SUPPORTING INFORMATION

Chiral Lewis Acid Catalysis in Nitrile Oxide Cycloadditions

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General Experimental Procedures. Methylene chloride was distilled from calcium hydride prior to use. Tetrahydrofuran was distilled from sodium benzophenone ketyl prior to use. Lewis acids were purchased and used as received. Oximes were synthesized using hydroxylamine monohydrochloride with corresponding aldehyde according to the literature.¹ Hydroximinoyl chlorides (nitrile oxide precursors) **7b-7g** were synthesized by chlorination of oximes with *N*-chlorosuccinimide (NCS) according to the literature.^{2,3} 2,4,6-Trimethylbenzonitrile oxide **7a** was prepared from 2,4,6-trimethylbenzohydroximinoyl chloride.^{1,2} α,β -Unsaturated imides **5a-5d** were prepared by previously reported methods.^{4,5,6} The ligands **6a, 6b** and α,β -unsaturated imides **5e-5f** were synthesized according to the method reported by our laboratory.⁷ Powdered molecular sieves 4Å (MS 4A) was purchased from Aldrich Chemical and dried at 300 °C under vacuum before use. L-Selectride® (1 M solution in THF) was purchased from Aldrich Chemical. Sodium borohydride (powder) was purchased from Lancaster Synthesis. Flash chromatography was performed using EM Science silica gel 60 (230-400 mesh). All glassware was oven dried, assembled hot, and cooled under a stream of dry nitrogen before use. Reactions with air sensitive materials were carried out by standard syringe techniques.

Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. ¹H NMR was recorded on a Varian Unity/Inova-500 NB (500 MHz), or a Varian Mercury-400 (400 MHz). Chemical shifts are reported in parts per million (ppm)

down field from TMS, using residual CDCl_3 (7.27 ppm) or C_6D_6 (7.15 ppm) as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sep = septet, dd = doublets of doublets, dt = doublets of triplets, dq = doublets of quartets, m = multiplet, br = broad, AB sys = AB system), coupling constant(s) and integration. ^{13}C NMR was recorded on a Varian Unity/Inova-500 NB (125 MHz) or a Varian Mercury-400 (100 MHz) spectrometers using broad band proton decoupling. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of CDCl_3 (77.23 ppm) as an internal standard. HPLC analyses were carried out on Waters 515 HPLC pump and a 2487 dual λ absorbance detector connected to a PC with millennium workstation. Rotations were recorded on a JASCO-DIP-370 instrument. High-resolution mass spectra (HRMS) [EI+ or FAB] were obtained from the Mass Spectrometry Laboratory, Ohio State University, Columbus, Ohio.

I. Preparation of intermediates and substrates

General procedure for the *N*(1)-alkylation of pyrazolidinones: The synthesis of pyrazolidinone **12** has been reported in the literature.⁸ *N*(1)-Alkyl pyrazolidinones were prepared by selective alkylation at the more basic *N*(1)-nitrogen.⁹ The corresponding alkyl bromide (1 eq.), K_2CO_3 (1 eq.) and a catalytic amount of NaI (0.1 eq.) were added to a solution of corresponding pyrazolidinone (1 eq.) in 2-butanone. The solution was allowed to reflux overnight. After the reaction mixture was cooled to room temperature, water was added, followed by extraction with CH_2Cl_2 (3x). The organics were combined, dried over magnesium sulfate, then filtered, and solvent was removed under reduced pressure. The products were purified by flash chromatography on silica gel.

1-Benzyl-5,5-dimethyl-pyrazolidin-3-one (13a):

White solid; yield: 90%; mp 105-106 °C (Hexane-Ethyl Acetate), [lit.² 105-106 °C]; ¹H NMR (CDCl₃, 500 MHz) δ 1.37 (s, 6H), 2.42 (s, 2H), 3.79 (s, 2H), 6.81 (s, 1H), 7.30-7.35 (m, 5H); ¹³C NMR (CDCl₃, 125 MHz) δ 25.6, 43.1, 57.3, 62.6, 128.0, 128.9, 129.5, 137.3, 174.4. See also reference.⁷

5,5-Dimethyl-1-(1-naphthylmethyl)- pyrazolidin-3-one (13b):

White solid; yield: 89%; mp 152-154 °C (Hexane-Ethyl Acetate), [lit.² 152-154 °C]; ¹H NMR (CDCl₃, 500 MHz) δ 1.51 (s, 6H), 2.50 (s, 2H), 4.26 (s, 2H), 6.43 (bs, 1H), 7.43-7.44 (m, 2H), 7.54-7.59 (m, 2H), 7.84-7.86 (m, 1H), 7.90 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 25.5, 43.4, 55.3, 62.9, 124.3, 125.5, 126.2, 126.5, 128.6, 129.0, 129.3, 132.3, 132.4, 134.3, 174.2 See also reference.⁷

1-Ethyl-5,5-dimethyl-pyrazolidinone (13c):

This compound was prepared by reductive amination with acetaldehyde from **12** (see scheme below).¹⁰ **Procedure:** At 0 °C, 1.4 mL of acetaldehyde (17 mmol) was added to a solution of **12** (1.9 g, 17 mmol) in 20 mL MeOH. The solution was warmed to rt and stirred for 1h. The reaction was cooled back to 0 °C and NaBH₄ (1.3g, 17 mmol) was added in small portions. The ice bath was removed after 10 min and the resulting reaction mixture was stirred at rt for an additional 30 min. Saturated NaHCO₃ solution (5 mL) and of H₂O (15 mL) were added, the aqueous layer was extracted with CH₂Cl₂ four times. The combined organic extracts were washed with brine and dried over magnesium sulfate, then filtered, and solvent was removed under reduced pressure to afford a white solid (2.2 g, 92% yield), mp 101-103 °C, [lit.¹⁰: 101-103 °C]; ¹H NMR (CDCl₃, 500 MHz) δ 1.13 (t, J = 7.1 Hz, 3H), 1.26 (s, 6H), 2.34 (s, 2H), 2.68 (q,

