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Asymmetric 1,3-Dipolar Cycloaddition Reactions of Nitrile Oxides Catalyzed by Chiral Binaphthyldiimine-Ni(II) Complexes

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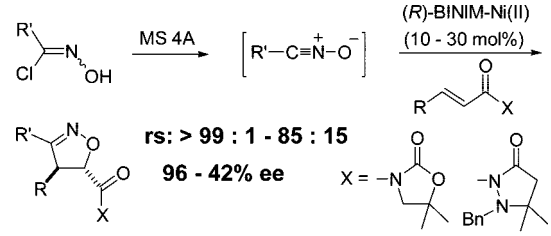

Asymmetric cycloaddition reactions between several nitrile oxides and 3-(2-alkenoyl)-2-oxazolidinones and 2-(2-alkenoyl)-3-pyrazolidinone derivatives were carried out in the presence of chiral binaphthyldiimine (BINIM)-Ni(II) complexes as catalysts. Using (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (30 mol %), good regioselectivity (4-Me/5-Me = 85:15) along with high enantioselectivity (96% ee) of the 4-Me adduct were obtained for the reaction between isolable 2,4,6-trimethylbenzonitrile oxide and 3-crotonoyl-5,5-dimethyl-2-oxazolidinone. Substituted and unsubstituted benzonitrile oxides and aliphatic nitrile oxides, which were generated from the corresponding hydroximoyl chloride in the presence of MS 4Å, were reacted with 3-crotonoyl-5,5-dimethyl-2-oxazolidinone, 5,5-dimethyl-3-(2-pentenoyl)-2-oxazolidinone, 5,5-dimethy-3-[3-(ethoxycarbonyl)propenoyl]-2-oxazolidinone, 1-benzyl-2-crotonoyl-5,5-dimethyl-3-pyrazolidinone, and 1-benzyl-2-[3-(ethoxycarbonyl)propenoyl]-5,5-dimethy-3-pyrazolidinone in the presence of (*R*)-BINIM-4Ph-2QN-Ni(II) or (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complexes (10−30 mol %) as catalysts to give the corresponding cycloadducts in high yields, with high regioselectively (4-R/5-R = 85:15−99:1) and with moderate to high enantioselectivities (42−95% ee) of the 4-R adducts. Higher enantioselectivities and regioselectivities were obtained for the reactions using pyrazolidinone derivatives as the dipolarophiles. For the cycloadditions of 2-(2-alkenoyl)-1-benzyl-5,5-dimethyl-3-pyrazolidinones catalyzed by (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (30 mol %), the enantioselectivity varied from 75% to 95% ee. The reactions between several nitrile oxides and 2-acryloyl-1-benzyl-5,5-dimethyl-3-pyrazolidinone in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (10 mol %) resulted in enantioselectivities (79−91% ee) that exceed those of previously reported enantioselective cycloadditions of acrylic acid derivatives. Furthermore, studies using a molecular modeling program using PM3 calculations were carried out to gain insight into the mechanisms of the asymmetric induction.

Introduction

From a synthetic point of view, nitrones and nitrile oxides can serve as highly useful 1,3-dipoles[1] because they allow the construction of chiral centers that bear nitrogen and oxygen functionalities in the cycloaddition step, while offering a facile reductive cleavage of the N−O bond of the cycloadducts. Accordingly, their use allows the synthesis of biologically important natural products containing several chiral centers.[1b−e] Classical diastereoselective cycloaddition procedures involving nitrones and nitrile oxides have been extensively studied and have resulted in the development of numerous successful

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methods.[1b−e] Efficient syntheses of chiral compounds using such methodologies, however, require the development of catalytic asymmetric cycloaddition reactions. For nitrones, numerous cycloadditions that are catalyzed by chiral Lewis acids have been developed during the past decade.[1c−e,2−4] For nitrile oxides, Ukaji and Inomata have developed the enantioselective cycloaddition with allylic alcohols using chiral zinc catalysts; presumably, the reaction involves an active dinuclear zinc species consisting of an allylic alcohol, a nitrile oxide, and chiral ligands.[5] To the best of our knowledge, however, only a few examples have been reported for the cycloaddition between nitrile oxides and electron-deficient olefins catalyzed by a chiral Lewis acid.

Recently, Sibi reported on the successful reaction (79−99% ee) using (2-alkenoyl)-3-pyrazolidinone derivatives featuring an aminoindanol-derived bisoxazoline-Mg(II) complex as the chiral Lewis acid catalyst. Although excellent enantioselectivity was obtained using 30 mol % of the catalyst,[6] lowering the catalytic loading from 30 to 10 to 5 mol % reduced both the regio- and the enantioselectivities of the reaction. For cycloadditions involving acrylic acid derivative as the dipolarophiles, Yamamoto was able to obtain good asymmetric induction (87% ee) for the reaction between benzonitrile oxide and *N*-acryloyl-2-imidazolidinone using the (*S*)-Pybox-*i*-Pr-Mg(II) complex (1 equiv).[7] More recently, for cycloadditions between nitrile oxides and methacrolein, Kündig has reported a highly enantiomeric reaction (93% ee, 60% yield) using *p*-trifluoromethylbenzonitrile oxide and a chiral ruthenium Lewis acid catalyst (5 mol %); unfortunately, other nitrile oxides exhibited only moderate enantioselectivities (60−76% ee).[8] Difficulty in obtaining successful asymmetric induction of the chiral Lewis acid catalyzed nitrile oxide cycloadditions may be owing to the instability of nitrile oxides, which are generally prepared in situ via treatment of a basic reagent, and the high donor ability of oxygen atom of the dipole. Structurally, in contrast to the bent structure of nitrones, the enantio-face of nitrile oxides is also obscured by its linear structure in the asymmetric induction step. The development of an efficient chiral Lewis acid catalyst, therefore, remains a challenging objective for the asymmetric cycloadditions of nitrile oxides and other unstable 1,3-dipoles.

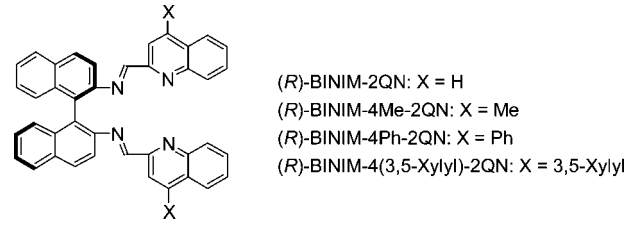
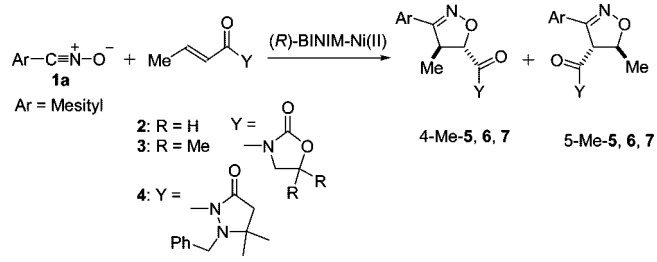


FIGURE 1. Structures of the BINIM ligands.

SCHEME 1. Reactions of 2,4,6-Trimethylbenzonitrile Oxide (1a) with Olefins 2, 3, or 4 Catalyzed by (*R*)-BINIM-Ni(II) Complexes



Recently, we reported on the effective use of chiral catalysts consisting of $Ni(ClO_4)_2 \cdot 6H_2O$ and chiral binaphthyldiimine (BINIM) ligands in achieving high levels of asymmetric induction in Diels−Alder reactions;[9a,b] 1,3-dipolar cycloadditions of nitrones,[9c] azomethine imines,[9d] and carbonyl ylides;[9e] and Michael additions of silyloxyfurans.[9f] To extend the scope of our chiral BINIM-Ni(II) catalysts toward other 1,3-dipolar cycloaddition reactions, our catalyst system was employed for the asymmetric cycloadditions of nitrile oxides. Herein, we describe the successful application of BINIM-Ni(II) complexes as chiral Lewis acid catalysts for the enantioselective cycloaddition of nitrile oxides with 3-(2-alkenoyl)-5,5-dimethyl-2-oxazolidinones and 2-(2-alkenoyl)-1-benzyl-5,5-dimethyl-3-pyrazolidinones.

Results and Discussion

Cycloaddition Reaction of 2,4,6-Trimethylbenzonitrile Oxide. Initially, the reactions of isolable 2,4,6-trimethylbenzonitrile oxide (**1a**) with 3-crotonoyl-2-oxazolidinone (**2**) in the presence of complexes consisting of quinoline-based BINIMs (Figure 1) and $Ni(ClO_4)_2 \cdot 6H_2O$ were investigated. The complexes were prepared by stirring the BINIM ligands, $Ni(ClO_4)_2 \cdot 6H_2O$, and 4Å molecular sieves (MS 4Å) in CH_2Cl_2 at room temperature for 6 h. The subsequent cycloaddition reactions between nitrile oxide **1a** and oxazolidinone **2** were carried out by stirring at room temperature (Scheme 1, Table 1, entries 2−4). In contrast to the cycloaddition reaction in the absence of the Lewis acid catalyst (entry 1), the presence of (*R*)-BINIM-4Ph-2QN-Ni(II) complex (10 mol %) (entry 2) favored the formation of the 4-Me cycloadduct; however, the resulting regioselectivity was moderate (62:38). Increasing the catalyst loading to 30 mol % (entry 3) improved the yield and regioselectivity (91:9), while the enantioselectivity remained

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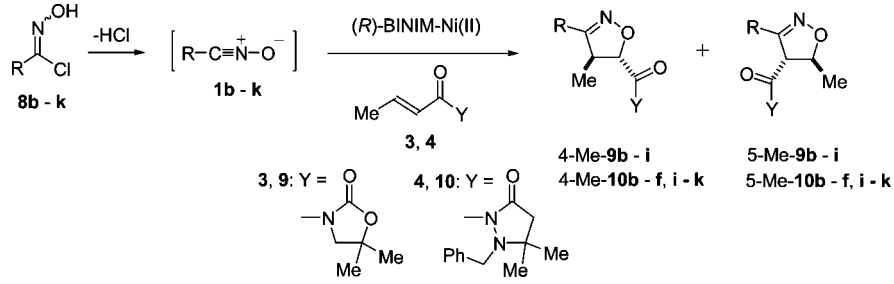
TABLE 1. Reactions of 2,4,6-Trimethylbenzonitrile Oxide (1a) with Olefins 2, 3, or 4 Catalyzed by (*R*)-BINIM-Ni(II) Complexes[a]

entry	mol %[b]	X(BINIM ligand)	olefin	time (h)	product	yield (%)	rs[c]	ee[d] (%)
1	none		**2**	118	**5**	74	29:71	
2	10	Ph (BINIM-4Ph-2QN)	**2**	64	**5**	66	62:38	62
3	30	Ph (BINIM-4Ph-2QN)	**2**	41	**5**	84	91:9	65
4	30	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**2**	51	**5**	81	90:10	73
5	30	Ph (BINIM-4Ph-2QN)	**3**	48	**6**	78	75:25	79
6	30	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**3**	50	**6**	80	85:15	96
7	10	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**4**	39	**7**	78	99:1	76
8	30	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**4**	39	**7**	94	99:1	92

[a] Reactions were carried out by stirring nitrile oxide **1a** with olefins **2**, **3**, or **4** (1 equiv) at rt in CH_2Cl_2 in the presence of (*R*)-BINIM-Ni(II) complexes. [b] Catalyst loading of (*R*)-BINIM-Ni(II) complexes. [c] Regioselectivity of cycloadducts (4-Me/5-Me). [d] Enantiomeric excess of the 4-Me adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$.

SCHEME 2. (*R*)-BINIM-Ni(II)-Catalyzed Reactions of Nitrile Oxides Generated from Hydroximoyl Chlorides with Olefins 3 or 4



unchanged. As a note, the enantioselectivity was determined by HPLC analysis (Daicel Chiralpak AD-H) after conversion of the 4-Me cycloadduct to the corresponding alcohol via reduction using $NaBH_4$ in THF/H_2O (see Experimental Section). The use of (*R*)-BINIM-4(3,5-xylyl)-2QN ligand, which possesses a bulky 3,5-xylyl substituent at the 4-position of the quinoline rings, exhibited enantioselectivity (73% ee) higher than that using the 4-Ph ligand (entry 4). In the case of the (*R*)-BINIM-4Ph-2QN-Ni(II)-catalyzed reaction of 3-crotonoyl-5,5-dimethyl-2-oxazolidinone (**3**) as the dipolarophile (entry 5), despite the slightly lower regioselectivity, higher enantioselectivity was obtained (entries 3 vs 5). To our delight, the reaction of oxazolidinone **3** in combination with the (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) catalyst resulted in an extremely high enantioselectivity (96% ee) for the 4-Me cycloadduct (entry 6). In the case of 1-benzyl-2-crotonoyl-5,5-dimethyl-3-pyrazolidinone (**4**) as the dipolarophile (entry 8), the reaction under similar conditions resulted in a slightly lower enantioselectivity (92% ee), but with high regioselectivity (99:1) of the 4-Me cycloadduct. Decreasing the catalyst loading to 10 mol % lowered the enantioselectivity even further (entry 7).

Cycloaddition Reaction of Benzonitrile Oxide. Next, reactions between olefin **3** and benzonitrile oxide (**1b**), which was generated in situ from the corresponding hydroximoyl chloride **8b**, were carried out in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (30 mol %) (Scheme 2, Table 2). When an equimolar amount of diisopropylethylamine (DIEA) (relative to hydroximoyl chloride **8b**) was employed during the generation of benzonitrile oxide **1b**, asymmetric induction for the 4-Me-**9b** cycloadduct was not observed (entry 1). Fortunately, decreasing the amount of DIEA to 10 or 5 mol % dramatically favored the formation of 4-Me-**9b**, with promising enantioselectivity ratios (entries 2 and 3), along with increased yields of the cycloadducts. Surprisingly, the reaction in the absence of DIEA (entry 4) also afforded the cycloadduct with similar yields as that in entry 3, along with high regioselectivity (96:4) and good enantioselectivity (89% ee). Kim has reported that molecular sieves, in the presence of dipolarophiles, can convert hydroximoyl chlorides into nitrile oxides, which then afford the cycloaddition products in good yields.[10] Similarly, the cycloaddition of crotonoyloxazolidinone **3** in the presence of MS 4Å (using the same amount as in the preparation of the BINIM-Ni(II) complex) and in the absence of the BINIM-Ni(II) complex at room temperature in CH_2Cl_2 for 54 h afforded the cycloadducts in 84% yield (4-Me/5-Me = 55:45).

The use of the BINIM-Ni(II) catalyst dramatically improved the regioselectivity, along with providing a slightly faster reaction rate. A survey of the BINIM ligands (entries 4−7) revealed that (*R*)-BINIM-4Ph-2QN was the most effective in terms of the enantioselectivity of the 4-Me cycloadduct (90% ee, entry 7). It is noteworthy that the use of 10 mol % of the (*R*)-BINIM-4Ph-2QN-Ni(II) catalyst afforded the cycloadduct in a high yield, with regioselectivity (93:7) comparable to that using 30 mol % of the catalyst and without a significant loss of enantioselectivity (89% ee) (entry 9).

