then extracted with THF (3×2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=7/3) to give 114 mg (86%) of product **3a**. The enantiomeric purity was determined by chiral HPLC analysis with a chiral stationary phase column.

4.2.1. (−)-(S)-3-(3-Phenylthiobutanoyl)-2-oxazolidinone (3a)[6]

^1H NMR (400 MHz, $CDCl_3$) 1.36 (d, *J*=6.6 Hz, 3H), 3.14 (dd, *J*=17.2, 7.0 Hz, 1H), 3.27 (dd, *J*=16.9, 7.0 Hz, 1H), 3.74−3.82 (m, 1H), 3.90−4.01 (m, 2H), 4.33−4.44 (m, 2H), 7.23−7.33 (m, 3H), 7.44−7.47 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) 21.17, 38.86, 42.20, 42.33, 61.98, 127.25, 128.80, 132.68, 134.00, 153.27, 170.90. Colorless oil; $[\alpha]_D^{24}$ −12.70 (*c* 1.26, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −11.05 (*c* 1.23, $CHCl_3$)} {90% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALPAK AD-H, hexane/*i*-PrOH=5/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=11 min, t_R(*S*)=16 min)}.

4.2.2. (−)-(S)-3-[3-(p-Methoxyphenylthio)butanoyl]-2-oxazolidinone (3b)[6]

^1H NMR (400 MHz, $CDCl_3$) 1.30 (d, *J*=6.8 Hz, 3H), 3.06 (dd, *J*=17.0, 7.0 Hz, 1H), 3.24 (dd, *J*=16.8, 7.0 Hz, 1H), 3.58−3.61 (m, 1H), 3.80 (s, 3H), 3.96 (t, *J*=7.9 Hz, 2H), 4.37 (t, *J*=7.9 Hz, 2H), 6.85 (d, *J*=8.8 Hz, 2H), 7.43 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) 21.09, 39.84, 42.19, 42.38, 55.27, 62.01, 114.34, 123.80, 136.24, 153.30, 159.72, 171.08. Colorless oil; $[\alpha]_D^{25}$ −6.70 (*c* 2.13, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −5.95 (*c* 2.05, $CHCl_3$)} {86% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALCEL OD-H, hexane/*i*-PrOH=9/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=34 min, t_R(*S*)=40 min)}.

4.2.3. (−)-(S)-3-[3-(p-Chlorophenylthio)butanoyl]-2-oxazolidinone (3c)[9b]

^1H NMR (500 MHz, $CDCl_3$) 1.35 (d, *J*=6.9 Hz, 3H), 3.12 (dd, *J*=17.0, 6.9 Hz, 1H), 3.26 (dd, *J*=17.0, 6.9 Hz, 1H), 3.71−3.76 (m, 1H), 3.96−3.99 (d, *J*=7.8 Hz, 2H), 4.40 (t, *J*=7.8 Hz, 2H), 7.27 (d, *J*=7.6 Hz, 2H), 7.39 (d, *J*=7.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 21.16, 39.24, 42.17, 42.40, 62.06, 129.02, 132.54, 133.57, 134.21, 153.31, 170.84. Colorless powder; $[\alpha]_D^{25}$ −16.47 (*c* 2.15, $CHCl_3$) {lit.[9b] $[\alpha]_D^{20}$ −21 (*c* 1.0, CH_2Cl_2)} {87% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALPAK AD-H, hexane/*i*-PrOH=5/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=19 min, t_R(*S*)=23 min)}.

4.2.4. (−)-(S)-3-(3-o-Tolylthiobutanoyl)-2-oxazolidinone (3d)[6]

^1H NMR (500 MHz, $CDCl_3$) 1.35 (d, *J*=6.9 Hz, 3H), 2.41 (s, 3H), 3.13 (dd, *J*=17.0, 6.9 Hz, 1H), 3.24 (dd, *J*=17.0, 6.9 Hz, 1H), 3.74−3.78 (m, 1H), 3.89 (t, *J*=7.8 Hz, 2H), 4.33 (t, *J*=7.8 Hz, 2H), 7.12−7.19 (m, 3H), 7.41−7.43 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 20.78, 21.10, 38.24, 42.34, 42.36, 62.01, 126.27, 127.24, 130.31, 132.68, 133.68, 140.36, 153.29, 171.01. Colorless oil; $[\alpha]_D^{26}$ −29.95 (*c* 2.13, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −30.33 (*c* 2.09, $CHCl_3$)} {95% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALCEL OD-H, hexane/*i*-PrOH=19/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=32 min, t_R(*S*)=45 min)}.