$J = 7.1$ Hz, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.5, 25.5, 43.1, 47.0, 62.7. See also reference.⁷

General procedure for the *N*(2)-acylation of pyrazolidinones (To prepare **5e-5g**, *N*(2)-acroylation of pyrazolidinone **13**) To a stirred solution of the appropriate pyrazolidinone **13** in anhydrous THF (0.3 M) at -78 °C was added 1.0 eq of *n*-BuLi. After 30 min, 1.1 eq of the *trans*-crotonoyl chloride was added. The mixture was stirred at -78 °C for 2 to 3 h (TLC). The reaction was quenched with saturated aqueous ammonium chloride, and the slurry was concentrated under reduced pressure. The residue was redissolved in CH_2Cl_2 and then washed with saturated aqueous sodium bicarbonate. The combined organic extracts were washed with brine and dried over magnesium sulfate, then filtered, and solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

2-[(*E*)-2-butenoyl]-1-ethyl-5,5-dimethyl-pyrazolidin-3-one (5e**):**

Yellow oil; yield: 93%; ^1H NMR (CDCl_3 , 300 MHz) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.29 (s, 6H), 1.91 (dd, $J = 6.9, 1.2$ Hz, 3H), 2.56 (s, 2H), 2.97 (q, $J = 7.3$ Hz, 2H), 6.98-7.20 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 13.0, 18.7, 26.0, 44.2, 47.6, 60.7, 123.1, 146.6, 164.2, 175.4. For ^1H NMR and ^{13}C NMR data also see reference.⁷

1-Benzyl-2-[(*E*)-2-butenoyl]-5,5-dimethyl-pyrazolidin-3-one (5f**):**

White solid; yield: 94%; mp 102.5 - 103.5 °C (Hexane-Ethyl Acetate), [lit²: 98 - 101 °C]; ^1H NMR (CDCl_3 , 500 MHz) δ 1.31 (s, 6H), 1.85 (dd, $J = 6.9, 1.5$ Hz, 3H), 2.56 (s, 2H), 4.08 (s, 2H), 6.83 (d, $J = 15.3$ Hz, 1H),

6.93-6.98 (m, 1H), 7.24-7.32 (m, 3H), 7.40-7.41 (m, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) $\square$ 18.7, 26.4, 44.0, 57.2, 61.1, 123.0, 127.9, 128.6, 129.9, 137.3, 145.8, 163.5, 174.7. For ^1H NMR and ^{13}C NMR data also see reference.⁷

2-[(*E*)-2-butenoyl]- 5,5-dimethyl-1-(1-naphthylmethyl)- pyrazolidin-3-one (5g):

White solid; yield: 93%; mp 136-137 °C (Hexane-Ethyl Acetate), [lit²: 138-140 °C]; ^1H NMR (CDCl_3 , 500 MHz) $\square$ 1.11 (d, J = 6.4 Hz, 3H), 1.48 (s, 6H), 2.78 (s, 2H), 4.44 (s, 2H), 5.88 (d, J = 15.3 Hz, 2H), 6.28-6.35 (m, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 6.6 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 8.2 Hz, 1H), 8.22 (d, J = 8.6 Hz, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) $\square$ 17.8, 26.2, 43.3, 55.8, 61.7, 122.6, 123.6, 125.7, 125.9, 126.6, 129.0, 129.2, 130.1, 131.6, 132.9, 133.9, 144.4, 164.2, 174.2. For ^1H NMR and ^{13}C NMR data also see reference.⁷

1-Benzyl-5,5-dimethyl-2-[(*E*)-2-pentenoyl]- pyrazolidin-3-one (5h):

White solid; yield: 88%; mp 81-83 °C (Hexane-Ethyl Acetate); ^1H NMR (CDCl_3 , 400 MHz) $\square$ 1.01 (t, J = 6.8 Hz, 3H), 1.26 (s, 6H), 2.16 (m, 2H), 2.53 (s, 2H), 4.04 (s, 2H), 6.76 (d, J = 15.2 Hz, 1H), 6.97 (dt, J = 15.2, 6.4 Hz, 1H), 7.21-7.38 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz) $\square$ 12.4, 25.9, 26.3, 43.9, 57.2, 61.1, 120.6, 127.8, 128.6, 129.8, 137.3, 152.0, 163.7, 174.6. HRMS calcd. for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_2\text{Na}^+$ is 309.1573 and Observed = 309.1559.

1-Benzyl-2-[(*E*)-2-cinnamoyl]-5,5-dimethyl-pyrazolidin-3-one (5i):

White solid; yield: 93%; mp 99-100 °C (Hexane-Ethyl Acetate); ^1H NMR (CDCl_3 , 400 MHz) $\square$ 1.31 (s, 6H), 2.58 (s, 2H), 4.09 (s, 2H), 7.17-7.43 (m, 9H), 7.48-7.51 (m, 2H), 7.62 (d, J = 16.0 Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) $\square$ 26.3, 44.0, 57.3, 61.2, 118.5, 127.9, 128.6, 128.7, 129.0,

129.9, 130.4, 135.1, 137.1, 145.3, 163.7, 174.6. HRMS calcd. for $C_{21}H_{22}N_2O_2Na^+$ is 357.1573 and Observed = 357.1588.

1-Benzyl-2-[(*E*)-3-(ethoxycarbonyl)propenoyl]-5,5-dimethyl-pyrazolidin-3-one (5j):

The acid chloride was prepared using a literature method.¹¹ Yellow solid; yield: 75%; mp 98-100 °C (Hexane-Ethyl Acetate); ¹H NMR (CDCl₃, 400 MHz) δ 1.29 (t, *J* = 6.8 Hz, 3H), 1.33 (s, 6H), 2.60 (s, 2H), 3.99 (s, 2H), 4.21 (q, *J* = 6.8 Hz, 2H), 6.47 (d, *J* = 16.0 Hz, 1H), 7.19-7.30 (m, 5H), 7.42 (d, *J* = 11.6 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.3, 26.1, 43.2, 57.6, 61.2, 61.7, 128.2, 128.7, 130.6, 132.3, 133.2, 136.2, 162.3, 165.3, 174.2. HRMS calcd. for $C_{18}H_{22}N_2O_4Na^+$ is 353.1472 and Observed = 353.1481.