In the case of 2-crotonoyl-1-benzyl-5,5-dimethyl-3-pyrazolidinone (**4**) (entry 10), which has exhibited excellent enantioselectivities in several cycloadditions including those with nitrile oxide,[6,11] the reaction with benzonitrile oxide proceeded smoothly in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) (30 mol %) to give the cycloadduct with high regioselectivity (99:1) and enantioselectivity (95% ee), as compared to those of oxazolidinone **3**. Decreasing the catalyst loading to 10 mol % (entry 11) did not significantly affect the enantioselectivity (91% ee) nor the regioselectivity (99:1).

Cycloaddition Reactions of Other Nitrile Oxides with Crotonoyloxazolidinone 3. To investigate the generality of our

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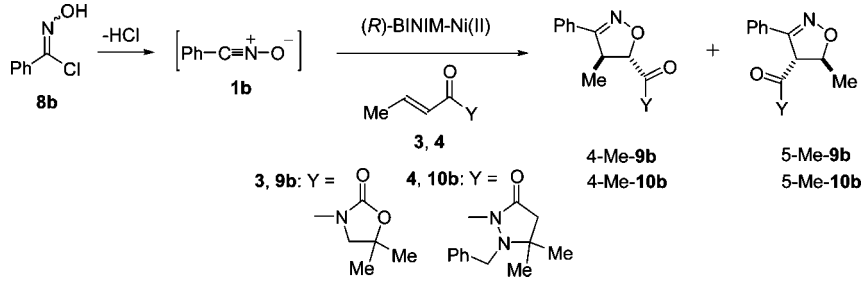
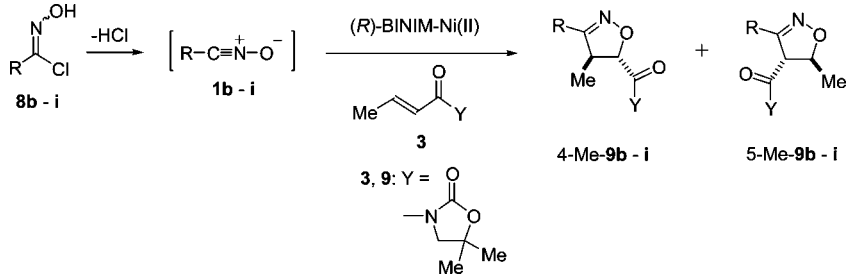
TABLE 2. Reactions of Benzonitrile Oxide (1b) with Olefins 3 or 4 Catalyzed by (*R*)-BINIM-Ni(II) Complexes[a]



entry	DIEA[b] (mol %)	X (BINIM ligand)	olefin	temp (°C)	time (h)	yield (%)	rs[c]	ee[d] (%)
1	100	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**3**	rt	14	39	55:45	0
2	10	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**3**	rt	26	58	93:7	86
3	5	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**3**	rt	26	70	95:5	88
4	none	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**3**	rt	29	74	96:4	89
5	none	H (BINIM-2QN)	**3**	rt	24	81	91:9	77
6	none	Me (BINIM-4Me-2QN)	**3**	rt	24	95	92:8	83
7	none	Ph (BINIM-4Ph-2QN)	**3**	rt	24	99	93:7	90
8	none	Ph (BINIM-4Ph-2QN)	**3**	0	120	74	96:4	90
9[e]	none	Ph (BINIM-4Ph-2QN)	**3**	rt	52	93	93:7	89
10	none	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**4**	rt	24	94	99:1	95
11[e]	none	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	**4**	rt	24	90	99:1	91
12[e]	none	Ph (BINIM-4Ph-2QN)	**4**	rt	24	96	99:1	87

[a] Reactions were carried out by stirring hydroximoyl chloride **8b** (2 equiv) with olefins **3** or **4** at rt in CH_2Cl_2 in the presence of (*R*)-BINIM-Ni(II) complexes and MS 4Å. [b] The mol % of DIEA relative to hydroximoyl chloride **8b**. [c] Regioselectivity of cycloadducts (4-Me/5-Me). [d] Enantiomeric excess of the 4-Me adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$. [e] 10 mol % of catalyst was used.

TABLE 3. Reactions of Hydroximoyl Chloride 8b−8i with Olefin 3 Catalyzed by (*R*)-BINIM-4Ph-2QN-Ni(II) Complex[a]

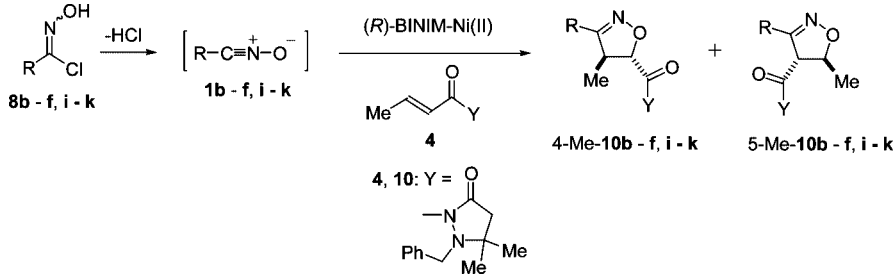


entry	R	**8**	mol %	time (h)	product **9**	yield (%)	rs[b]	ee[c] (%)
1	Ph	**8b**	30	24	**9b**	99	93:7	90
2	Ph	**8b**	10	52	**9b**	93	93:7	89
3	*p*-$MeOC_6H_4$	**8c**	30	16	**9c**	91	95:5	92
4	*p*-$MeOC_6H_4$	**8c**	10	43	**9c**	84	88:12	83
5	*p*-MeC_6H_4	**8d**	30	20	**9d**	87	95:5	91
6	*p*-MeC_6H_4	**8d**	10	29	**9d**	88	90:10	85
7	*p*-ClC_6H_4	**8e**	30	24	**9e**	78	86:14	84
8	*p*-ClC_6H_4	**8e**	10	27	**9e**	55	88:12	76
9	*o*-ClC_6H_4	**8f**	30	24	**9f**	quant	90:10	83
10	*o*-ClC_6H_4	**8f**	10	22	**9f**	quant	86:14	75
11	*p*-$NO_2C_6H_4$	**8g**	30	48	**9g**	48	90:10	78
12	*p*-$NO_2C_6H_4$	**8g**	10	66	**9g**	60	87:13	62
13	*p*-NCC_6H_4	**8h**	30	48	**9h**	60	90:10	73
14	*p*-NCC_6H_4	**8h**	10	66	**9h**	71	85:15	54
15	*i*-Bu	**8i**	30	13	**9i**	82	93:7	72
16	*i*-Bu	**8i**	10	48	**9i**	91	87:13	51

[a] Reactions were carried out by stirring hydroximoyl chloride **8b−8i** (2 equiv) with olefin **3** at rt in CH_2Cl_2 in the presence of the (*R*)-BINIM-4Ph-2QN-Ni(II) complexes and MS 4Å. [b] Regioselectivity of the cycloadducts (4-Me/5-Me). [c] Enantiomeric excess of the 4-Me adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$.

catalyst toward other nitrile oxides, reactions between several substituted benzohydroximoyl chlorides and crotonoyloxazolidinone **3** were carried out (Scheme 2, Table 3). Using the (*R*)-BINIM-4Ph-2QN-Ni(II) catalyst (30 mol %), the cycloadditions of the substituted benzonitrile oxides afforded the corresponding cycloadducts with high regioselectivities (86:14−94:6), along with moderate to high enantioselectivities (73−92% ee) of the 4-Me cycloadducts (entries 3, 5, 7, 9, 11, and 13). The enantioselectivities for the benzonitrile oxides with electron-withdrawing substituents were slightly lower (entries 7−14) than those for the unsubstituted benzonitrile oxide (entries 1 and 2) or with electron-releasing substituents (*p*-methoxy, entries 3 and 4; *p*-methyl groups, entries 5 and 6). The cycloaddition between aliphatic nitrile oxide **1i** (R = *i*-Bu) and oxazolidinone **3** also

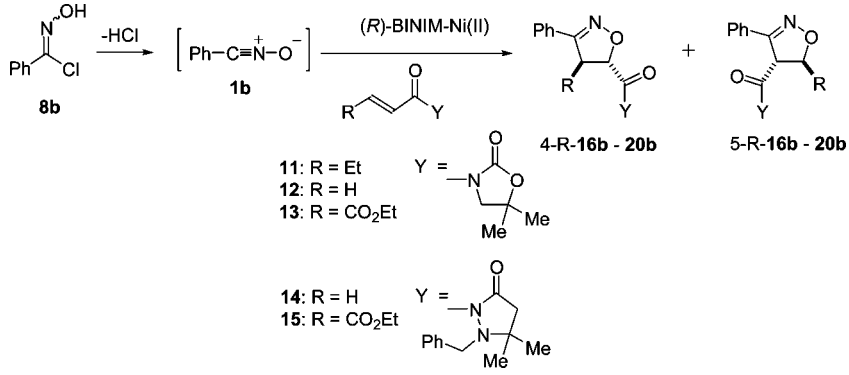
TABLE 4. Reactions of Hydroximoyl Chlorides 8b−8f and 8i−8k with Olefin 4 Catalyzed by (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) Complex[a]



entry	R	8	mol %	time (h)	product 10	yield (%)	rs[b]	ee[c] (%)
1	Ph	**8b**	30	24	**10b**	94	99:1	95
2	Ph	**8b**	10	24	**10b**	90	99:1	91
3	*p*-$MeOC_6H_4$	**8c**	10	39	**10c**	97	99:1	92
4	*p*-MeC_6H_4	**8d**	10	17	**10d**	84	99:1	88
5	*p*-ClC_6H_4	**8e**	30	14	**10e**	93	99:1	91
6	*p*-ClC_6H_4	**8e**	10	65	**10e**	81	99:1	79
7	*o*-ClC_6H_4	**8f**	30	18	**10f**	quant	99:1	90
8	*o*-ClC_6H_4	**8f**	10	17	**10f**	91	99:1	83
9	*i*-Bu	**8i**	30	14	**10i**	99	99:1	87
10	*i*-Bu	**8i**	10	61	**10i**	91	98:2	76
11	*n*-Bu	**8j**	10	56	**10j**	73	99:1	84
12	*t*-Bu	**8k**	30	37	**10k**	94	99:1	77
13	*t*-Bu	**8k**	10	72	**10k**	86	99:1	42

[a] Reaction were carried out by stirring hydroximoyl chlorides **8b−8f** and **8i−8k** (2 equiv) with olefin **4** at rt in CH_2Cl_2 in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex and MS 4Å. [b] Regioselectivity of the cycloadducts (4-Me/5-Me). [c] Enantiomeric excess of the 4-Me adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$.

SCHEME 3. Reactions Between Benzonitrile Oxide (1b) and Olefins 11−15 Catalyzed by (*R*)-BINIM-Ni(II)



proceeded smoothly under similar conditions (30 mol % catalyst) to preferentially afford the 4-Me cycloadduct (4-Me/5-Me = 93:7) in a high yield with moderate enantioselectivity of the 4-Me adduct (72% ee) (entry 15). Decreasing the catalyst loading to 10 mol % resulted in lower enantioselectivities and, to a lesser extent, decreased regioselectivities (entries 4, 6, 8, 10, 12, 14, and 16).

Cycloaddition Reactions of Other Nitrile Oxide with Crotonylpyrazolidinone 4. The reactions of several nitrile oxides with pyrazolidinone **4** in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (10−30 mol %) were also investigated (Scheme 2, Table 4, entries 3−13). When compared against those of oxazolidinone **3** (entries 3−10), the cycloadditions were highly regioselective (4-Me/5-Me = 98:2−99:1), with relatively high enantioselectivities (76−92% ee) of the 4-Me adducts. For the benzonitrile oxides with electron-releasing *p*-substituents (entries 3 and 4), the cycloadditions exhibited satisfactory asymmetric induction (88−92% ee), even with only 10 mol % catalyst. In the cases of electron-deficient *p*-chloro- and *o*-chlorobenzonitrile oxides (entries 5−8), although high enantioselectivites (90−91% ee) were observed using 30 mol % catalyst, lowering the catalytic loading from 30 to 10 mol % reduced the enantioselectivity without affecting the regioselectivity. For aliphatic nitrile oxides (entries 9 and 12), cycloaddition with pyrazolidinone **4** in the presence of 30 mol % catalyst was highly regioselective, with good enantioselectivity. It is noteworthy that the cycloaddition of pentanenitrile oxide (entry 11), a straight-chain aliphatic nitrile oxide that can readily undergo dimerization, also showed good enantioselectivity (84% ee) with high regioselectivity (99:1) even with only 10 mol % catalyst. Among the aliphatic nitrile oxides, the sterically hindered nitrile oxides exhibited lower enantioselectivities.

Cycloadditon Reactions with 2-Pentenoyl, (Ethoxycarbonyl)propenoyl, and Acryloyl Derivatives. To investigate the applicability of our methodology to olefinic dipolarophiles, the cycloadditions of benzonitrile oxide (**1b**) in the presence of 30 mol % catalyst were carried out using various oxazolidinones as dipolarophiles (Scheme 3, Table 5, entries 1−3). In the case of 5,5-dimethyl-3-(2-pentenoyl)-2-oxazolidinone (**11**, entry 1), the reaction was highly regio- and enantioselective (90% ee) and was comparable to that of crotonoyloxazolidinone **3**. The cycloaddition with 3-acryloyl-5,5-dimethyl-2-oxazolidinone (**12**,

TABLE 5. (*R*)-BINIM-Ni(II)-Catalyzed Reactions of Benzonitrile Oxide (1b) with Olefins 11−15[a]

entry	R	olefin	X (BINIM ligand)	time (h)	product	yield (%)	rs[b]	ee[c] (%)
1[d]	Et	**11**	Ph (BINIM-4Ph-2QN)	48	**16b**	73	90:10	90
2	H	**12**	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	2	**17b**	86	>99:1	74
3[d]	CO_2Et	**13**	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	3	**18b**	99	85:15	51
4	H	**14**	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	2	**19b**	93	<99:1	92
5	CO_2Et	**15**	3,5-xylyl (BINIM-4(3,5-xylyl)-2QN)	4	**20b**	93	99:1	75

[a] Reactions were carried out by stirring hydroximoyl chloride **8b** (2 equiv) with olefins **11**−**15** at rt in CH_2Cl_2 in the presence of (*R*)-BINIM-Ni(II) complexes (30 mol %). [b] Regioselectivity of the cycloadducts (4-R/5-R). [c] Enantiomeric excess of the 4-R adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$. [d] The reaction was carried out under high concentration (0.167 mol/L solution of olefin in CH_2Cl_2).