4.2.5. (−)-(S)-3-(3-p-Tolylthiobutanoyl)-2-oxazolidinone (3e)[6]

^1H NMR (500 MHz, $CDCl_3$) 1.26 (d, *J*=6.9 Hz, 3H), 2.25 (s, 3H), 3.03 (dd, *J*=17.0, 6.9 Hz, 1H), 3.17 (dd, *J*=17.0, 6.9 Hz, 1H), 3.59−3.64 (m, 1H), 3.88 (t, *J*=7.8 Hz, 2H), 4.30 (t,

J=7.8 Hz, 2H), 7.04 (d, J=7.8 Hz, 2H), 7.29 (d, J=7.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 21.03, 21.16, 39.24, 42.22, 42.37, 62.00, 129.59, 130.04, 133.56, 137.61, 153.28, 171.03. Colorless oil; $[\alpha]_D^{24}$ −17.74 (*c* 2.65, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −20.85 (*c* 2.67, $CHCl_3$)} {90% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALCEL OD-H, hexane/*i*-PrOH=19/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=37 min, t_R(*S*)=46 min)}.

4.2.6. (−)-(S)-3-[3-(2-Naphthylthio)butanoyl]-2-oxazolidinone (3f)[6]

^{1}H NMR (500 MHz, $CDCl_3$) 1.41 (d, J=6.9 Hz, 3H), 3.17 (dd, J=17.0, 6.6 Hz, 1H), 3.34 (dd, J=17.0, 6.6 Hz, 1H), 3.84 (t, J=7.8 Hz, 2H), 3.85−3.94 (m, 1H), 4.25 (t, J=7.8 Hz, 2H), 7.45−7.54 (m, 3H), 7.76−7.81 (m, 3H), 7.94 (d, J=1.79 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) 21.29, 39.00, 42.32, 42.44, 61.94, 126.22, 126.49, 127.44, 127.60, 128.37, 130.16, 131.47, 131.61, 132.35, 133.53, 153.27, 170.96. Colorless powder; $[\alpha]_D^{25}$ −17.5 (*c* 2.86, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −17.27 (*c* 2.90, $CHCl_3$)} {89% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALCEL OD-H, hexane/*i*-PrOH=19/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=50 min, t_R(*S*)=59 min)}.

4.2.7. (−)-(S)-3-(3-Benzylthiobutanoyl)-2-oxazolidinone (3g)[6]

^{1}H NMR (500 MHz, $CDCl_3$) 1.33 (d, J=6.4 Hz, 3H), 3.03−3.07 (m, 1H), 3.22−3.29 (m, 2H), 3.77 (d, J=13.3 Hz, 1H), 3.80 (d, J=13.3 Hz, 1H), 3.93−3.99 (m, 2H), 4.33−4.37 (m, 2H), 7.20−7.34 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) 21.48, 35.14, 35.46, 42.27, 42.31, 61.93, 126.79, 128.32, 128.72, 138.30, 153.26, 170.80. Colorless oil; $[\alpha]_D^{20}$ −5.87 (*c* 2.25, $CHCl_3$) {lit.[6] $[\alpha]_D^{25}$ −3.77 (*c* 2.28, $CHCl_3$)} {17% ee estimated on the basis of the HPLC using a chiral column (Daicel CHIRALCEL OD-H, hexane/*i*-PrOH=19/1 v/v, flow rate=1.0 mL/min, t_R(*R*)=48 min, t_R(*S*)=58 min)}.

4.3. General procedure of cobalt-catalyzed conjugate addition of thiols to (E)-3-crotonoyloxazolin-2-one (entry 11 in Table 3)

The reaction conditions and results are shown in Tables 3 and 4. A typical procedure is given for the reaction of (−)-(*S*)-3-(3-phenylthiobutanoyl)-2-oxazolidinone (**3a**) (Table 3, entry 11). To a solution of $Co(ClO_4)_2\cdot 6H_2O$ (18.4 mg, 0.05 mmol), (*S*,*S*)-*ip*-pybox (15.1 mg, 0.05 mmol), (*E*)-3-crotonoyl-2-oxazolidinone (**2**) (78 mg, 0.50 mmol), and MS 4 Å (17 mg) in THF (0.8 mL) was added benzenethiol (**1a**) (78 mg, 0.75 mmol) at −20 °C, then stirred for 72 h. The reaction mixture was quenched with satd NH_4Cl, then extracted with ether (3×2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=7/3) to give 117 mg (88%) of a mixture of conjugate adducts **3a**. The enantiomeric purity was determined by chiral HPLC analysis with a chiral stationary phase column (Daicel CHIRALPAK AD-H).

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