II. Cycloaddition of nitrile oxides with electron-deficient olefins; General procedure for the preparation of the racemic samples (8e-8j and 9e-9j): A vial was charged with substrate (0.60 mmol) and 2,4,6-trimethylbenzonitrile oxide (1.2 mmol), and CH₂Cl₂ (6 mL). The mixture was then stirred at room temperature for 168 h (TLC). The solvent was removed in vacuo and the crude material purified by column chromatography using FC (silica gel, hexane/ethyl acetate 4:1), giving standard samples (see scheme below). Both C-adduct and O-adduct were isolable by FC.

Ent	Subst.	R ₁	R ₂	Solvent	Temp, °C	Time, h	C/O Ratio ^a	Yield, % ^b
1	5e	Me	Me	CH ₂ Cl ₂	rt	168	2.3:1 (8e:9e)	99
2	5f	Ph	Me	CH ₂ Cl ₂	rt	168	2.1:1 (8f:9f)	93
3	5g	1-Naph	Me	Toluene	80 °C	48	1.4:1 (8g:9g)	75
4	5h	Ph	Et	Toluene	70 °C	5	1.9:1 (8h:9h)	80
5	5i	Ph	Ph	Toluene	70 °C	8	2.5:1 (8i:9i)	91
6	5j	Ph	CO ₂ Et	Toluene	70 °C	1	1.3:1 (8j:9j)	88

^aDiastereomer ratio determined by ¹H NMR (500 MHz). ^bIsolated yield.

III. General procedure for the preparation of the racemic samples (8k-8p and 9k-9p): To a stirred solution of substrate (0.60 mmol) and hydroximinoyl chloride (1.2 mmol) in toluene (6 mL) at rt was added triethylamine (1.2 mmol). The mixture was allowed to warm to 70 °C for several hours (TLC). The solvent was removed in vacuo and the crude material purified by column chromatography using FC (silica gel, hexane/ethyl acetate 4:1), giving standard samples (see scheme below). Both C-adduct and O-adduct were isolable each by FC.

Ent	R ₁	Time, h	C/O Ratio ^a	Yield, % ^b
1	Ph	5	2.2:1 (8k:9k)	70
2	2-Cl-Ph	5	3.8:1 (8l:9l)	71
3	4-Cl-Ph	5	2.2:1 (8m:9m)	63
4	4-MeOPh	5	2.2:1 (8n:9n)	52
5	t-Bu	8	47:1 (8o:9o)	61
6	i-Bu	8	25:1 (8p:9p)	50

^aDiastereomer ratio determined by ¹H NMR (500 MHz). ^bIsolated yield.

IV. General procedure for the enantioselective 1,3-Dipolar cycloadditions (Reactions of 2,4,6-trimethylbenzonitrile oxide and □,□-unsaturated imides, Table 1, 2 and Table 3: Entry 1-4): A flame-dried vial was charged with MgI₂ (or other Lewis acid) (0.054 mmol), the corresponding ligand (0.059 mmol) and dried MS 4A (90 mg) under a stream of nitrogen. Dry CH₂Cl₂ (1.8 mL) was added under nitrogen, and the mixture was then stirred at room temperature for 2 h. To the light yellow solution □,□-unsaturated imide (0.18 mmol) was added. After the mixture was stirred at room temperature for 15 min, 2,4,6-trimethylbenzonitrile oxide (0.36 mmol) was added to the reaction mixture. The solution was then stirred at room temperature for the appropriate time. After the completion of reaction, the mixture was filtered through Celite. Saturated aqueous ammonium chloride was added and the mixture was extracted with dichloromethane (5

mL x 3). The combined extracts were washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under reduced pressure to give the crude product, which was used to determine the diastereomer ratio with ^1H NMR, comparing to the data of the standard C-adduct and O-adduct samples. If the reaction was not complete, it was quenched by passing through a silica gel column. After removing mesitylnitrile oxide, a mixture of dipolarophile and the cycloadduct(s) were isolated and the diastereomer ratio determined by ^1H NMR. All diastereomers were separated by FC. The *ee* was estimated on the basis of HPLC analysis using a chiral column (Diacel Chiralcel column with hexane/*i*-PrOH as eluent).

The anhydrous complex of **6a**-Ni(SbF₆)₂ and **6a**-Ni(ClO₄)₂ were prepared by previously reported methods.¹² The anhydrous complex of **6a**-Mg(SbF₆)₂ was prepared from **6a**, MgBr₂·OEt₂ and AgSbF₆ according to the literature.¹²

V. General procedure for the enantioselective 1,3-Dipolar cycloadditions under base free condition (Use of hydroximinoyl chlorides as a nitrile oxide precursors, Table 3:

Entry 5-10): A flame-dried vial was charged with MgI₂ (0.111 mmol), the corresponding ligand (0.122 mmol) and dried MS 4A (185 mg) under a stream of nitrogen. Dry CH₂Cl₂ (2.4 mL) was added under nitrogen, and the mixture was then stirred at room temperature for 2 h. To the light yellow solution □,□-unsaturated imide (0.37 mmol) was added. After the mixture was stirred at room temperature for 15 min, a dry CH₂Cl₂ solution (2.5 mL) of hydroximinoyl chloride (0.74 mmol) was added slowly to the reaction mixture through the column which was filled with Amberlyst[®] A21 (230 mg) via syringe for 25 min with controlling slow addition rate by a syringe pump (see scheme below). After the completion of slow addition, dry CH₂Cl₂ (1 ml) was added to the reaction mixture through the column for 5 min. The solution was then stirred at room temperature for the appropriate time. The mixture was filtered through Celite. Saturated aqueous ammonium

chloride was added and the mixture was extracted with dichloromethane (10 mL x 3). The combined extracts were washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under reduced pressure to give the crude product, which was used to determine the diastereomer ratio with ^1H NMR, comparing to the data of the standard C-adduct and O-adduct samples. All diastereomers were separated by FC. The *ee* was estimated on the basis of HPLC analysis using a chiral column (Diacel Chiralcel column with hexane/*i*-PrOH as eluent).