SCHEME 4. (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II)-Catalyzed Reactions between Nitrile Oxides and 2-Acryloylpyrazolidinone 14

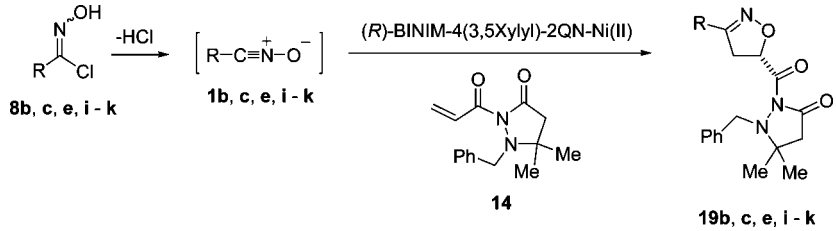


TABLE 6. (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) Catalyzed Reactions between Nitrile Oxides and 2-Acryloylpyrazolidinone 14[a]

entry	R	conditions[b]	catalyst (mol %)	time (h)[c]	product	yield (%)	rs[d]	ee[e] (%)
1	Ph	A	30	2	**19b**	93	>99:1	92
2	*p*-$MeOC_6H_4$	A	30	1	**19c**	95	>99:1	87
3	*p*-ClC_6H_4	A	30	1	**19e**	quant	>99:1	84
4	*i*-Bu	A	30	1	**19i**	91	>99:1	91
5	Ph	B	30	1	**19b**	92	>99:1	87
6	Ph	C	30	0.5	**19b**	90	>99:1	91
7	Ph	D	30	1	**19b**	93	>99:1	93
8	Ph	A	10	2	**19b**	99	>99:1	77
9	Ph	C	10	0	**19b**	90	>99:1	91
10	Ph	D	10	1	**19b**	80	>99:1	90
11	*p*-$MeOC_6H_4$	D	10	1	**19c**	67	>99:1	90
12	*p*-ClC_6H_4	D	10	1	**19e**	78	>99:1	79
13	*i*-Bu	D	10	1	**19i**	92	>99:1	83
14	*n*-Bu	D	10	1	**19j**	73	>99:1	87
15	*t*-Bu	D	10	1	**19k**	92	>99:1	86

[a] Reactions were carried out under conditions A−D by reacting the corresponding hydroximoyl chloride (2 equiv) with olefin **14** at rt in CH_2Cl_2 in the presence of the (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex. [b] Condition A: olefin **14**, hydroximoyl chloride, and CH_2Cl_2 were successively added within 30 s. Condition B: a solution of hydroximoyl chloride in CH_2Cl_2 was added to a mixture of olefin **14** and the catalyst. Condition C: a solution of olefin **14** in CH_2Cl_2 was added to a mixture of hydroximoyl chloride and the catalyst. Condition D: a solution of hydroximoyl chloride and olefin **14** in CH_2Cl_2 was added to the catalyst. [c] Stirring time after the addition of substrates. [d] Regioselectivity of the cycloadducts. [e] Enantiomeric excess of 4-Me adduct was determined by chiral HPLC after reduction to the corresponding alcohol using $NaBH_4$.

entry 2) in the presence of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex resulted in a lower enantioselectivity (74% ee) but with an extremely high regioselectivity (>99:1). Under similar conditions, only moderate enantioselectivity, with reduced regioselectivity, was observed for the reaction with 5,5-dimethy-3-[3-(ethoxycarbonyl)propenoyl]-2-oxazolidinone (**13**, entry 3).

To investigate the applicability of our methodology to 2-alkenoylpirazolidinone derivatives, cycloadditions were carried out using 2-acryloyl-1-benzyl-5,5-dimethyl-3-pyrazolidinone (**14**) and 1-benzyl-2-[3-(ethoxycarbonyl)propenoyl]-5,5-dimethy-3-pyrazolidinone (**15**) (Scheme 3, Table 5, entries 4 and 5). In contrast to that of acryloyloxazolidinone **12**, the reaction of 2-acryloylpyrazolidinone **14** (entry 4) using (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (30 mol %) was high-yielding while highly regio- (>99:1) and enantioselective (92% ee). Similarly, the reaction of [(ethoxycarbonyl)propenoyl]pyrazolidinone **15** (entry 5) exhibited regio- (99:1) and enantioselectivities (75% ee) higher than those of oxazolidinone **13**.

Cycloaddition Reactions of Several Nitrile Oxides with 2-Acryloylpyrazolidinone 14. On the basis of the highly enantioselective asymmetric cycloaddition between benzonitrile oxide and an acrylic acid derivative (Table 5, entry 4), we extended our studies using other nitrile oxides while varying the catalyst loading (Scheme 4, Table 6). The catalyzed cycloaddition between *p*-substituted benzonitrile oxides and 2-acryloylpyrazolidinone **14** in the presence of the (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex (30 mol %), regardless of the electronic character of *p*-substituents (entries 2 and 3), proceeded smoothly to give the corresponding 5-substituted cycloadduct exclusively in high yields with good enantioselectivity. Similarly, the reaction of 3-methylbutanenitrile oxide (entry 4) yielded the 5-substituted adduct quantitatively with high enantioselectivity (91% ee). For the reaction between benzonitrile oxide (**1b**) and 2-acryloylpyrazolidinone **14** (entry 8), decreasing the catalyst loading to 10 mol % resulted in lowering the enantioselectivity (77% ee). To improve the selectivity, the reaction condition was modified by the slow addition of hydroximoyl chloride **8b** (Condition B), 2-acryloylpyrazolidinone **14** (Condition C), or a mixture of **8b** and **14** (Condition D) over a period of 1 h. Our results showed that conditions C

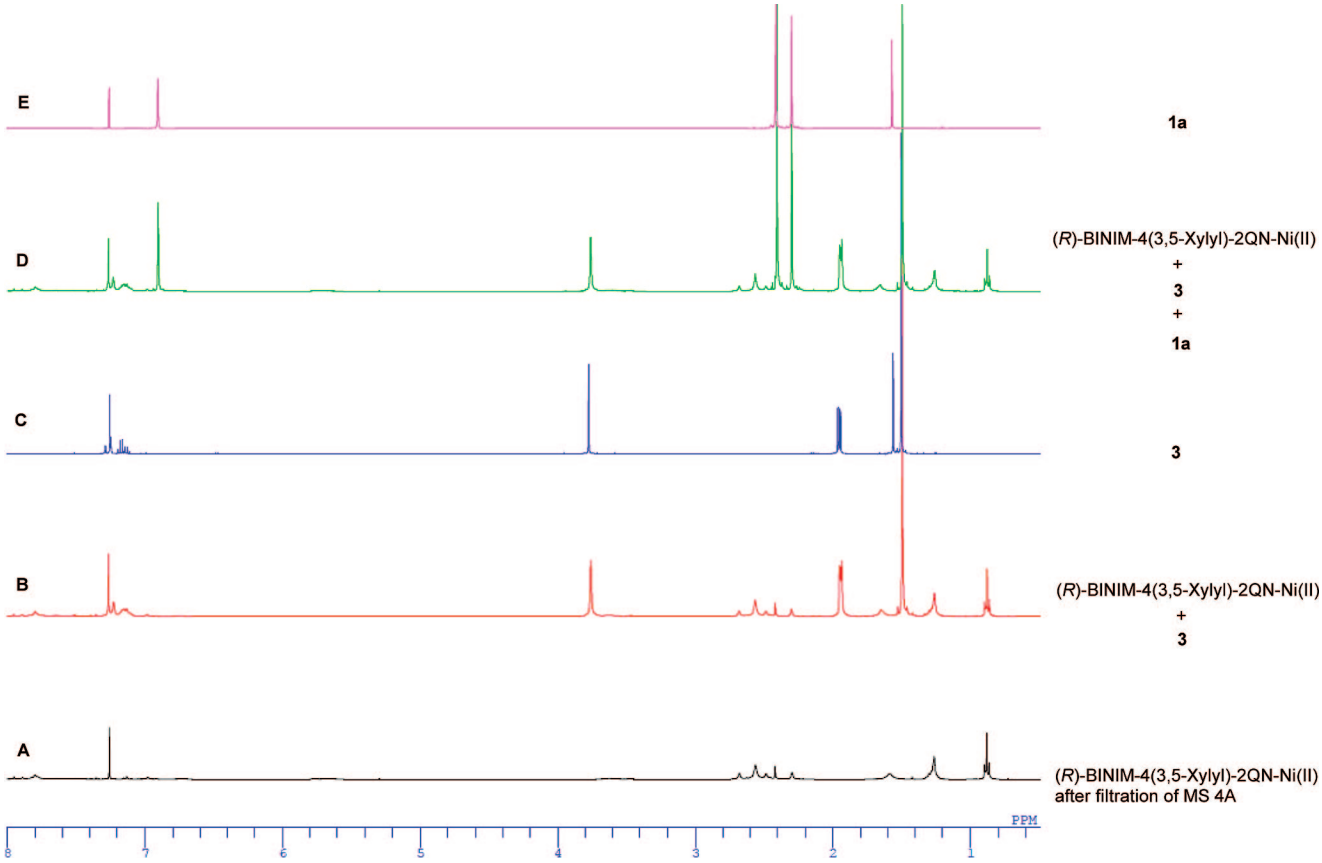


FIGURE 2. ^{1}H NMR study of (*R*)-BINIM-4(3,5-xylyl)-2QN complex in $CDCl_3$ (see Supporting Information for good resolution).

and D improved the enantioselectivities to over 90% ee, even for the reactions using only 10 mol % catalyst (entries 6, 7, 9, and 10). Under condition D, the reactions between 2-acryloylpyrazolidinone **14** and the *para*-substituted benzonitrile oxides or aliphatic nitrile oxides using 10 mol % catalyst (entries 11−15) also exhibited good enantioselectivities (79−90% ee) with high regioselectivities (>99:1).

^{1}H NMR Studies of the Cycloaddition Reaction of 2,4,6-Trimethylbenzonitrile Oxide (1a). To gain insight into the efficient activation of nitrile oxides under high catalyst loading, ^{1}H NMR studies were carried out for the reaction between 2,4,6-trimethylbenzonitrile oxide (**1a**) and crotonoyloxazolidinone **3** catalyzed by the (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) complex. The Ni(II) catalyst was prepared by stirring (*R*)-BINIM-4(3,5-xylyl)-2QN (28.9 mg, 0.038 mmol), $Ni(ClO_4)_2\cdot 6H_2O$ (13.7 mg, 0.038 mmol), and MS 4Å (95.3 mg) in $CDCl_3$ (1.5 mL) at room temperature for 6 h. Following removal of MS 4Å by filtration, the resulting Ni(II) catalyst was washed with $CDCl_3$ (0.75 mL). The ^{1}H NMR spectrum of the catalyst (about 0.012 mol dissolved in 0.6 mL $CDCl_3$) (Figure 2, **A**) did not exhibit any significant signals, except for those corresponding to hydrocarbon impurities. Upon the addition of oxazolidinone **3** (6.1 mg, 0.13 mmol), the ^{1}H NMR spectrum of the resulting solution exhibited signals that correspond to **3** (Figure 2, **B**) but slightly broader than those without the Lewis acid (Figure 2, **C**). Subsequent addition of nitrile oxide **1a** (4.4 mg, 0.13 mmol) to the above solution caused the appearance of sharp signals, which were assigned to nitrile oxide **1a**, while the signals of oxazolinedinone **3** remained broadened (Figure 2, **D**). The ^{1}H NMR spectra were also measured after allowing the mixture to stand for 24 h (Figure 3, **F**) and 7 days (Figure 3, **G**), in which the H_a and H_b signals of cycloadduct 4-Me-**6** exhibited a significant shift to higher field with slightly broadening, as compared to those of 4-Me-**6** without the Lewis acid (Figure 3, **H**). These results suggest that, as the reaction proceeds, the BINIM-Ni(II) catalyst coordinates not only with dipolarophile **3** but also with cycloadduct 4-Me-**6**, which in turn deactivates the catalyst. Accordingly, it is difficulty to decrease the catalyst loading in the BINIM-Ni(II)-catalyzed cycloaddition reactions of some nitrile oxides.

Proposed Mechanism for Asymmetric Induction. Attempts to form single crystals of the complexes between chiral BINIMs and $Ni(ClO_4)_2\cdot 6H_2O$ for X-ray structure analysis were unsuccessful. Consequently, on the basis of the X-ray structural analysis of DBFOX/Ph-$Ni(ClO_4)_2\cdot 3H_2O$, as reported by Kanemasa,[12] the structure of (*R*)-BINIM-4-(3,5-xylyl)-2QN-Ni(II)·crotonylpyrazolidinone **4** complex was proposed as a hexacoordinated octahedral structure. A similar structure has been suggested for BINIM-Ni(II)-catalyzed azomithine imine cycloaddition,[9d] by means of a molecular modeling program using PM3 calculations (Figure 4).[13] Ball-and-spoke models of the optimized complex are shown in Figure 4. As shown in the lower side view, the *re*-face of crotonylpyrazolidinone **4** is effectively shielded by the 4-(3,5-xylyl)quinoline moiety and the benzyl group of **4**. In contrast, as shown in the top side view, the *si*-face is located in a relatively open space. The high enantioselectvity of the cycloaddition reactions of nitrile oxides with crotonylpyrazolidinone **4**, therefore, is attributable to the

(12) Kanemasa, S.; Oderaotoshi, Y.; Sakaguchi, S.; Yamamoto, H.; Tanaka, J.; Wada, E.; Curran, D. P. *J. Am. Chem. Soc.* **1998**, *120*, 3074.

(13) The structure of the complex was optimized by PM3 calculations (Spartan 04).

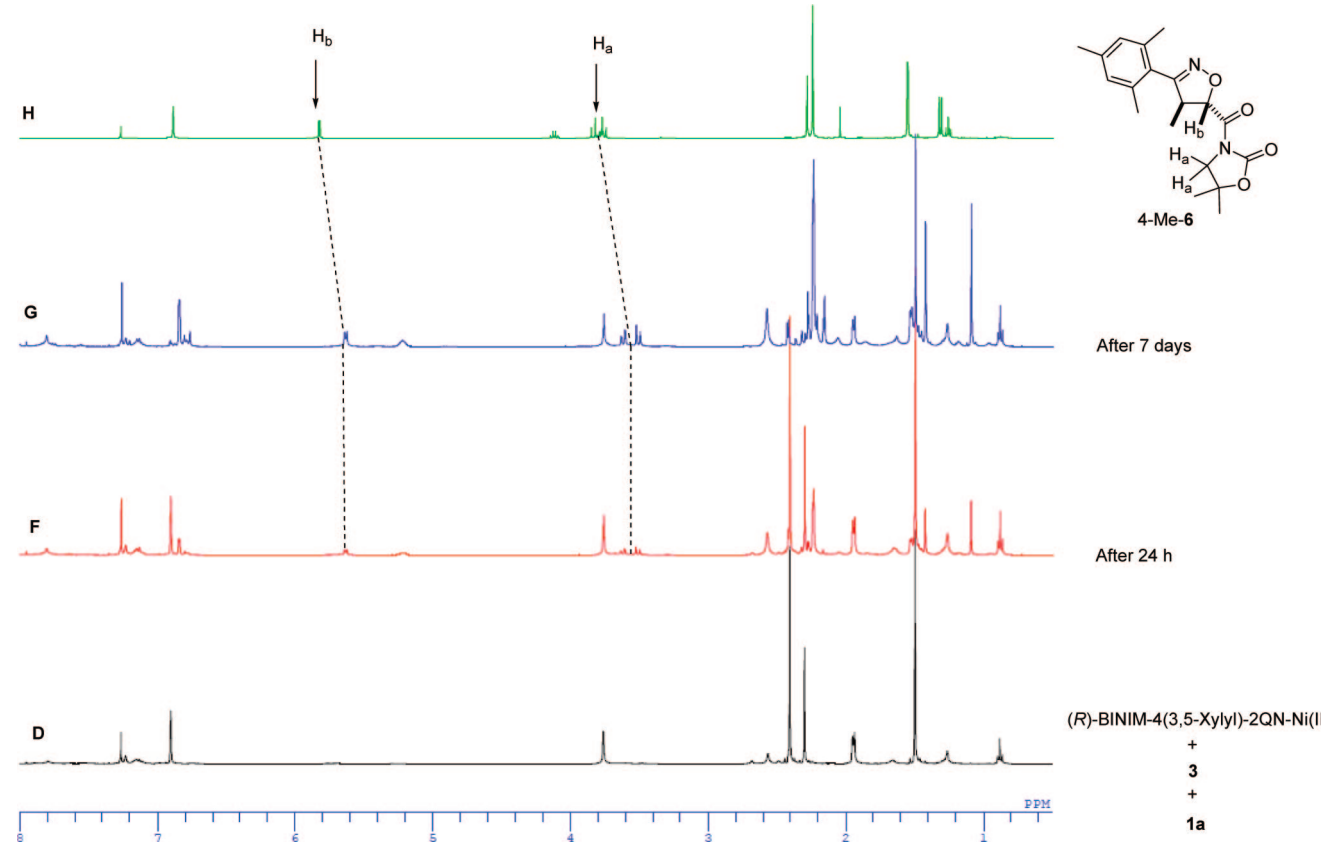


FIGURE 3. ^{1}H NMR study for (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II)-catalyzed reaction of **1a** with **3** (see Supporting Information for good resolution).

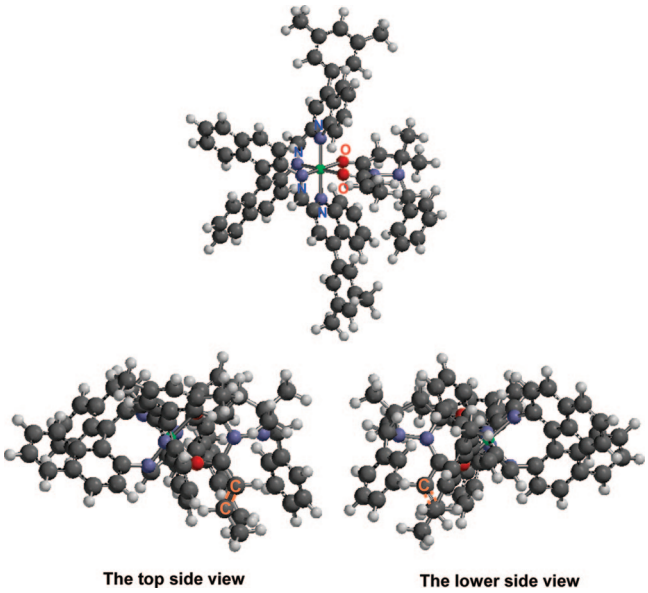


FIGURE 4. Proposed structure of (*R*)-BINIM-4-(3,5-xylyl)-2QN-Ni(II)·crotonylpyrazolidinone **4** complex.

highly selective approach of the nitrile oxides toward the *si*-face of the proposed hexa-coordinated Ni(II) complex (Figure 5). This *si*-face approach can reasonably explain the selective formation of (4*S*,5*S*)-cycloadducts 4-Me-**9b** and 4-Me-**10b**, which have the same configuration determined by the optical rotation[5c,6a] after reduction to the corresponding alcohol (see Experimental Section).

Conclusions

We have developed a novel synthetic scheme featuring BINIM-Ni(II) complexes as chiral Lewis acid catalysts for the asymmetric cycloadditions of nitrile oxide. The best result, in terms of enantioselectivity (96% ee), was achieved for the reaction of isolable 2,4,6-trimethylbenzonitrile oxide (**1a**) using the combination of (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II) catalyst (30 mol %) and 3-crotonoyl-5,5-dimethyl-2-oxazolidinone (**3**) as the dipolarophile. For this reaction, decreasing the catalyst loading resulted in lower enantioselectivities. For the catalyzed reactions of substituted and unsubstituted benzonitrile oxides and aliphatic nitrile oxides, which were generated from the corresponding hydroximoyl chloride in the presence of MS 4Å, the enantio- and regioselectivities were higher for 1-benzyl-2-crotonoyl-5,5-dimethyl-3-pyrazolidinone (**4**) as the dipolarophile than those using oxazolidinone **3**. For the reactions of benzonitrile oxide, *para*- and *ortho*-substituted benzonitirile oxides, and a straight chain aliphatic nitrile oxide, moderate to high enantioselectivities (79−92% ee) were observed for pyrazolidinone **4** as the dipolarophile, even in the presence of only 10 mol % catalyst. For the asymmetric cycloadditions of acrylic acid derivatives, specifically, reactions between several nitrile oxides and 2-acryloyl-1-benzyl-5,5-dimethyl-3-pyrazolidinone (**14**), relatively high enantioselectivities (79−91% ee) were attained with a catalyst loading of 10 mol %. We believe that our results have contributed toward the development of chiral Lewis acid catalyzed asymmetric cycloaddition reactions of unstable 1,3-dipoles.

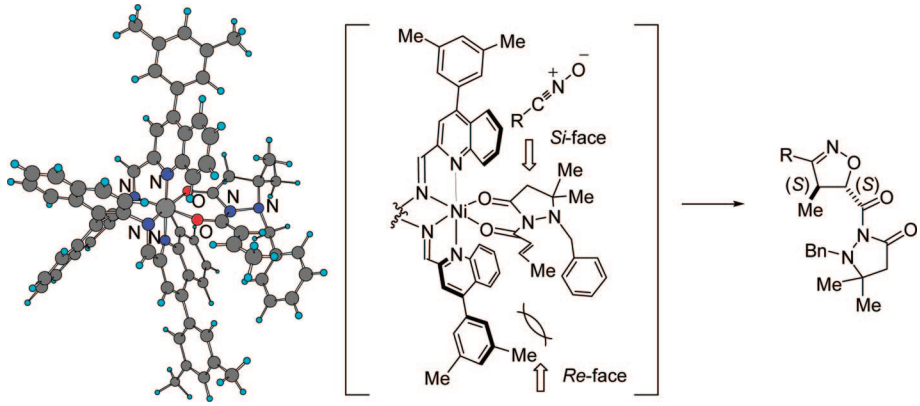


FIGURE 5. Proposed mechanism for BINIM-Ni(II)-catalyzed asymmetric cycloadditions of nitrile oxides.

Experimental Section

For general methods and materials, see Supporting Information.

General Procedure for (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II)-Catalyzed Reaction of 2,4,6-Trimethylbenzonitrile Oxide (1a) with 3-Crotonoyl-5,5-dimethyl-2-oxazolidinone (3). A suspension of (*R*)-BINIM-4(3,5-xylyl)-2QN (115.7 mg, 0.15 mmol), powdered MS 4Å (381 mg), and $Ni(ClO_4)_2 \cdot 6H_2O$ (54.9 mg, 0.15 mmol) in CH_2Cl_2 (6.0 mL) was stirred for 6 h at room temperature. Oxazolidinone **3** (91.6 mg, 0.50 mmol), nitrile oxide **1a** (80.6 mg, 0.50 mmol), and CH_2Cl_2 (3.0 mL) were added successively to the catalyst suspension. After stirring at room temperature for 50 h, the reaction was quenched with saturated NH_4Cl solution (7.5 mL) and water (7.5 mL) and then filtered through Celite. The filtrate was extracted with CH_2Cl_2 (5.0 mL × 3). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane−ethyl acetate (7:3 v/v) as an eluent to give cycloadduct (121.2 mg, 80%). Regioselectivity was determined to be 4-Me/5-Me = 85:15 by ^{1}H NMR (400 MHz) analysis of the crude mixture. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:39 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after conversion to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 40.4 min, t_{major} = 62.0 min.

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole (4-Me-6). Colorless plates, mp 185.0−186.0 °C (CH_2Cl_2−hexane), IR (KBr) 3492, 2964, 1770, 1703, 1614, 1462, 1388, 1325, 1292, 1203, 1165, 1122, 1093, 1020, 987, 929, 883, 850, 760, 684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, d, J = 7.3 Hz), 1.55 (3H, s), 1.56 (3H, s), 2.25 (6H, s), 2.29 (3H, s), 3.76 (1H, d, J = 11.0 Hz), 3.79 (1H, dq, J = 4.2, 7.3 Hz), 3.84 (1H, d, J = 11.0 Hz), 5.83 (1H, d, J = 4.2 Hz), 6.89 (2H, s); ^{13}C NMR ($CDCl_3$) δ 16.3 (CH_3), 20.1 (CH_3), 21.2 (CH_3), 27.3 (CH_3), 27.4 (CH_3), 51.0 (CH), 54.4 (CH_2), 80.0 (C), 83.2 (CH), 124.1 (C), 128.5 (CH), 137.1 (C), 138.7 (C), 152.4 (C), 160.4 (C), 169.5 (C), MS (EI) *m*/*z* 344 (M^+), 316, 202, 172. HRMS (EI) calcd for $C_{19}H_{24}N_2O_4$ (M^+): 344.1736, found 344.1725. Anal. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.37; H, 7.22; N, 7.83.

Conversion to (4*S*,5*S*)-5-Hydroxymethyl-4-methyl-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole.[14] To a solution of 4-Me-**6** (34.4 mg, 0.10 mmol) in THF (2.0 mL) and water (0.66 mL) was added $NaBH_4$ (15.1 mg, 0.40 mmol) at 20−25 °C. After stirring the mixture for 1.5 h, the reaction was quenched with 2 mol/L hydrochloric acid, and the mixture was extracted with ethyl acetate (5.0 mL × 3). The organic layer was washed with saturated NaCl solution (10 mL × 2), and the dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane−ethyl acetate (3:2 v/v) as an eluent to give the corresponding alcohol (21.3 mg, 99%). Colorless oil; $[\alpha]^{25}_D$ = +191.5 (*c* 0.13, MeOH, 96% ee); IR (neat) 3461, 3220, 2974, 2930, 1520, 1456, 1215, 1033, 929, 852, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (3H, d, J = 7.3 Hz), 2.06 (1H, brs), 2.25 (6H, s), 2.29 (3H, s), 3.55 (1H, dq, J = 8.1, 7.3 Hz), 3.70−3.76 (1H, m), 3.92−3.97 (1H, m), 4.39 (1H, ddd, J = 3.2, 4.4, 8.1 Hz), 6.90 (2H, s); ^{13}C NMR ($CDCl_3$) δ 15.8 (CH_3), 20.2 (CH_3), 21.3 (CH_3), 47.4 (CH), 62.8 (CH_2), 87.9 (CH), 125.2 (C), 128.5 (CH), 136.9 (C), 138.4 (C), 161.9 (C); MS (EI) *m*/*z* 233 (M^+), 202, 172, 159, 146, 119, 91, 77, 57, 28. HRMS (EI) calcd for $C_{14}H_{19}NO_2$ (M^+): 233.1416, found 233.1454. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:39 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C. t_{minor} = 40.4 min, t_{major} = 62.0 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole (5-Me-6). Although 5-Me-**6** could not be separated by chromatography from a mixture with major 4-Me-**6**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.10 (3H, s), 1.43 (3H, s), 1.55 (3H, d, J = 6.6 Hz), 2.25 (9H, s), 3.52 (1H, d, J = 11.0 Hz), 3.61 (1H, d, J = 11.0 Hz), 5.27 (1H, dq, J = 7.1, 6.6 Hz), 5.65 (1H, d, J = 7.1 Hz), 6.85 (2H, s).

(4*S*,5*S*)-4-Methyl-5-[(2-oxo-3-oxazolidinyl)carbonyl]-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole (4-Me-5). Colorless prisms; 159.5−160.5 °C (CH_2Cl_2−hexane); IR (KBr) 3445, 2982, 1788, 1705, 1610, 1477, 1386, 1317, 1217, 1120, 974, 912, 850, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, d, J = 7.3 Hz), 2.24 (6H, s), 2.29 (3H, s), 3.81 (1H, dq, J = 4.2, 7.3 Hz), 4.02−4.16 (2H, m), 4.53 (2H, t, J = 7.6 Hz), 5.83 (1H, d, J = 4.2 Hz), 6.89 (2H, s); ^{13}C NMR ($CDCl_3$) δ 16.3 (CH_3), 20.1 (CH_3), 21.2 (CH_3), 42.7 (CH_2), 50.8 (CH), 62.9 (CH_2), 82.9 (CH), 124.0 (C), 128.5 (CH), 137.1 (C), 138.8 (C), 153.2 (C), 160.4 (C), 169.2 (C); MS (EI) *m*/*z* 316 (M^+), 202, 172, 88. HRMS (EI) calcd for $C_{17}H_{20}N_2O_4$ (M^+): 316.1423, found 316.1421.

5-Methyl-4-[(2-oxo-3-oxazolidinyl)carbonyl]-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole (5-Me-5). Although 5-Me-**5** could not be separated by chromatography from a mixture with major 4-Me-**5**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.55 (3H, d, J = 6.3 Hz), 2.27 (3H, s), 2.28 (6H, s), 3.80−3.87 (1H, m), 3.93−4.00 (1H, m), 4.11−4.16 (1H, m), 4.30−4.36 (1H, m), 5.19 (1H, dq, J = 6.6, 6.3 Hz), 5.59 (1H, d, J = 6.6 Hz), 6.86 (2H, s).

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-4-methyl-3-[(2,4,6-trimethyl)phenyl]-4,5-dihydroisoxazole (4-Me-7). Colorless prisms, mp 143 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +226.8 (*c* 0.50, $CHCl_3$, 92% ee); IR (KBr) 2972, 2930, 1749, 1714, 1455, 1375, 1307, 1234, 853, 699 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.76 (3H, s), 0.77 (3H, s), 0.98 (3H, d, J = 7.6 Hz), 1.97 (1H, d, J = 16.9 Hz), 2.04 (1H, d, J = 16.9 Hz), 2.04 (3H, s), 2.27 (6H, s), 3.67 (1H, d, J = 14.1 Hz), 3.71 (1H, d, J = 14.1 Hz), 4.01 (1H, dq, J = 4.1, 7.6 Hz), 5.93 (1H, d, J = 4.1 Hz), 6.64 (2H, s),

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7.03−7.06 (3H, m), 7.50−7.52 (2H, m); ^{13}C NMR ($CDCl_3$) δ 16.2 (CH_3), 20.2 (CH_3), 21.2 (CH_3), 25.8 (CH_3), 26.8 (CH_3), 43.3 (CH_2), 49.5 (CH), 56.9 (CH_2), 61.6 (C), 84.0 (CH), 124.2 (C), 127.6 (CH), 128.3 (CH), 128.4 (CH), 129.4 (CH), 136.8 (C), 137.2 (C), 138.6 (C), 160.6 (C), 166.0 (C), 174.5 (C); MS (EI) *m*/*z* 433(M^+), 204, 189, 113, 91, 37. Anal. Calcd for $C_{26}H_{31}N_3O_3$: C, 72.03; H, 7.21; N, 9.69. Found: C, 71.85; H, 6.92; N, 9.57. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:39 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 40.4 min, t_{major} = 62.0 min.