Additional data for reactions with oxazolidinones:

Entry	Subs.	Yield ^c	Time, h	10:11 Ratio ^d	10 (ee) ^e	11 (ee) ^e
1	5a	81	96	2.2:1 (8a:9a)	82	13
2	5b	87	96	1.3:1 (8b:9b)	23	02
3	5c	88	96	3:1 (8c:9c)	84	08

3-[4', 5'-*trans*-Dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-2-oxazolidinone (8a):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 96 h. Enantioselectivity was determined by chiral HPLC after reductive conversion to known alcohol **10** (for details of the HPLC conditions see information on page 28). Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 65 °C; ¹H NMR (CDCl₃, 500 MHz) δ 1.30 (d, J = 7.3 Hz, 3H), 2.24 (s, 6H), 2.28 (s, 3H), 3.80 (dq, 1H, J = 7.3, 4.2 Hz, 1H), 4.02-4.14 (m, 2H), 4.52 (t, J = 7.9 Hz, 1H), 5.82 (d, J = 4.2 Hz, 1H), 6.88 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 16.4, 20.2, 21.3, 42.8, 50.9, 63.2, 83.2, 124.4, 128.9, 137.5, 139.2, 153.7, 160.9, 169.7; HRMS calcd. for C₁₇H₂₀N₂O₄Na⁺ is 339.1315 and Observed = 339.1323.

3-[4', 5'-*trans*-Dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-4,4-dimethyl-2-oxazolidinone (8b):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 96 h. Enantioselectivity was determined by chiral HPLC after reductive conversion to alcohol **10** (for details of the HPLC conditions see information on page 28). Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 8/1 (v/v) – 4/1 (v/v)]; mp 161 °C; ¹H NMR (CDCl₃, 500 MHz) δ 1.31 (d, J = 7.1 Hz, 3H), 1.59 (s, 3H), 1.63 (s, 3H), 2.22 (s, 6H), 2.27 (s, 3H), 3.64 (dq, 1H, J = 7.1, 3.4 Hz, 1H), 4.13 (AB sys, J = 8.5 Hz, 1H), 4.13 (AB sys, J = 8.5 Hz, 1H), 5.73 (d, J = 3.4 Hz, 1H), 6.87 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 16.5, 20.1, 21.3, 24.7, 24.9, 51.5, 60.9, 76.2, 84.5, 124.5, 128.9, 137.4, 139.1, 154.3, 160.8, 170.7; HRMS calcd. for C₁₉H₂₄N₂O₄Na⁺ is 367.1628 and Observed = 367.1629.

3-[4', 5'-*trans*-Dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-5,5-dimethyl-2-oxazolidinone (8c):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 96 h. Enantioselectivity was determined by chiral HPLC after reductive conversion to alcohol **10** (for details of the HPLC conditions see information on page 28). Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 8/1 (v/v) – 4/1 (v/v)]; mp 55 °C; ¹H NMR (CDCl₃, 500 MHz) δ 1.30 (d, J = 7.3 Hz, 3H), 1.53 (s, 3H), 1.54 (s, 3H), 2.23 (s, 6H), 2.27 (s, 3H), 3.76 (AB sys, J = 10.8 Hz, 1H), 3.77 (dq, 1H, J = 7.3, 4.2 Hz, 1H), 3.79 (AB sys, J = 10.8 Hz, 1H), 5.81 (d, J = 4.2 Hz, 1H), 6.87 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 16.4, 20.1, 21.3, 27.4, 27.5, 51.1, 54.6, 80.3, 83.4, 124.4, 128.9, 137.4, 139.1, 152.8, 160.8, 169.9; HRMS calcd. for C₁₉H₂₄N₂O₄Na⁺ is 367.1628 and Observed = 339.1604.

1-[4', 5'-*trans*-Dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-3,5-dimethylpyrazole (8d):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 96 h. Enantioselectivity was determined by chiral HPLC after reductive conversion to alcohol **10** (for details of the HPLC conditions see information on page 28). Colorless viscous oil [silica gel column chromatography eluted by hexane/diethyl ether = 10/1 (v/v)]; ¹H NMR (CDCl₃, 500 MHz) δ 1.37 (d, J = 7.3 Hz, 3H), 2.24 (s, 6H), 2.25 (s, 3H), 2.28 (s, 3H), 2.58 (s, 3H), 3.83 (dq, 1H, J = 7.3, 5.4 Hz, 1H), 5.91 (d, J = 5.4 Hz, 1H), 6.03 (s, 1H), 6.88 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.1, 14.3, 16.4, 20.2, 21.3, 51.9, 84.1, 111.8, 124.6, 128.9, 137.5, 139.0, 144.9, 153.4, 160.6, 169.5; HRMS calcd. for C₁₉H₂₃N₃O₂Na⁺ is 348.1682 and Observed = 348.1681.

2-[4', 5'-*trans*-Dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-1-ethyl-5,5-dimethylpyrazolidine-3-one (8e):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 18 h. Enantioselectivity was determined by chiral HPLC in comparison with authentic

materials and after reductive conversion to known alcohol **10** (for details of the HPLC conditions see information on page 28). Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 90 °C; $[\alpha]_D^{25} = +292.0$ (*c* 0.39, CHCl₃) [95% ee estimated by chiral HPLC analysis on Daicel Chiral Cell AD, hexane / 2-propanol (9:1 v/v), 1 mL/min, *t_r* (main) = 12.4 min, *t_r* (major) = 15.8 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.77 (s, 3H), 0.78 (s, 3H), 0.90 (t, *J* = 7.1 Hz, 3H), 1.43 (AB sys, *J* = 17.0 Hz, 1H), 2.01 (s, 3H), 2.02 (AB sys, *J* = 17.0 Hz, 1H), 2.24 (s, 6H), 2.51-2.58 (m, 2H), 4.05 (dq, 1H, *J* = 7.1, 4.2 Hz, 1H), 5.97 (d, *J* = 4.2 Hz, 1H), 6.62 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 12.8, 16.3, 20.3, 21.3, 25.6, 26.5, 43.9, 47.3, 49.7, 61.4, 84.4, 124.6, 128.9, 137.6, 139.1, 161.3, 167.6, 175.7; HRMS calcd. for C₂₁H₂₉N₃O₃Na⁺ is 394.2101 and Observed = 394.2097.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-5,5-dimethylpyrazolidine-3-one (8g):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 2.5 h. Enantioselectivity was determined by chiral HPLC. The adduct was reduced to