General Procedure for (*R*)-BINIM-4Ph-2QN-Ni(II)-Catalyzed Reaction of Hydroximyl Chloride with 3-Crotonoyl-5,5-dimethyl-2-oxazolidione (3) Exemplified by the Reaction of *p*-Methylbenzohydroximoyl Chloride (8e). A suspension of (*R*)-BINIM-4Ph-2QN (53.6 mg, 0.075 mmol), powdered MS 4Å (190.5 mg), and $Ni(ClO_4)_2 \cdot 6H_2O$ (27.5 mg, 0.075 mmol) in CH_2Cl_2 (3.0 mL) was stirred for 6 h at room temperature. Oxazolidinone **3** (45.8 mg, 0.25 mmol), hyroximoyl chloride **8e** (84.8 mg, 0.50 mmol), and CH_2Cl_2 (1.5 mL) were added successively to the catalyst suspension. After stirring at room temperature for 20 h, the reaction was quenched with saturated NH_4Cl solution (2.5 mL) and water (2.5 mL) and then filtered through Celite. The filtrate was extracted with CH_2Cl_2 (5.0 mL × 3). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane−ethyl acetate (73:27 v/v) as an eluent to give cycloadduct **9e** (69.2 mg, 87%). Regioselectivity was determined to be 4-Me/5-Me = 95:5 by ^{1}H NMR (400 MHz) analysis of the crude mixture. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:29 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after conversion to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 97.1 min, t_{major} = 127.0 min.

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-3-phenyl-4,5-dihydroisoxazole (4-Me-9b). Colorless needles; mp 148.0−149.0 °C (CH_2Cl_2−hexane); IR (KBr) 3460, 3030, 2978, 2935, 2878, 1988, 1778, 1697, 1466, 1379, 1350, 1294, 1209, 1109, 1080, 1037, 979, 937, 873, 852, 760, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, s), 1.52 (3H, d, *J* = 6.3 Hz), 1.54 (3H, s), 3.75 (1H, d, *J* = 11.0 Hz), 3.79 (1H, d, *J* = 11.0 Hz), 3.85 (1H, dq, *J* = 2.7, 6.3 Hz), 5.76 (1H, d, *J* = 2.7 Hz), 7.37−7.42 (3H, m), 7.68−7.73 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 27.2 (CH_3), 47.2 (CH), 54.1 (CH_2), 80.2 (C), 84.6 (CH), 127.0 (CH), 127.5 (C), 128.5 (CH), 130.0 (CH), 152.5 (C), 160.0 (C), 169.0 (C); MS (EI) *m*/*z* 302 (M^+), 161, 132, 117, 104, 77, 55, 37, 24. Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.60; H, 6.17; N, 9.06.

(4*S*,5*S*)-5-Hydroxymethyl-4-methyl-3-phenyl-4,5-dihydroisoxazole. Colorless prisms; mp 79.5−80.5 °C (CH_2Cl_2−hexane); $[\alpha]^{25}_D$ = +76.2 (*c* 0.31, MeOH, 89% ee); IR (KBr) 3452, 3055, 2966, 2922, 1689, 1620, 1458, 1379, 1350, 1261, 1159, 1078, 1057, 1016, 887, 854, 767 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (3H, d, *J* = 7.3 Hz), 2.15 (1H, brs), 3.62 (1H, dq, *J* = 5.2, 7.3 Hz), 3.68 (1H, dd, *J* = 12.0, 5.1 Hz), 3.78 (1H, dd, *J* = 12.0, 3.7 Hz), 4.44 (1H, ddd, *J* = 3.7, 5.1, 5.2 Hz), 7.39−7.43 (3H, m), 7.65−7.69 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.8 (CH_3), 43.7 (CH), 63.4 (CH_2), 88.6 (CH), 126.9 (CH), 128.4 (C), 128.7 (CH), 129.9 (CH), 161.0 (C); MS (EI) *m*/*z* 191 (M^+), 146, 77, 39. HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+): 191.0946, found 191.0964. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:49 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 116.0 min, t_{major} = 135.4 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-3-phenyl-4,5-dihydroisoxazole (5-Me-9b). Although 5-Me-**9b** could not be separated by chromatography from a mixture with major 4-Me-**9b**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.51 (3H, d, *J* = 6.6 Hz), 1.54 (3H, s), 1.55 (3H, s), 3.73 (2H, d, *J* = 11.2 Hz), 3.74 (1H, d, *J* = 11.2 Hz), 4.93 (1H, dq, *J* = 4.1, 6.6 Hz), 5.43 (1H, d, *J* = 4.1 Hz), 7.36−7.40 (3H, m), 7.59−7.64 (2H, m).

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-3-(*p*-methoxyphenyl)-4-methyl-4,5-dihydroisoxazole (4-Me-9c). Colorless prisms; mp 154.0−155.0 °C (CH_2Cl_2−hexane); IR (KBr) 3432, 2984, 2937, 1772, 1714, 1608, 1566, 1518, 1450, 1398, 1371, 1296, 1261, 1205, 1188, 1113, 1012, 962, 931, 883, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, d, *J* = 7.3 Hz), 1.54 (6H, s), 3.72 (1H, d, *J* = 11.0 Hz), 3.80 (1H, d, *J* = 11.0 Hz), 3.81 (1H, dq, *J* = 2.4, 7.3 Hz), 3.84 (3H, s), 5.73 (1H, d, *J* = 2.4 Hz), 6.90−6.93 (2H, m), 7.63−7.67 (2H, m); ^{13}C NMR ($CDCl_3$) δ 18.0 (CH_3), 27.4 (CH_3), 47.6 (CH), 54.3 (CH_2), 55.4 (CH_3), 80.2 (C), 84.6 (CH), 114.1 (CH), 120.2 (C), 128.7 (CH), 152.6 (C), 159.7 (C), 161.0 (C), 169.4 (C); MS (EI) *m*/*z* 332 (M^+), 190, 162, 135, 77, 55, 37. Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.35; H, 6.16; N, 8.42.

(4*S*,5*S*)-5-Hydroxymethyl-3-(*p*-methoxyphenyl)-4-methyl-4,5-dihydroisoxazole. Colorless prisms; mp 141.0−142.5 °C (CH_2Cl_2−hexane); $[\alpha]^{25}_D$ = +76.2 (*c* 0.26, $CHCl_3$, 93% ee); IR (KBr) 3439, 2957, 1653, 1608, 1591, 1516, 1458, 1423, 1386, 1251, 1018, 943, 881 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (3H, d, *J* = 7.1 Hz), 2.31 (1H, brs), 3.62 (1H, dq, *J* = 5.1, 7.1 Hz), 3.66 (1H, dd, *J* = 5.6, 12.2 Hz), 3.75 (1H, dd, *J* = 3.7, 12.2 Hz), 3.84 (3H, s), 4.41 (1H, ddd, *J* = 3.7, 5.1, 5.6 Hz), 6.90−6.99 (2H, m), 7.59−7.63 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.8 (CH_3), 43.9 (CH), 55.4 (CH_3), 63.4 (CH_2), 88.3 (CH), 114.1 (CH), 120.8 (C), 128.4 (CH), 160.6 (C), 160.8 (C); MS (EI) *m*/*z* 221 (M^+), 190, 162, 135, 77, 28. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.41; H, 6.94; N, 5.96. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:49 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 99.7 min, t_{major} = 116.3 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-3-(*p*-methoxyphenyl)-5-methyl-4,5-dihydroisoxazole (5-Me-9c). Although **5**-Me-**9c** could not be separated by chromatography from a mixture with major 4-Me-**9c**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, d, *J* = 6.3 Hz), 1.53 (3H, s), 1.54 (3H, s), 3.73 (1H, d, *J* = 11.0 Hz), 3.76 (1H, d, *J* = 11.0 Hz), 4.89 (1H, dq, *J* = 4.2, 6.3 Hz), 5.40 (1H, d, *J* = 4.2 Hz), 6.89−6.92 (2H, m), 7.55−7.59 (2H, m).

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-3-(*p*-methylphenyl)-4,5-dihydroisoxazole (4-Me-9d). Colorless plates; mp 145.0−146.0 °C (CH_2Cl_2−hexane); IR (KBr) 3452, 3042, 2980, 2968, 2930, 1772, 1716, 1606, 1558, 1514, 1460, 1396, 1371, 1313, 1298, 1261, 1209, 1167, 1105, 1020, 960, 843 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, d, *J* = 7.1 Hz), 1.54 (6H, s), 2.37 (3H, s), 3.72 (1H, d, *J* = 11.0 Hz), 3.80 (1H, d, *J* = 11.0 Hz), 3.83 (1H, dq, *J* = 2.7, 7.1 Hz), 5.74 (1H, d, *J* = 2.7 Hz), 7.20−7.22 (2H, m), 7.58−7.61 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.9 (CH_3), 21.6 (CH_3), 27.4 (CH_3), 47.5 (CH), 54.2 (CH_2), 80.2 (C), 84.6 (CH), 124.7 (C), 127.0 (CH), 129.3 (CH), 142.5 (C), 152.6 (C), 160.0 (C), 169.3 (C); MS (EI) *m*/*z* 316 (M^+), 301, 174, 146, 118, 91, 59, 37. Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.86. Found: C, 64.55; H, 6.37; N, 8.85.

(4*S*,5*S*)-5-Hydroxymethyl-4-methyl-3-(*p*-methylphenyl)-4,5-dihydroisoxazole. Colorless prisms; mp 111.0−112.0 °C (CH_2Cl_2−hexane); $[\alpha]^{25}_D$ = +99.3 (*c* 0.33, $CHCl_3$, 91% ee); IR (KBr) 3441, 2974, 2943, 2878, 1718, 1608, 1514, 1458, 1410, 1379, 1346, 1236, 1076, 993, 941 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, *J* = 7.3 Hz), 2.23 (1H, brs), 2.38 (3H, s), 3.60 (1H, dq, *J* = 5.1, 7.3 Hz), 3.66 (1H, dd, *J* = 5.6, 12.2 Hz), 3.76 (1H, dd, *J* = 3.7, 12.2 Hz), 4.42 (1H, ddd, *J* = 3.7, 5.1, 5.6 Hz), 7.20−7.22 (2H, m), 7.54−7.56 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.8 (CH_3), 21.5 (CH_3), 43.7 (CH), 63.6 (CH_2), 88.4 (CH), 125.4 (C), 127.0 (CH), 129.3 (CH), 140.0 (C), 160.9 (C); MS (EI) *m*/*z* 205 (M^+), 174, 146, 131, 91, 65. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.29; H, 7.42; N, 6.71. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:29 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 97.1 min, t_{major} = 127.0 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-3-(*p*-methylphenyl)-4,5-dihydroisoxazole (5-Me-9d). Although 5-Me-**9d** could not be separated by chromatography from a mixture with major 4-Me-**9d**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, s), 1.51 (3H, d, J = 6.3 Hz), 1.54 (3H, s), 2.36 (3H, s), 3.73 (1H, d, J = 11.0 Hz), 3.76 (1H, d, J = 11.0 Hz), 4.91 (1H, dq, J = 4.4, 6.3 Hz), 5.42 (1H, d, J = 4.4 Hz), 7.07−7.09 (2H, m), 7.50−7.52 (2H, m).

(4*S*,5*S*)-3-(*p*-Chlorophenyl)-5-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-4,5-dihydroisoxazole (4-Me-9e). Colorless prisms; mp 180.0−181.5 °C (CH_2Cl_2−hexane); IR (KBr) 3457, 3069, 2980, 2947, 1782, 1716, 1593, 1560, 1493, 1464, 1394, 1365, 1317, 1300, 1261, 1209, 1165, 1111, 1012, 962, 933, 889, 854 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50 (3H, d, J = 7.1 Hz), 1.54 (3H, s), 1.55 (3H, s), 3.72 (1H, d, J = 11.0 Hz), 3.82 (1H, d, J = 11.0 Hz), 3.83 (1H, dq, J = 2.7, 7.1 Hz), 5.78 (1H, d, J = 2.7 Hz), 7.36−7.40 (2H, m), 7.63−7.66 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.8 (CH_3), 27.4 (CH_3), 47.2 (CH), 54.3 (CH_2), 80.3 (C), 85.0 (CH), 126.2 (C), 128.4 (CH), 129.0 (CH), 136.2 (C), 152.6 (C), 159.3 (C), 169.0 (C); MS (EI) *m*/*z* 338 (M^++2), 336 (M^+), 321, 308, 196, 166, 131, 116, 75, 56, 37, 26. Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57.13; H, 5.32; N, 8.03.

(4*S*,5*S*)-3-(*p*-Chlorophenyl)-5-hydroxymethyl-4-methyl-4,5-dihydroisoxazole. Colorless prisms; mp 82.0−83.0 °C (CH_2Cl_2−hexane); $[\alpha]^{25}_D$ = +87.3 (*c* 0.39, $CHCl_3$, 84% ee); IR (KBr) 3431, 2978, 2939, 1647, 1595, 1494, 1456, 1381, 1234, 1097, 1012, 993, 941, 883 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, J = 7.1 Hz), 2.11 (1H, brs), 3.60 (1H, dq, J = 5.1, 7.1 Hz), 3.67 (1H, dd, J = 5.1, 12.2 Hz), 3.79 (1H, dd, J = 3.7, 12.2 Hz), 4.44 (1H, dt, J = 3.7, 5.1 Hz), 7.36−7.40 (2H, m), 7.58−7.61 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.6 (CH_3), 43.5 (CH), 63.2 (CH_2), 88.9 (CH), 126.8 (C), 128.1 (CH), 128.9 (CH), 135.8 (C), 160.1 (C); MS (EI) *m*/*z* 225 (M^+), 194, 166, 131, 111, 75, 28. Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.54; H, 5.61; N, 5.96. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:29 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 94.9 min, t_{major} = 112.9 min.

3-(*p*-Chlorophenyl)-4-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-4,5-dihydroisoxazole (5-Me-9e). Although 5-Me-**9e** could not be separated by chromatography from a mixture with major 4-Me-**9e**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.51 (3H, d, J = 6.3 Hz), 1.55 (6H, s), 3.73 (1H, d, J = 11.2 Hz), 3.76 (1H, d, J = 11.2 Hz), 4.93 (1H, dq, J = 4.2, 6.3 Hz), 5.38 (1H, d, J = 4.2 Hz), 7.34−7.38 (2H, m), 7.55−7.58 (2H, m).

(4*S*,5*S*)-3-(*o*-Chlorophenyl)-5-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-4,5-dihydroisoxazole (4-Me-9f). Colorless amorphous; IR (KBr) 3446, 2987, 2935, 1776, 1714, 1653, 1591, 1558, 1508, 1475, 1458, 1375, 1265, 1207, 1168, 1109, 1032, 954, 931, 877, 761 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, J = 6.8 Hz), 1.56 (6H, s), 3.78 (1H, d, J = 11.2 Hz), 3.84 (1H, d, J = 11.2 Hz), 4.20 (1H, dq, J = 3.7, 6.8 Hz), 5.84 (1H, d, J = 3.7 Hz), 7.29−7.44 (3H, m), 7.54−7.57 (1H, m); ^{13}C NMR ($CDCl_3$) δ 16.8 (CH_3), 27.2 (CH_3), 27.3 (CH_3), 49.2 (CH), 54.3 (CH_2), 80.2 (C), 84.4 (CH), 126.8 (CH), 127.2 (C), 130.1 (CH), 130.9 (CH), 131.3 (CH), 132.8 (C), 152.4 (C), 160.2 (C), 168.8 (C); MS (EI) *m*/*z* 338 (M^++2), 336 (M^+), 321, 301, 273, 196, 166, 130, 116, 102, 71, 65, 37, 26. HRMS (EI) calcd for $C_{17}H_{17}N_3O_4$ (M^+): 336.0877, found 336.0856.