alcohol **10** and its ee was also evaluated by HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 122 °C; $[\alpha]_D^{25} = +274.7$ (*c* 0.77, CHCl₃) [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD,

hexane / 2-propanol (9:1 v/v), 0.8 mL/min, t_r (minor) = 26.2 min, t_r (major) = 34.1 min]; Colorless solid; mp. 122 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.74 (s, 3H), 0.75 (s, 3H), 0.95 (d, J = 7.3 Hz, 3H), 1.97 (AB sys + d, J = 16.9, 1.8 Hz, 1H), 2.00 (s, 3H), 2.04 (AB sys + d, J = 16.9, 1.8 Hz, 1H), 3.65 (AB sys, J = 14.3 Hz), 3.68 (AB sys, J = 14.3, 1H), 3.94-3.99 (m, 1H), 5.89 (d, J = 3.6 Hz, 1H), 6.61 (s, 2H), 7.02 (app t, J = 7.5 Hz, 1H), 7.10-7.13 (m, 2H), 7.78 (d, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 16.2, 20.3, 21.3, 25.9, 26.9, 43.6, 49.6, 57.1, 61.9, 84.2, 124.6, 127.9, 128.7, 128.8, 129.8, 137.2, 137.6, 138.9, 161.1, 166.5, 174.9; HRMS calcd. for $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_3\text{Na}^+$ is 456.2257 and Observed = 456.2263.

2-[4', 5'-*trans*-dihydro-4-methyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-1-naphthylmethyl-5,5-dimethylpyrazolidine-3-one (8g):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 24 h. Enantioselectivity was determined by chiral HPLC. The adduct was reduced to

alcohol **10** and its ee was also evaluated by HPLC (see page 28 for details). Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 201 °C; $[\alpha]_{\text{D}}^{25} = +199.6$ (c 0.57, CHCl_3). [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD, hexane / 2-propanol (9:1 v/v), 0.8 mL/min, t_r (minor) = 46.7 min, t_r (major) = 71.4 min]; ^1H NMR (C_6D_6 , 500 MHz) δ 0.70 (br s, 3H), 0.78 (s, 3H), 0.83 (s, 3H), 1.98 (s, 3H), 2.05 (AB sys, J = 17.1 Hz, 1H), 2.14 (s, 6H), 2.16 (AB sys, J = 17.1 Hz, 1H), 3.77-3.83 (m, 1H), 3.97 (AB sys, J = 13.7 Hz, 1H), 4.19 (AB sys, J = 13.7 Hz), 5.60 (br s, 1H), 6.58 (s, 2H), 7.19-7.26 (m, 2H), 7.36-7.40 (m, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.70 (br s, 1H), 8.28 (d, J = 8.3 Hz, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 15.2, 20.2, 21.2, 25.6, 27.3, 43.2, 48.4, 55.5, 62.3, 83.5, 123.6, 124.5, 125.7,

126.2, 126.9, 128.7, 128.9, 129.1, 129.6, 131.9, 132.3, 133.9, 137.6, 138.8, 161.1, 166.7, 174.7; HRMS calcd. for $C_{30}H_{33}N_3O_3Na^+$ is 506.2414 and Observed = 506.2424.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-ethyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-5,5-dimethylpyrazolidine-3-one (8h):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 6 h. Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 55 °C; $[\alpha]_D^{25} = +289.9$ (c 0.79, $CHCl_3$) [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD, hexane / 2-propanol (9:1 v/v), 0.8 mL/min, t_r (minor) = 19.1 min, t_r (major) = 40.7 min]; 1H NMR (C_6D_6 , 500 MHz) δ 0.61 (t, J = 7.3 Hz, 3H), 0.73 (s, 3H), 0.78 (s, 3H), 1.25-1.40 (m, 2H), 2.01 (s, 3H), 2.06 (AB sys, J = 17.1 Hz, 1H), 2.07 (AB sys, J = 17.1 Hz, 1H), 2.27 (s, 3H), 3.69 (AB sys, J = 14.5 Hz, 1H), 3.72 (AB sys, J = 14.5 Hz, 1H), 4.11 (qn, J = 5.0 Hz, 1H), 6.16 (d, J = 5.0 Hz, 1H), 6.63 (s, 2H), 7.02 (m, 1H), 7.12 (m, 2H), 7.49 (d, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.5, 20.5, 21.3, 23.9, 26.4, 26.5, 43.6, 55.5, 57.1, 61.7, 82.6, 125.2, 127.9, 128.7, 128.9, 129.6, 137.3, 137.6, 138.9, 160.5, 166.4, 174.9; HRMS calcd. for $C_{27}H_{33}N_3O_3Na^+$ is 470.2414 and Observed = 470.2423.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-phenyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-5,5-dimethylpyrazolidine-3-one (8i):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 14 h. Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 189 °C; $[\alpha]_D^{25} =$