(4*S*,5*S*)-3-(*o*-Chlorophenyl)-5-hydroxymethyl-4-methyl-4,5-dihydroisoxazole. Colorless viscous oil; $[\alpha]^{25}_D$ = +94.8 (*c* 0.31, $CHCl_3$, 83% ee); IR (neat) 3452, 2932, 2361, 1732, 1591, 1456, 1217, 1062, 1035, 893, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.16 (3H, d, J = 7.3 Hz), 2.30 (1H, brs), 3.78 (1H, dd, J = 5.1, 12.2 Hz), 3.89 (1H, dd, J = 3.2, 12.2 Hz), 3.94 (1H, dq, J = 7.6, 7.3 Hz), 4.44 (1H, ddd, J = 3.2, 5.1, 7.6 Hz), 7.29−7.39 (2H, m), 7.43−7.49 (2H, m); ^{13}C NMR ($CDCl_3$) δ 16.4 (CH_3), 45.4 (CH), 62.8 (CH_2), 88.8 (CH), 126.8 (CH), 128.1 (C), 130.1 (CH), 130.7 (CH), 131.1 (CH), 132.6 (C), 161.6 (C); MS (EI) *m*/*z* 227 (M^++2), 225 (M^+), 194, 166, 131, 102, 75, 28. Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.76; H, 5.44; N, 5.92. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:29 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 76.1 min, t_{major} = 86.8 min.

3-(*o*-Chlorophenyl)-4-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-4,5-dihydroisoxazole (5-Me-9f). Although 5-Me-**9f** could not be separated by chromatography from a mixture with major 4-Me-**9f**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.43 (3H, s), 1.51 (3H, s), 1.60 (3H, d, J = 6.6 Hz), 3.67 (1H, d, J = 11.2 Hz), 3.70 (1H, d, J = 11.2 Hz), 4.97 (1H, dq, J = 5.1, 6.6 Hz), 5.67 (1H, d, J = 5.1 Hz), 7.29−7.40 (3H, m), 7.74−7.76 (1H, m).

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-3-(*p*-nitrophenyl)-4,5-dihydroisoxazole (4-Me-9g). Colorless prisms; mp 206.0−208.0 °C (CH_2Cl_2−hexane); IR (KBr) 3452, 3113, 2980, 2935, 1776, 1709, 1604, 1575, 1521, 1460, 1377, 1294, 1265, 1207, 1170, 1109, 954, 931 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52 (3H, d, J = 7.1 Hz), 1.56 (6H, s), 3.74 (1H, d, J = 10.7 Hz), 3.89 (1H, d, J = 10.7 Hz), 3.89 (1H, dq, J = 2.9, 7.1 Hz), 5.86 (1H, d, J = 2.9 Hz), 7.87−7.90 (2H, m), 8.24−8.28 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 27.4 (CH_3), 46.7 (CH), 54.2 (CH_2), 80.5 (C), 85.5 (CH), 123.9 (CH), 127.8 (CH), 128.8 (C), 148.3 (C), 152.6 (C), 158.7 (C), 168.6 (C); MS (EI) *m*/*z* 347 (M^+), 332, 149, 105, 77, 57, 37. HRMS (EI) calcd for $C_{16}H_{17}N_3O_6$ (M^+): 347.1117, found 347.1128.

(4*S*,5*S*)-5-Hydroxymethyl-4-methyl-3-(*p*-nitrophenyl)-4,5-dihydroisoxazole. Colorless viscous oil; $[\alpha]^{25}_D$ = +88.9 (*c* 0.25, $CHCl_3$, 78% ee); IR (neat) 3601, 2932, 1722, 1602, 1521, 1456, 1348, 1072, 991, 906, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (3H, d, J = 7.3 Hz), 1.97 (1H, brs), 3.70 (1H, dq, J = 5.4, 7.3 Hz,), 3.71 (1H, dd, J = 4.9, 12.2 Hz), 3.85 (1H, dd, J = 3.7, 12.2 Hz), 4.52 (1H, ddd, J = 3.7, 4.9, 5.4 Hz), 7.82−7.86 (2H, m), 8.25−8.29 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 43.1 (CH), 63.2 (CH_2), 89.7 (CH), 123.9 (CH), 127.6 (CH), 134.6 (C), 148.2 (C), 159.4 (C); MS (EI) *m*/*z* 236 (M^+), 205, 177, 149, 130, 103, 76, 57, 37. HRMS (EI) calcd for $C_{11}H_{12}N_2O_4$ (M^+): 236.0797, found 236.0795. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:9 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 48.8 min, t_{major} = 101.0 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-3-(*p*-nitrophenyl)-4,5-dihydroisoxazole (5-Me-9g). Although 5-Me-**9g** could not be separated by chromatography from a mixture with major 4-Me-**9g**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.55 (3H, s), 1.56 (3H, s), 1.61 (1H, d, J = 6.8 Hz), 3.76 (1H, d, J = 11.0 Hz), 3.78 (1H, d, J = 11.0 Hz), 5.00 (1H, dq, J = 4.1, 6.8 Hz), 5.40 (1H, d, J = 4.1 Hz), 7.79−7.81 (2H, m), 8.26−8.27 (2H, m).

(4*S*,5*S*)-3-(*p*-Cyanophenyl)-5-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-4,5-dihydroisoxazole (4-Me-9h). Colorless needles; mp 203.0−204.5 °C (CH_2Cl_2−hexane); IR (KBr) 3422, 2986, 1780, 1714, 1608, 1589, 1508, 1460, 1369, 1300, 1263, 1209, 1168, 1114, 958, 933, 896 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.51 (3H, d, J = 7.3 Hz), 1.55 (3H, s), 1.56 (3H, s), 3.73 (1H, d, J = 11.2 Hz), 3.81 (1H, d, J = 11.2 Hz), 3.85 (1H, dq, J = 2.9, 7.3 Hz), 5.84 (1H, d, J = 2.9 Hz), 7.78−7.86 (4H, m); ^{13}C NMR ($CDCl_3$) δ 17.6 (CH_3), 27.4 (CH_3), 46.6 (CH), 54.2 (CH_2), 80.4 (C), 85.4 (CH), 113.5 (C), 118.0 (C), 127.5 (CH), 132.4 (CH), 152.5 (C), 158.9 (C), 168.6 (C); MS (EI) *m*/*z* 327 (M^+), 312, 185, 157, 130, 116, 102, 56. HRMS (EI) calcd for $C_{17}H_{17}N_3O_4$ (M^+): 327.1219, found 327.1234.

(4*S*,5*S*)-3-(*p*-Cyanophenyl)-5-hydroxymethyl-4-methyl-4,5-dihydroisoxazole. Colorless viscous oil; $[\alpha]^{25}_D$ = +74.9 (*c* 0.24, $CHCl_3$, 73% ee); IR (neat) 3406, 2932, 2229, 1736, 1589, 1489, 1456, 1348, 1076, 993, 902, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (3H, d, J = 7.1 Hz), 1.81 (1H, brs), 3.65 (1H, dq, J = 5.4, 7.1 Hz),

3.69 (1H, dd, J = 4.4, 12.6 Hz), 3.84 (1H, dd, J = 3.9, 12.6 Hz), 4.50 (1H, ddd, J = 3.9, 4.4, 5.4 Hz), 7.69−7.72 (2H, m), 7.76−7.79 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 43.1 (CH), 63.2 (CH_2), 89.5 (CH), 113.3 (C), 118.1 (C), 127.3 (CH), 132.4 (CH), 132.9 (C), 159.7 (C); MS (EI) m/z 216 (M^+), 185, 157, 142, 102. HRMS (EI) calcd for $C_{12}H_{12}N_2O_2$ (M^+): 216.0899, found 216.0898. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, i-PrOH−hexane (1:9 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 55.0 min, t_{major} = 65.6 min.

3-(*p*-Cyanophenyl)-4-[(5,5-dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-4,5-dihydroisoxazole (5-Me-9h). Although 5-Me-**9h** could not be separated by chromatography from a mixture with major 4-Me-**9h**, it could be characterized by ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ 1.48 (3H, d, J = 3.2 Hz), 1.54 (3H, s), 1.56 (3H, s), 3.75 (1H, d, J = 6.6 Hz), 3.77 (1H, d, J = 6.6 Hz), 4.98 (1H, dq, J = 3.7, 3.2 Hz), 5.37 (1H, d, J = 3.7 Hz), 7.73−7.45 (2H, m), 7.95−7.98 (2H, m).

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-methyl-3-(2-methylpropyl)-4,5-dihydroisoxazole (4-Me-9i). Colorless prisms; mp 126.0−127.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +103.4 (c 0.50, $CHCl_3$, 67% ee); IR (KBr) 2965, 2872, 1778, 1705, 1390, 1370, 1294, 1107, 958 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, d, J = 6.6 Hz), 1.00 (3H, d, J = 6.6 Hz), 1.36 (3H, d, J = 7.3 Hz), 1.53 (6H, s), 1.87−2.02 (1H, m), 2.14−2.29 (2H, m), 3.28−3.41 (1H, m), 3.71 (1H, d, J = 11.0 Hz), 3.79 (1H, d, J = 11.0 Hz), 5.61 (1H, d, J = 3.7 Hz); ^{13}C NMR ($CDCl_3$) δ 16.6 (CH_3), 22.0 (CH_3), 22.2 (CH_3), 26.4 (CH), 27.4 (CH_3), 34.3 (CH_2), 49.2 (CH), 54.3 (CH_2), 79.9 (C), 82.8 (CH), 152.4 (C), 161.3 (C), 169.7 (C); MS (EI) m/z 282 (M^+), 267, 209, 152, 112, 98, 72, 38. HRMS (EI) calcd for $C_{14}H_{22}N_2O_4$ (M^+): 282.1596, found 282.1610. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, i-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 57.1 min, t_{major} = 85.9 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-methyl-3-(2-methylpropyl)-4,5-dihydroisoxazole (5-Me-9i). Colorless prisms; mp 80.0−82.0 °C (Et_2O−hexane); IR (KBr) 2962, 2870, 1775, 1694, 1467, 1376, 1294, 1107 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (3H, d, J = 6.8 Hz), 1.00 (3H, d, J = 6.3 Hz), 1.42 (3H, d, J = 6.3 Hz), 1.54 (6H, s), 1.85−2.01 (1H, m), 2.18 (1H, dd, J = 5.6, 15.1 Hz), 2.29 (1H, dd, J = 9.0, 15.1 Hz), 3.78 (2H, s), 4.74−7.85 (1H, m), 4.90 (1H, d, J = 5.6 Hz); ^{13}C NMR ($CDCl_3$) δ 20.5 (CH_3), 22.2 (CH_3), 23.1(CH_3), 26.2 (CH), 27.3 (CH_3), 27.3 (CH_3), 36.1 (CH_2), 54.6 (CH_2), 60.3 (CH), 79.4 (C), 81.2 (CH), 152.4 (C), 155.1 (C), 169.1 (C); MS (EI) m/z 282 (M^+), 267, 209, 152, 112, 98, 72, 38. Anal. Calcd for $C_{14}H_{22}N_2O_4$: C, 59.56; H, 7.85; N, 9.92. Found: C, 59.75; H, 7.94; N, 9.65.

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-ethyl-3-phenyl-4,5-dihydroisoxazole (4-Et-16b). Colorless prisms; mp 141.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +124.5 (c 0.22, $CHCl_3$, 88% ee); IR (KBr) 2973, 2935, 1775, 1708, 1375, 1295, 1207, 1109, 761, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (3H, t, J = 7.3 Hz), 1.55 (3H, s), 1.55 (3H, s), 1.76−1.84 (1H, m), 1.96−2.05 (1H, m), 3.74 (1H, d, J = 11.2 Hz), 3.80 (1H, d, J = 11.2 Hz), 3.99 (1H, ddd, J = 3.2, 4.1, 7.3 Hz), 5.93 (1H, d, J = 3.2 Hz), 7.39−7.42 (3H, m), 7.70−7.73 (2H, m); ^{13}C NMR ($CDCl_3$) δ 9.9 (CH_3), 23.8 (CH_2), 27.3 (CH_3), 27.4 (CH_3), 52.5 (CH), 54.4 (CH_2), 80.1 (C), 82.3 (CH), 127.1 (CH), 127.9 (C), 128.7 (CH), 130.2 (CH), 152.4 (C), 158.7 (C), 169.5 (C); MS (EI) m/z 316 (M^+), 219, 175, 117, 104, 91, 71, 55, 38. Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.86. Found: C, 64.76; H, 6.33; N, 8.68. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, i-PrOH−hexane (3:97 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol. t_{minor} = 78.7 min, t_{major} = 90.3 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-ethyl-3-(2-methylpropyl)-4,5-dihydroisoxazole (5-Et-16b). Colorless prisms; mp 105.0−106.0 °C (Et_2O−hexane); IR (KBr) 2972, 1770, 1743, 1697, 1375, 1031, 1238, 1199, 1110, 881 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (3H, t, J = 7.3 Hz), 1.49 (3H, s), 1.54 (3H, s), 1.82−1.89 (2H, m), 3.73 (1H, d, J = 11.5 Hz), 3.76 (1H, d, J = 11.5 Hz), 4.78 (1H, ddd, J = 4.8, 5.6, 11.7 Hz), 5.62 (1H, d, J = 4.8 Hz), 7.36−7.41 (3H, m), 7.62−7.64 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 27.1 (CH_3), 27.2 (CH_3), 54.5 (CH_2), 55.8 (CH), 62.4 (CH_2), 79.8 (C), 83.0 (CH), 127.0 (CH) 128.8 (CH), 130.5 (CH), 152.4 (C), 154.7 (C), 167.8 (C), 168.1 (C); MS (EI) m/z 316 (M^+), 243, 184, 172, 144, 116, 98, 77, 35. Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.86. Found: C, 64.42; H, 6.50; N, 8.57.

(5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-3-phenyl-4,5-dihydroisoxazole (17b). Colorless prisms; mp 196.0 °C (Et_2O); $[\alpha]^{25}_D$ = +55.2 (c 0.5, $CHCl_3$, 62% ee); IR (KBr) 2981, 1774, 1713, 1374, 1294, 1107, 921, 760, 687 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55 (6H, s), 3.58 (1H, dd, J = 6.1, 16.8 Hz), 3.76 (1H, d, J = 10.7 Hz), 3.83 (1H, d, J = 10.7 Hz), 3.83 (1H, dd, J = 11.7, 16.8 Hz), 6.14 (1H, dd, J = 11.7, 6.1 Hz), 7.38−7.43 (3H, m), 7.67−7.70 (2H, m); ^{13}C NMR ($CDCl_3$) δ 27.3 (CH_3), 39.1 (CH_2), 54.5 (CH_2), 78.3 (CH), 80.6 (C), 127.4 (CH), 129.1 (C), 129.2 (CH), 130.9 (CH), 153.0 (C), 156.4 (C), 170.1 (C); MS (EI) m/z 288 (M^+), 260, 146, 118, 104, 91, 77, 35. Anal. Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.61; H, 5.43; N, 9.76. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, i-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 53.9 min, t_{major} = 62.8 min.