+352.0 (*c* 0.65, CHCl₃) [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell ODH, hexane / 2-propanol (4:1 v/v), 0.5 mL/min, *t_r* (major) = 20.3 min, *t_r* (minor) = 30.4 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.71 (s, 3H), 0.78 (s, 3H), 1.90 (s, 3H), 1.96 (AB sys, *J* = 17.1 Hz, 1H), 2.02 (AB sys, *J* = 17.1 HZ, 1H), 2.16 (s, 3H), 3.62 (AB sys, *J* = 14.3 Hz, 1H), 3.67 (AB sys, *J* = 14.3 Hz, 1H), 5.36 (d, *J* = 4.0 Hz, 1H), 6.49 (s, 2H), 6.56 (br s, 1H), 6.82-6.87 (m, 2H), 6.98 (app t, *J* = 7.3 Hz, 1H), 7.07-7.15 (m, 5H), 7.46 (d, *J* = 7.3 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.2, 21.2, 25.9, 26.8, 43.4, 57.3, 59.3, 61.9, 84.3, 124.2, 127.9, 128.1, 128.7, 128.9, 129.7, 136.5, 136.8, 137.7, 138.8, 159.6, 166.1, 174.7 (two carbons are overlapped); HRMS calcd. for C₃₁H₃₃N₃O₃Na⁺ is 518.2414 and Observed = 518.2423.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-ethoxycarbonyl-3-(2,4,6-trimethylphenyl)isoxazol-5-yl]-5,5-dimethylpyrazolidine-3-one (8j):

General procedure for the enantioselective 1,3-dipolar cycloadditions was used. 1 h. Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel

column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 57 °C; [α]_D²⁵ = +340.0 (*c* 0.59, CHCl₃) [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell ODH, hexane / 2-propanol (4:1 v/v), 0.5 mL/min, *t_r* (major) = 27.2 min, *t_r* (minor) = 31.3 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.61 (dt, *J* = 7.1, 1.6 Hz, 3H), 0.69 (s, 3H), 0.72 (s, 3H), 1.96 (AB sys, *J* = 17.0 Hz, 1H), 2.02 (AB sys, *J* = 17.0 HZ, 1H), 2.26 (s, 3H), 3.56 (AB sys, *J* = 13.9 Hz, 1H), 3.63 (AB sys, *J* = 13.9 Hz, 1H), 3.73-3.80 (m, 2H), 5.18 (d, *J* = 5.8 Hz, 1H), 6.58 (s, 2H), 6.88 (br s, 1H), 7.00-7.03 (m, 1H), 7.08-7.12 (m, 2H), 7.45 (d, *J* = 7.1 HZ, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.9, 20.1, 21.3, 26.0, 26.7, 43.2, 57.3, 58.6, 61.9, 62.1, 81.2, 123.9, 127.9, 128.7, 128.7, 129.8, 136.8, 137.6, 139.2, 153.9,

165.0, 167.3, 174.6; HRMS calcd. for $C_{28}H_{33}N_3O_5Na^+$ is 514.2312 and Observed = 514.2318.

1-Benzyl-2-[(4'S, 5'S)-*trans*-dihydro-4-methyl-3-phenyl-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8k):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow addition rate = 35 min/3.5 mL. Total reaction time = 2 h. The

absolute configuration was determined on the basis of the reported optical rotation in comparison with known alcohol **15** which was obtained by reductive conversion of titled compound. Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 58 °C; $[\alpha]_D^{25} = +152.0$ (c 0.55, $CHCl_3$) [98% ee estimated by chiral HPLC analysis on Daicel Chiral Cell ODH, hexane / 2-propanol (9:1 v/v), 0.5 mL/min, t_r (minor) = 54.2 min, t_r (major) = 74.5 min]; 1H NMR (C_6D_6 , 500 MHz) δ 0.72 (s, 3H), 0.74 (s, 3H), 1.05 (d, J = 7.1 Hz, 3H), 2.00 (s, 2H), 3.63 (s, 2H), 3.95 (dq, J = 7.1, 3.0 Hz), 5.80 (d, J = 3.0 Hz, 1H), 6.95-7.16 (m, 6H), 7.43 (d, J = 7.3 Hz, 2H), 7.57-7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.7, 26.4, 26.5, 43.4, 45.9, 57.2, 61.9, 85.6, 127.5, 127.8, 128.2, 128.6, 128.9, 129.3, 129.5, 130.4, 137.3, 160.8, 166.3, 175.1; HRMS calcd. for $C_{23}H_{25}N_3O_3Na^+$ is 414.1788 and Observed = 414.1787.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(2-chlorophenyl)-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8l):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow

addition rate = 35 min/3.5 mL. Total reaction time = 4.5 h. Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 53 °C; $[\alpha]_D^{25} = +183.6$ (*c* 0.77, CHCl₃) [86% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD, hexane / 2-propanol (9:1 v/v), 1 mL/min, *t_r* (minor) = 28.0 min, *t_r* (major) = 45.9 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.73 (s, 3H), 0.74 (s, 3H), 0.98 (d, *J* = 7.3 Hz, 3H), 1.96 (AB sys, *J* = 17.1 Hz, 1H), 2.02 (AB sys, *J* = 17.1 Hz, 1H), 3.65 (AB sys, *J* = 14.1 Hz, 1H), 3.69 (AB sys, *J* = 14.1 Hz, 1H), 4.46 (dq, *J* = 4.4, 7.3 Hz, 1H), 5.87 (d, *J* = 4.4 Hz, 1H), 6.64-6.70 (m, 2H), 6.96-7.03 (m, 2H), 7.09-7.12 (m, 2H), 7.36 (dd, *J* = 2.0 Hz and *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 16.7, 26.1, 26.8, 43.5, 48.1, 57.0, 61.9, 85.6, 127.1, 127.7, 127.9, 128.7, 129.5, 130.5, 131.2, 131.7, 133.3, 137.5, 160.8, 165.9, 175.0; HRMS calcd. for C₂₃H₂₄ClN₃O₃Na⁺ is 448.1398 and Observed = 448.1393.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(4-chlorophenyl)-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8m):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow addition rate = 35 min/3.5 mL. Total reaction time = 3 h.

Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 132 °C; $[\alpha]_D^{25} = +122.5$ (*c* 0.59, CHCl₃) [96% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD, hexane / 2-propanol (9:1 v/v), 0.8 mL/min, *t_r* (minor) = 38.4 min, *t_r* (major) = 47.7 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.73 (s, 3H), 0.75 (s, 3H), 0.98 (d, *J* = 7.1 Hz, 3H), 2.00 (s, 2H), 3.63 (s, 2H), 3.81 (dq, *J* = 3.2, 7.1 Hz, 1H), 5.77 (d, *J* = 3.2 Hz, 1H), 6.91-6.99 (m, 3H), 7.08 (app t, *J* = 7.5 Hz, 2H), 7.25-7.27 (m, 2H), 7.42 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 17.6, 26.4, 26.5, 43.4, 45.7, 57.2, 61.9, 85.8, 126.7, 127.9, 128.6,

128.7, 129.3, 129.5, 136.4, 137.2, 159.9, 166.2, 175.1; HRMS calcd. for $C_{23}H_{24}ClN_3O_3Na^+$ is 448.1398 and Observed = 448.1404.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(4-methoxyphenyl)-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8n):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used.

Slow addition rate = 35 min/3.5 mL. Total reaction time = 10.5 h. Enantioselectivity was determined by chiral HPLC. Pale yellow solid [silica gel column chromatography eluted by hexane/ethyl acetate = 2/1 (v/v)]; mp 55 °C; $[\alpha]_D^{25} = +139.0$ (c 0.51, $CHCl_3$) [99% ee estimated by chiral HPLC analysis on Daicel Chiral Cell ODH, hexane / 2-propanol (4:1 v/v), 0.5 mL/min, t_r (minor) = 41.9 min, t_r (major) = 59.3 min]; 1H NMR (C_6D_6 , 500 MHz) δ 0.73 (s, 3H), 0.76 (s, 3H), 1.12 (d, J = 7.1 Hz, 3H), 2.02 (s, 2H), 3.17 (s, 3H), 3.65 (s, 2H), 3.86-4.01 (m, 1H), 5.81 (d, J = 1.8 Hz, 1H), 6.59-6.61 (m, 2H), 6.98-7.12 (m, 3H), 7.43 (d, J = 7.3 Hz, 2H), 7.55-7.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.8, 26.4, 26.5, 43.5, 46.2, 55.6, 57.1, 61.9, 85.4, 114.4, 120.7, 127.8, 128.6, 129.1, 129.5, 137.3, 160.3, 161.4, 166.5, 175.1; HRMS calcd. for $C_{24}H_{27}N_3O_4Na^+$ is 444.1893 and Observed = 444.1885.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(*tert*-butyl)-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8o):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow addition rate = 60 min/3.5 mL. Total reaction time = 240 h.

Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 146 °C; $[\alpha]_D^{25} = +165.1$

(*c* 0.53, CHCl₃) [92% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OD-ODH doubly connected column, hexane / 2-propanol (9:1 v/v), 0.5 mL/min, *t_r* (major) = 58.2 min, *t_r* (minor) = 66.0 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.83 (s, 3H), 0.85 (s, 3H), 1.13 (d, *J* = 7.1 Hz, 3H), 1.14 (s, 9H), 2.11 (AB sys, *J* = 17.1 Hz, 1H), 2.16 (AB sys, *J* = 17.1 Hz, 1H), 3.53 (dq, *J* = 3.0, 7.1 Hz, 1H), 5.68 (d, *J* = 3.0 Hz, 1H), 7.10 (app t, *J* = 7.3 Hz, 1H), 7.18-7.21 (m, 2H), 7.55 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 18.3, 26.1, 26.9, 29.3, 33.6, 43.5, 46.3, 57.1, 61.8, 85.4, 127.9, 128.7, 129.6, 137.4, 166.6, 169.5, 174.9; HRMS calcd. for C₂₁H₂₉N₃O₃Na⁺ is 394.2101 and Observed = 394.2092.

1-Benzyl-2-[4', 5'-*trans*-dihydro-4-methyl-3-(*iso*-propyl)-isoxazol-5-yl]-5,5-dimethyl-pyrazolidine-3-one (8p):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow addition rate = 35 min/3.5 mL. Total reaction time = 168 h.

Enantioselectivity was determined by chiral HPLC. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 73 °C; [α]_D²⁵ = +125.9 (*c* 0.57, CHCl₃) [79% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OJ-OJ doubly connected column, hexane / 2-propanol (4:1 v/v), 0.5 mL/min, *t_r* (minor) = 50.2 min, *t_r* (major) = 55.7 min]; ¹H NMR (C₆D₆, 500 MHz) δ 0.72 (s, 3H), 0.75 (s, 3H), 0.76 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 1H), 1.71-1.83 (m, 2H), 1.95-2.02 (m, 3H), 3.40-3.45 (m, 1H), 3.65 (s, 2H), 5.66 (d, *J* = 3.4 Hz, 1H), 7.01-7.12 (m, 3H), 7.45 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 16.3, 22.2, 23.3, 26.1, 26.4, 26.7, 34.5, 43.5, 47.8, 57.1, 61.8, 83.8, 127.9, 128.7, 129.7, 137.3, 161.9, 166.7, 174.9; HRMS calcd. for C₂₁H₂₉N₃O₃Na⁺ is 394.2101 and Observed = 394.2105.

3-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-2-oxazolidinone (9a):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 42 °C; ¹H NMR (CDCl₃, 500 MHz) δ 1.54 (d, J = 6.4 Hz, 3H), 2.61 (s, 3H), 2.27 (s, 6H), 3.79-3.84 (m, 1H), 3.91-3.97 (m, 1H), 4.04-4.13 (m, 1H), 4.28-4.34 (m, 1H), 3.53 (qn, J = 6.4 Hz, 1H), 5.58 (d, J = 6.4 Hz, 1H), 6.85 (s, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.9, 20.6, 21.3, 43.2, 61.1, 62.4, 81.3, 124.7, 128.7, 137.9, 139.3, 153.1, 153.7, 168.7; HRMS calcd. for C₁₇H₂₀N₂O₄Na⁺ is 339.1315 and Observed = 339.1305.