(4*S*,5*S*)-5-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-4-ethoxycarbonyl-3-phenyl-4,5-dihydroisoxazole (4-CO_2Et-18b). Colorless prisms; mp 121.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +81.4 (c 0.4, $CHCl_3$, 51% ee); IR (KBr) 2977, 1764, 1739, 1375, 1297, 1263, 1238, 1177, 1111, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (3H, t, J = 7.1 Hz), 1.55 (3H, s), 1.56 (3H, s), 3.75 (1H, d, J = 11.0 Hz), 3.81 (1H, d, J = 11.0 Hz), 4.20 (1H, dq, J = 11.7, 7.1 Hz), 4.23 (1H, dq, J = 11.7, 7.1 Hz),, 4.76 (1H, d, J = 4.6 Hz), 6.40 (1H, d, J = 4.6 Hz), 7.36−7.42 (3H, m), 7.77−7.86 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 27.3 (CH_3), 27.4 (CH_3), 54.2 (CH_2), 57.0 (CH), 62.5 (CH_2), 80.4 (C), 82.3 (CH), 127.3 (CH), 127.4 (C), 128.5 (CH), 130.5 (CH), 152.2 (C), 153.6 (C), 167.5 (C), 167.6 (C); MS (EI) m/z 360 (M^+), 332, 218, 190, 172, 144, 77, 55, 37. Anal. Calcd for $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77. Found: C, 59.96; H, 5.67; N, 7.73. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, i-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 54.9 min, t_{major} = 68.5 min.

4-[(5,5-Dimethyl-2-oxo-3-oxazolidinyl)carbonyl]-5-ethoxycarbonyl-3-phenyl-4,5-dihydroisoxazole (5-CO_2Et-18b). Colorless prisms; mp 165.5−166.5 °C (Et_2O−hexane) IR (KBr) 1768, 1743, 1697, 1376, 1338, 1332, 1238, 1199, 1110, 881, 768 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, t, J = 7.1 Hz), 1.47 (3H, s), 1.55 (3H, s), 3.72 (1H, d, J = 11.0 Hz), 3.76 (1H, d, J = 11.0 Hz), 4.29 (1H, dq, J = 14.1, 7.1 Hz), 4.30 (1H, dq, J = 14.1, 7.1 Hz), 5.22 (1H, d, J = 5.4 Hz), 6.20 (1H, d, J = 5.4 Hz), 7.36−7.42 (3H, m), 7.63−7.67 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.4 (CH_3), 27.1 (CH_3), 27.2 (CH_3), 54.4 (CH_2), 55.8 (CH), 62.4 (CH_2), 79.8 (C), 83.2 (CH), 127.0 (CH), 127.7 (C), 128.8 (CH), 130.5 (CH), 152.4 (C), 154.8 (C), 167.8 (C), 168.1 (C); MS (EI) m/z 360 (M^+), 287, 218, 184, 172, 116, 98, 77. HRMS (EI) calcd for $C_{18}H_{20}N_2O_6$ (M^+): 360.1321, found 360.1341.

General Procedure for the (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II)-Catalyzed Reaction of Hydroximyl Chloride with 1-Benzyl-2-crotonoyl-5,5-dimethyl-3-pyrazolidinone (4) Exemplified by the Reaction of Benzohydroximoyl Chloride (8b). A suspension of (*R*)-BINIM-4(3,5-xylyl)-2QN (19.3 mg, 0.025 mmol), powdered MS 4Å (190.5 mg), and $Ni(ClO_4)_2\cdot 6H_2O$ (9.2 mg, 0.025 mmol) in CH_2Cl_2 (3.0 mL) was stirred for 6 h at room temperature. Pyrazolidinone **4** (68.1 mg, 0.25 mmol), hyroximoyl chloride **8b** (77.8 mg, 0.50 mmol), and CH_2Cl_2 (1.5 mL) were added successively to the catalyst suspension. After stirring at room temperature

for 24 h, the reaction was quenched with saturated NH_4Cl solution (2.5 mL) and water (2.5 mL) and then filtered through Celite. The filtrate was extracted with CH_2Cl_2 (5.0 mL × 3). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane−ethyl acetate (73:27 v/v) as an eluent to give cycloadduct **10b** (88.0 mg, 90%). Regioselectivity was determined to be 4-Me/5-Me = 99:1 by ^{1}H NMR (400 MHz) analysis of the crude mixture. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 41.6 min, t_{major} = 49.5 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-4-methyl-3-phenyl-4,5-dihydroisoxazole (4-Me-10b).[6] Colorless prisms; mp 111.0−112.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +115.4 (*c* 0.51, $CHCl_3$, 95% ee); IR (KBr) 2977, 2933, 1749, 1709, 1455, 1346, 1305, 1233, 925, 881, 768, 696 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.75 (3H, s), 0.77 (3H, s), 1.09 (3H, d, *J* = 7.3 Hz), 2.04 (2H, s), 3.66 (2H, s), 3.99 (1H, dq, *J* = 2.7, 7.3 Hz), 5.83 (1H, d, *J* = 2.7 Hz), 6.97−7.18 (6H, m), 7.44−7.47 (2H, m), 7.59−7.63 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.6 (CH_3), 26.3 (CH_3), 26.4 (CH_3), 43.3 (CH_2), 45.8 (CH), 56.9 (CH_2), 61.7 (C), 85.3 (CH), 127.1 (CH), 127.4 (CH), 127.8 (C), 128.2 (CH), 128.6 (CH), 129.1 (CH), 130.0 (CH), 136.8 (C), 160.3 (C), 165.8 (C), 174.6 (C); MS (EI) *m*/*z* 391 (M^+), 204, 189, 113, 91, 77, 37. Anal. Calcd for $C_{23}H_{25}N_3O_3$: C, 70.57; H, 6.44; N, 10.73. Found: C, 70.53; H, 6.38; N, 10.72. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 41.6 min, t_{major} = 49.5 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(*p*-methoxyphenyl)-4-methyl-4,5-dihydroisoxazole (4-Me-10c).[6] Colorless prisms; mp 121.0−121.5 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +111.6 (*c* 0.51, $CHCl_3$, 92% ee); IR (KBr) 2973, 2937, 1753, 1709, 1604, 1515, 1261, 1229, 1176, 925, 886, 840, 699 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.76 (3H, s), 0.78 (3H, s), 1.15 (3H, d, *J* = 7.3 Hz), 2.04 (2H, s), 3.19 (3H, s), 3.67 (2H, s), 4.02 (1H, dq, *J* = 2.9, 7.3 Hz), 5.85 (1H, d, *J* = 2.9 Hz), 6.61−6.64 (2H, m), 7.00−7.04 (1H, m), 7.11−7.19 (2H, m), 7.47−7.49 (2H, m), 7.57−7.61 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 26.3 (CH_3), 26.4 (CH_3), 43.3 (CH_2), 46.1 (CH), 55.4 (CH_3), 56.9 (CH_2), 61.7 (C), 85.1 (CH), 114.0 (CH), 120.2 (C), 127.4 (CH), 128.2 (CH), 128.6 (CH), 129.1 (CH), 136.8 (C), 159.9 (C), 160.8 (C), 166.0 (C), 174.6 (C); MS (EI) *m*/*z* 421 (M^+), 204, 190, 133, 113, 92, 77. Anal. Calcd for $C_{24}H_{27}N_3O_4$: C, 68.39; H, 6.46; N, 9.97. Found: C, 68.17; H, 6.16; N, 9.84. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 51.9 min, t_{major} = 69.1 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-4-methyl-3-*p*-tolyl-4,5-dihydroisoxazole (4-Me-10d). Colorless prisms; mp 170.0−171.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +121.2 (*c* 0.5, $CHCl_3$, 88% ee); IR (KBr) 2995, 2971, 2930, 1754, 1705, 1304, 1235, 1210, 952, 883, 817 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.76 (3H, s), 0.79 (3H, s), 1.14 (3H, d, *J* = 7.3 Hz), 2.00 (3H, s), 2.06 (2H, s), 3.67 (2H, s), 4.02 (1H, dq, *J* = 7.3, 2.9 Hz), 5.84 (1H, d, *J* = 2.9 Hz), 6.85−6.87 (2H, m), 7.01−7.04 (1H, m), 7.10−7.19 (2H, m), 7.45−7.49 (2H, m), 7.57−7.62 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 21.5 (CH_3), 26.3 (CH_3), 26.4 (CH_3), 43.3 (CH_2), 46.0 (CH), 56.9 (CH_2), 61.7 (C), 85.2 (CH), 124.9 (C), 127.0 (CH), 127.4 (CH), 128.2 (CH), 129.1 (CH), 129.2 (CH), 136.8 (C), 140.3 (C), 160.2 (C), 165.9 (C), 174.5 (C); MS (EI) *m*/*z* 405 (M^+), 204, 189, 174, 146, 113, 92, 77. Anal. Calcd for $C_{24}H_{27}N_3O_3$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.29; H, 6.34; N, 10.22. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 56.7 min, t_{major} = 75.0 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(*p*-chlorophenyl)-4-methyl-4,5-dihydroisoxazole (4-Me-10e).[6] Colorless prisms; mp 154.5−155.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +100.8 (*c* 0.59, $CHCl_3$, 79% ee); IR (KBr) 2981, 2938, 1751, 1722, 1496, 1304, 1217, 1093, 929, 887, 834, 694 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.75 (3H, s), 0.77 (3H, s), 0.99 (3H, d, *J* = 7.3 Hz), 2.02 (2H, s), 3.65 (2H, s), 3.85 (1H, dq, *J* = 2.9, 7.3 Hz), 5.81 (1H, d, *J* = 2.9 Hz), 6.93−7.02 (3H, m), 7.09−7.19 (2H, m), 7.27−7.30 (2H, m), 7.44−7.46 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.5 (CH_3), 26.4 (CH_3), 26.4 (CH_3), 43.2 (CH_2), 45.6 (CH), 57.0 (CH_2), 61.7 (C), 85.5 (CH), 126.3 (C), 127.4 (CH), 128.2 (CH), 128.3 (CH), 128.8 (CH), 129.1 (CH), 136.0 (C), 136.7 (C), 159.4 (C), 165.6 (C) 174.6 (C); MS (EI) *m*/*z* 425 (M^+), 205, 189, 131, 111, 92. Anal. Calcd for $C_{23}H_{24}N_3O_3Cl$: C, 64.86; H, 5.68; N, 9.87. Found: C, 64.96; H, 5.39; N, 9.68. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 55.9 min, t_{major} = 67.5 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(*o*-chlorophenyl)-4-methyl-4,5-dihydroisoxazole (4-Me-10f).[6] Colorless prisms; mp 53.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +100.3 (*c* 0.34, $CHCl_3$, 83% ee); IR (KBr) 3061, 3028, 2975, 2935, 1747, 1714, 1455, 1313, 1235, 874, 759, 698 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.77 (3H, s), 0.78 (3H, s), 1.02 (3H, d, *J* = 6.8 Hz), 1.99 (1H, d, *J* = 16.8 Hz), 2.05 (1H, d, *J* = 16.8 Hz), 3.68 (1H, d, *J* = 13.9 Hz), 3.72 (1H, d, *J* = 13.9 Hz), 4.45−4.53 (1H, m), 5.90 (1H, d, *J* = 4.1 Hz), 6.66−6.74 (2H, m), 6.98−7.13 (4H, m), 7.38−7.41 (1H, m), 7.50−7.53 (2H, m); ^{13}C NMR ($CDCl_3$) δ 16.6 (CH_3), 26.0 (CH_3), 26.7 (CH_3), 43.3 (CH_2), 47.9 (CH), 56.8 (CH_2), 61.6 (C), 85.2 (CH), 126.7 (CH), 127.3 (C), 127.4 (CH), 128.3 (CH), 129.1 (CH), 130.1 (CH), 130.8, (CH) 131.2 (CH), 132.9 (C), 137.0 (C), 160.3 (C), 165.4 (C), 174.5 (C); MS (EI) *m*/*z* 425 (M^+), 205, 189, 130, 111, 92, 77. HRMS (EI) calcd for $C_{23}H_{24}N_3O_3Cl$ (M^+): 425.1502, found 425.1512. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol.[14] t_{minor} = 48.5 min, t_{major} = 54.4 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-Dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-4-methyl-3-(2-methylpropyl)-4,5-dihydroisoxazole (4-Me-10i).[6] Colorless needles; mp 88.0−89.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +135.3 (*c* 0.57, $CHCl_3$, 76% ee); IR (KBr) 2957, 2933, 2872, 1750, 1709, 1471, 1265, 1237, 1204, 716 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.75 (3H, s), 0.78 (3H, s), 0.80 (3H, d, *J* = 6.6 Hz), 0.86 (3H, d, *J* = 6.6 Hz), 0.90 (3H, d, *J* = 7.3 Hz), 1.73−1.87 (2H, m), 1.97−2.07 (3H, m), 3.46 (1H, dq, *J* = 4.1, 7.3 Hz), 3.68 (2H, s), 5.70 (1H, d, *J* = 4.1 Hz), 7.03−7.19 (3H, m), 7.47−7.49 (2H, m); ^{13}C NMR ($CDCl_3$) δ 16.2 (CH_3), 22.0 (CH_3), 23.2 (CH_2), 26.0 (CH_3), 26.2 (CH_3), 26.6 (CH_3), 34.4 (CH_2), 43.3 (CH), 47.6 (CH), 56.9 (CH_2), 61.6 (C), 83.5 (CH), 127.5 (CH), 128.2 (CH), 129.3 (CH), 136.8 (C), 161.5 (C), 166.2 (C), 174.4 (C); MS (EI) *m*/*z* 371 (M^+), 356, 205, 189, 113, 92, 77, 65. Anal. Calcd for $C_{21}H_{29}N_3O_3$: C, 67.90; H, 7.87; N, 11.31. Found: C, 67.97; H, 7.87; N, 11.25. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak OJ, *i*-PrOH−hexane (1:9 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 26.6 min, t_{major} = 30.6 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-butyl-4-methyl-4,5-dihydroisoxazole (4-Me-10j). Colorless cottonlike needles; mp 88.0−89.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +53.5 (*c* 0.51, $CDCl_3$, 84% ee); IR (KBr) 2969, 2933, 2872, 1750, 1705, 1463, 1370, 1314, 1257, 1237, 1213, 772 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.76 (3H, t, *J* = 7.3 Hz), 0.77 (3H, s), 0.79 (3H, s), 0.90 (3H, d, *J* = 7.1 Hz), 1.11−1.27 (2H, m), 1.38−1.45 (2H, m), 1.86 (1H, dt, *J* = 15.4, 7.8 Hz), 2.04 (2H, s), 2.16 (1H, dt, *J* = 15.4, 7.8 Hz), 3.47 (1H, dq, *J* = 4.4, 7.1 Hz), 3.69 (2H, s), 5.69 (1H, d, *J* = 4.4 Hz), 7.03−7.72 (1H, m), 7.13−7.19 (2H, m), 7.46−7.51 (2H, m); ^{13}C NMR ($CDCl_3$) δ 13.8 (CH_3), 16.3 (CH_3), 22.5 (CH_2), 25.4 (CH_2), 26.1 (CH_3), 26.5 (CH_3), 28.3 (CH_2), 43.3

(CH_2), 47.4, (CH) 57.0 (CH_2), 61.6 (C), 83.7 (CH), 127.5 (CH), 128.2 (CH), 129.3 (CH), 136.9 (C), 162.2 (C), 166.1 (C), 174.4 (C); MS (EI) *m*/*z* 371 (M^+), 204, 189, 113, 91, 57. Anal. Calcd for $C_{21}H_{29}N_3O_3$: C, 67.90; H, 7.87; N, 11.31. Found: C, 67.82; H, 8.04; N, 11.36. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 60.8 min, t_{major} = 68.2 min.

(4*S*,5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-*tert*-butyl-4-methyl-4,5-dihydroisoxazole (4-Me-10k).[6] Colorless cottonlike needles; mp 155.0−156.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +67.1 (*c* 0.5, $CDCl_3$, 42% ee); IR (KBr) 2969, 2933, 1753, 1697, 1467, 1374, 1318, 1224, 881, 724, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.64 (3H, s), 0.67 (3H, s), 0.95 (3H, d, *J* = 7.3 Hz), 0.99 (9H, s), 1.88 (1H, d, *J* = 17.1 Hz), 1.92 (1H, d, *J* = 17.1 Hz), 3.35−3.43 (1H, m), 3.55 (1H, d, *J* = 14.1 Hz), 3.59 (1H, d, *J* = 14.1 Hz), 5.54 (1H, d, *J* = 2.0 Hz), 6.92−6.95 (1H, m), 7.00−7.08 (2H, m), 7.34−7.39 (2H, m); ^{13}C NMR ($CDCl_3$) δ 18.2 (CH_3), 25.9 (CH_3), 26.7 (CH_3), 29.1 (CH_3), 33.5 (C), 43.3 (CH_2), 46.1 (CH), 56.9 (CH_2), 61.6 (C), 85.1 (CH), 127.4 (CH), 128.3 (CH), 129.2 (CH), 136.9 (C), 166.0 (C), 169.0 (C), 174.4 (C); MS (EI) *m*/*z* 371 (M^+), 356, 204, 189, 113, 91, 69, 57. Anal. Calcd for $C_{21}H_{29}N_3O_3$: C, 67.90; H, 7.87; N, 11.31. Found: C, 68.04; H, 7.73; N, 11.31. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 41.2 min, t_{major} = 52.3 min.

General Procedure for (*R*)-BINIM-4(3,5-xylyl)-2QN-Ni(II)-Catalyzed Reaction of Hydroximyl Chloride with 2-Acryloyl-1-benzyl-5,5-dimethyl-3-pyrazolidinone (14) Exemplified by the Reaction of Benzohydroximoyl Chloride (8b). A suspension of (*R*)-BINIM-4(3,5-xylyl)-2QN (19.3 mg, 0.025 mmol), powdered MS 4Å (190.5 mg), and $Ni(ClO_4)_2 \cdot 6H_2O$ (9.2 mg, 0.025 mmol) in CH_2Cl_2 (3.0 mL) was stirred for 6 h at room temperature. A solution of pyrazolidinone **14** (63.5 mg, 0.25 mmol) and hyroximoyl chloride **8b** (77.8 mg, 0.50 mmol) in CH_2Cl_2 (1.0 mL) were added to the catalyst suspension over a period of 1 h by syringe pump. The syringe was washed with CH_2Cl_2 (0.5 mL). After stirring the mixture at room temperature for 1 h, the reaction mixture was quenched with saturated NH_4Cl solution (2.5 mL) and water (2.5 mL) and then filtered through Celite. The filtrate was extracted with CH_2Cl_2 (5.0 mL × 3). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed on silica gel with hexane−ethyl acetate (72: 28 v/v) as an eluent to give cycloadduct **19b** (75.6 mg, 80%). Regioselectivity was determined to be 4-Me/5-Me = >99:1 by ^1H NMR (400 MHz) analysis of the crude mixture. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 53.9 min, t_{major} = 62.8 min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-phenyl-4,5-dihydroisoxazole (19b). Colorless prisms; mp 195.0−196.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +165.5 (*c* 0.50, $CHCl_3$, 90% ee); IR (KBr) 2981, 2696, 1753, 1693, 1353, 1233, 881, 768, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3H, s), 1.33 (3H, s), 2.60 (1H, d, *J* = 17.1 Hz), 2.68 (1H, d, *J* = 17.1 Hz), 3.45 (2H, d, *J* = 7.1 Hz), 4.06 (1H, d, *J* = 13.7 Hz), 4.11 (1H, d, *J* = 13.7 Hz), 5.84 (1H, brt, *J* = 7.1 Hz), 7.14−7.31 (3H, m), 7.34−7.47 (5H, m), 5.84−7.63 (2H, m); ^{13}C NMR ($CDCl_3$) δ 26.1 (CH_3), 26.4 (CH_3), 37.8 (CH_2), 43.2 (CH_2), 57.0 (CH_2), 61.7 (C), 78.3 (CH), 126.8 (CH), 127.5 (CH), 128.3 (CH), 128.5 (CH), 128.7 (C), 129.3 (CH), 130.1 (CH), 136.7 (C), 155.7 (C), 165.9 (C), 174.3 (C); MS (EI) *m*/*z* 377 (M^+), 205, 189, 146, 118, 92, 77, 65. Anal. Calcd for $C_{22}H_{23}N_3O_3$: C, 70.01; H, 6.14; N, 11.13. Found: C, 69.95; H, 6.10; N, 11.24. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 53.9 min, t_{major} = 62.8 min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(*p*-methoxyphenyl)-4,5-dihydroisoxazole (19c). Colorless needles; mp 121.0−121.5 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +148.5 (*c* 0.40, $CHCl_3$, 91% ee); IR (KBr) 2966, 2928, 1755, 1698, 1607, 1515, 1362, 1246, 1227, 1179, 1025, 838, 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3H, s), 1.32 (3H, s), 2.61 (1H, d, *J* = 17.1 Hz), 2.67 (1H, d, *J* = 17.1 Hz), 3.42 (2H, d, *J* = 7.3 Hz), 3.83 (3H, s), 4.06 (1H, d, *J* = 13.7 Hz), 4.11 (1H, d, *J* = 13.7 Hz), 5.81 (1H, brt, *J* = 7.3 Hz), 6.88−6.92 (2H, m), 7.18−7.29 (3H, m), 7.40−7.44 (2H, m), 7.53−7.60 (2H, m); ^{13}C NMR ($CDCl_3$) δ 26.1 (CH_3), 26.4 (CH_3), 38.1 (CH_2), 43.2 (CH_2), 55.4 (CH_3), 57.0 (CH_2), 61.6 (C), 78.1 (CH), 113.9 (CH), 121.2 (C), 127.5 (CH), 128.2 (CH), 128.3 (CH), 129.2 (CH), 136.7 (C), 155.2 (C), 160.9 (C), 166.1 (C), 174.3 (C); MS (EI) *m*/*z* 407 (M^+), 204, 189, 113, 91, 77, 56. Anal. Calcd for $C_{23}H_{25}N_3O_4$: C, 67.80; H, 6.18; N, 10.31. Found: C, 67.75; H, 6.16; N, 10.38. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 111.4 min, t_{major} = 124.2 min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(*p*-chlorophenyl)-4,5-dihydroisoxazole (19e). Colorless needles; mp 128.0−129.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +82.4 (*c* 0.50, $CDCl_3$, 79% ee); IR (KBr) 3034, 2977, 1757, 1701, 1491, 1349, 1240, 1216, 825, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3H, s), 1.33 (3H, s), 2.62 (1H, d, *J* = 17.1 Hz), 2.69 (1H, d, *J* = 17.1 Hz), 3.41 (2H, d, *J* = 7.1 Hz), 4.05 (1H, d, *J* = 13.2 Hz), 4.11 (1H, d, *J* = 13.2 Hz), 5.84 (1H, brt, *J* = 7.1 Hz), 7.18−7.29 (3H, m), 7.33−7.44 (4H, m), 7.53−7.61 (2H, m); ^{13}C NMR ($CDCl_3$) δ 26.4 (CH_3), 26.1 (CH_3), 37.6 (CH_2), 43.2 (CH_2), 57.1 (CH_2), 61.7 (C), 78.5 (CH), 127.1 (C), 127.5 (CH), 128.0 (CH), 128.3 (CH), 128.8 (CH), 129.3 (CH), 136.1 (C), 136.6 (C), 154.8 (C), 165.7 (C), 174.3 (C); MS (EI) *m*/*z* 411 (M^+), 204, 189, 113, 91, 75, 56. Anal. Calcd for $C_{22}H_{22}N_3O_3Cl$: C, 64.15; H, 5.38; N, 10.20. Found: C, 64.23; H, 5.24; N, 10.27. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 72.0 min, t_{major} = 83.7 min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-(2-methylpropyl)-4,5-dihydroisoxazole (19i). Colorless cottonlike needles; mp 77.0−78.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +118.5 (*c* 0.50, $CHCl_3$, 83% ee); IR (KBr) 2957, 2876, 1757, 1693, 1390, 1224, 886, 833, 716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (3H, d, *J* = 6.8 Hz), 0.95 (3H, d, *J* = 6.8 Hz), 1.28 (3H, s), 1.31 (3H, s), 1.87 (1H, quint, *J* = 6.8 Hz), 2.20 (2H, d, *J* = 7.3 Hz), 2.56 (1H, d, *J* = 17.1 Hz), 2.66 (1H, d, *J* = 17.1 Hz), 2.90−3.08 (2H, m), 4.03 (1H, d, *J* = 13.7 Hz), 4.11 (1H, d, *J* = 13.7 Hz), 5.65 (1H, brt, *J* = 7.3 Hz), 7.24−7.32 (3H, m), 7.41−7.43 (2H, m); ^{13}C NMR ($CDCl_3$) δ 22.5 (CH_3), 22.6 (CH_3), 26.0 (CH_3), 26.3 (CH), 26.5 (CH_3), 36.1 (CH_2), 39.8 (CH_2), 43.2 (CH_2), 57.0 (CH_2), 61.5 (C), 76.8 (CH), 127.5 (CH), 128.2 (CH), 129.3 (CH), 136.7 (C), 157.5 (C), 166.3 (C), 174.2 (C); MS (EI) *m*/*z* 357 (M^+), 204, 189, 113, 91, 57. Anal. Calcd for $C_{20}H_{27}N_3O_3$: C, 67.20; H, 7.61; N, 11.76. Found: C, 67.18; H, 7.62; N, 11.72. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 92.1 min, t_{major} = 99.70. min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-butyl-4,5-dihydroisoxazole (19j). Colorless oil; $[\alpha]^{25}_D$ = +72.8 (*c* 0.50, $CHCl_3$, 87% ee); IR (neat) 2962, 2934, 1684, 1585, 1454, 1373, 1219, 754, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (3H, t, *J* = 7.3 Hz), 1.28 (3H, s), 1.31 (3H, s), 1.32−1.39 (2H, m), 1.48−1.59 (2H, m), 2.31 (2H, t, *J* = 7.3 Hz), 2.56 (1H, d, *J* = 17.3 Hz), 2.65 (1H, d, *J* = 17.3 Hz), 2.96−3.08 (2H, m), 4.04 (1H, d, *J* = 13.7 Hz), 4.11 (1H, d, *J* = 13.7 Hz), 5.66 (1H, brdd, *J* = 6.3, 7.8 Hz), 7.23−7.33 (3H, m), 7.42−7.44 (2H, m); ^{13}C NMR

($CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 26.3 (CH_3), 26.7 (CH_3), 27.3 (CH_2), 28.7 (CH_2), 40.0 (CH_2), 43.5 (CH_2), 57.3 (CH_2), 61.9 (C), 77.2 (CH), 127.7 (CH), 128.5 (CH), 129.5 (CH), 137.0 (C), 158.5 (C), 166.6 (C), 174.5 (C); MS (EI) *m*/*z* 357 (M^+), 204, 189, 119, 92, 82, 65. HRMS (EI) calcd for $C_{20}H_{27}N_3O_3$ (M^+): 357.2052, found 357.2017. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 92.6 min, t_{major} = 101.8 min.

(5*S*)-5-[(1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-3-*tert*-butyl-4,5-dihydroisoxazole (19k). Colorless cottonlike needles; mp 148.0−149.0 °C (Et_2O−hexane); $[\alpha]^{25}_D$ = +130.4 (*c* 0.50, $CHCl_3$, 86% ee); IR (KBr) 2971, 2870, 1751, 1712, 1251, 1232, 1213, 929, 863, 771 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (9H, s), 1.26 (3H, s), 1.31 (3H, s), 2.56 (1H, d, *J* = 17.1 Hz), 2.66 (1H, d, *J* = 17.1 Hz), 3.00 (1H, dd, *J* = 10.0, 16.6 Hz), 3.10 (1H, dd, *J* = 6.3, 16.6 Hz), 4.03 (1H, d, *J* = 13.4 Hz), 4.11 (1H, d, *J* = 13.4 Hz), 5.63 (1H, brdd, *J* = 6.3, 10.0 Hz), 7.24−7.33 (3H, m), 7.41−7.44 (2H, m); ^{13}C NMR ($CDCl_3$) δ 26.0 (CH_3), 26.5 (CH_3), 28.1 (CH_3), 33.0 (C), 36.9 (CH_2), 43.2 (CH_2), 57.1 (CH_2), 61.6 (C), 77.3 (CH), 127.5 (CH), 128.3 (CH), 129.3 (CH), 136.8 (C), 165.1 (C), 166.2, (C) 174.1 (C); MS (EI) *m*/*z* 357 (M^+), 205, 190, 113, 92, 77, 65. Anal. Calcd for $C_{20}H_{27}N_3O_3$: C, 67.20; H, 7.61; N, 11.76. Found: C, 67.19; H, 7.64; N, 11.74. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C). t_{minor} = 56.2 min, t_{major} = 63.0 min.

(4*S*,5*S*)-5-[((1-Benzyl-5,5-dimethyl-3-oxo-2-pyrazolidinyl)carbonyl]-4-ethoxycarbonyl-3-phenyl-4,5-dihydroisoxazole (4-CO_2Et-20b). Colorless oil; $[\alpha]^{25}_D$ = +143.8 (*c* 0.40, $CHCl_3$, 75% ee); IR (neat) 2988, 2971, 2938, 1763, 1734, 1701, 1337, 1235, 890, 694 cm^{-1}; ^1H NMR (C_6D_6) δ 0.70 (3H, s), 0.74 (3H, s), 0.74 (3H, t, *J* = 7.1 Hz), 1.92−2.03 (2H, m), 3.58 (2H, s), 3.70−3.86 (2H, m), 5.09 (1H, d, *J* = 4.4 Hz), 6.23 (1H, br), 6.95−7.18 (6H, m), 7.44−7.46 (2H, m), 7.85−7.87 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 25.2 (CH_3), 43.2 (CH_2), 56.8 (CH_2), 56.9 (CH_3), 62.5 (CH_2), 62.8 (C), 82.0 (CH), 126.8 (CH), 127.3 (CH), 127.5 (C), 127.8 (CH), 128.5 (CH), 128.5 (CH), 129.1 (CH), 130.5 (CH), 135.9 (C), 135.9 (C), 167.6 (C), 171.4 (C), 174.4 (C); MS (EI) *m*/*z* 449 (M^+), 204, 189, 144, 113, 91, 77. HRMS (EI) calcd for $C_{25}H_{27}N_3O_5$ (M^+): 449.1950, found 449.1925. The enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD-H, *i*-PrOH−hexane (1:19 v/v), detector: UV 254 nm, flow rate = 0.5 mL/min, 35 °C) after reduction to the corresponding alcohol by $NaBH_4$.[14] t_{minor} = 54.9 min, t_{major} = 68.5 min.

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Supporting Information Available: General methods and materials for experimental section and spectroscopic data of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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