3-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-4,4-dimethyl-2-oxazolidinone (9b):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 8/1 (v/v) – 4/1 (v/v)]; mp 88 °C; ¹H NMR (CDCl₃, 500 MHz) δ 1.21 (s, 3H), 1.48 (s, 3H), 1.56 (d, J = 6.4 Hz, 3H), 2.25 (s, 3H), 2.26 (s, 6H), 3.62 (AB sys, J = 8.3 Hz, 1H), 3.88 (AB sys, J = 8.3 Hz, 1H), 5.66 (dq, J = 6.4, 7.9 Hz, 1H), 5.65 (d, J = 7.9 Hz, 1H), 6.84 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.2, 20.3, 21.3, 23.6, 24.8, 61.3, 62.3, 75.2, 81.7, 124.8, 128.8, 137.7, 139.2, 153.9, 154.3, 169.8; HRMS calcd. for C₁₉H₂₄N₂O₄Na⁺ is 367.1628 and Observed = 336.1617.

3-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-5,5-dimethyl-2-oxazolidinone (9c):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 8/1 (v/v) – 4/1 (v/v)]; mp 188 °C; ^1H NMR (CDCl_3 , 500 MHz) δ 1.07 (s, 3H), 1.40 (s, 3H), 1.52 (d, J = 6.4 Hz, 3H), 2.23 (s, 9H), 3.50 (AB sys, J = 10.9 Hz, 1H), 3.60 (AB sys, J = 10.9 Hz, 1H), 5.24 (qn, J = 6.4 Hz, 1H), 5.63 (d, J = 6.7 Hz, 1H), 6.83 (s, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 19.9, 20.5, 21.9, 55.0, 61.4, 79.1, 80.8, 124.7, 128.8, 137.8, 139.3, 152.2, 153.6, 168.7; HRMS calcd. for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_4\text{Na}^+$ is 367.1628 and Observed = 367.1641.

1-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-3,5-dimethylpyrazole (9d):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Pale orange solid [silica gel column chromatography eluted by hexane/diethyl ether = 10/1 (v/v)]; mp 95 °C; ^1H NMR (CDCl_3 , 500 MHz) δ 1.59 (d, J = 6.4 Hz, 3H), 1.98 (s, 3H), 2.20 (s, 3H), 2.26 (s, 6H), 2.41 (s, 3H), 5.24 (dq, J = 6.4, 8.1 Hz, 1H), 5.60 (d, J = 8.1 Hz, 1H), 5.80 (s, 1H), 6.73 (s, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.6, 14.4, 20.1, 20.4, 21.2, 62.3, 80.9, 111.9, 125.3, 128.3, 137.4, 138.6, 144.0, 152.4, 154.5, 168.6; HRMS calcd. for $\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}_2\text{Na}^+$ is 348.1682 and Observed = 348.1710.

2-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-1-ethyl-5,5-dimethylpyrazolidine-3-one (9e):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known

alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 87 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.50 (s, 3H), 0.65 (t, J = 7.1 Hz, 3H), 0.70 (s, 3H), 1.48 (d, J = 6.2 Hz, 3H), 1.74 (AB sys, J = 17.3 Hz, 1H), 1.89 (AB sys, J = 17.3 Hz, 1H), 2.09 (s, 3H), 2.43-2.54 (m, 2H), 2.50 (s, 6H), 5.24 (m, 1H), 6.02 (d, J = 7.7 Hz, 1H), 6.70 (s, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 12.2, 20.1, 20.2, 21.2, 25.5, 25.6, 44.3, 46.9, 60.0, 62.2, 82.8, 124.9, 128.8, 137.9, 139.1, 154.7, 166.7, 175.7; HRMS calcd. for $\text{C}_{21}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}^+$ is 394.2101 and Observed = 394.2073.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-5,5-dimethylpyrazolidine-3-one (9f):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 73 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.37 (s, 3H), 0.53 (s, 3H), 1.35 (d, J = 6.4 Hz, 3H), 1.57 (AB sys, J = 17.1 Hz, 1H), 1.86 (AB sys, J = 17.1 Hz, 1H), 1.99 (s, 3H), 2.42 (s, 3H), 3.43 (AB sys, J = 14.1 Hz, 1H), 3.51 (AB sys, J = 14.1 Hz, 1H), 5.27 (qn, J = 6.5 Hz, 1H), 5.88 (d, J = 7.3 Hz, 1H), 6.99-7.02 (m, 1H), 7.06-7.10 (m, 2H), 7.34 (d, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.1, 20.4, 21.3, 25.2, 26.3, 43.7, 56.5, 60.5, 62.3, 82.4, 125.0, 127.9, 128.6, 128.8, 129.4, 137.2, 137.9, 139.0, 154.3, 165.8, 174.9; HRMS calcd. for $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_3\text{Na}^+$ is 456.2257 and Observed = 456.2278.

2-[4', 5'-*trans*-Dihydro-5-methyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-1-naphthylmethyl-5,5-dimethylpyrazolidine-3-one (9g):

Enantioselectivity was determined by chiral HPLC in comparison with authentic materials and after reductive conversion to known alcohol **11**. Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 65 °C; ¹H NMR (C₆D₆, 500 MHz) δ 0.37 (s, 3H), 0.52 (s, 3H), 1.32 (br s, 3H), 1.67 (AB sys, J = 17.3 Hz, 1H), 1.97 (AB sys, J = 17.3 Hz, 1H), 1.99 (s, 3H), 2.35 (s, 3H), 3.84 (AB sys, J = 14.1 Hz, 1H), 3.94 (AB sys, J = 14.1 Hz, 1H), 5.06 (br s, 1H), 5.80 (br s, 1H), 6.58 (s, 2H), 7.16 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 7.1 Hz, 1H), 7.35-7.38 (m, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.70 (br d, J = 5.4 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.0, 20.3, 21.3, 25.1, 26.1, 43.4, 54.3, 60.7, 62.2, 82.1, 123.4, 125.1, 125.5, 125.9, 126.4, 128.0, 128.5, 128.8, 129.1, 131.7, 132.8, 133.9, 137.9, 138.9, 153.9, 165.8, 174.6; HRMS calcd. for C₃₀H₃₃N₃O₃Na⁺ is 506.2414 and Observed = 506.2398.

1-Benzyl-2-[4', 5'-*trans*-dihydro-5-ethyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-5,5-dimethylpyrazolidine-3-one (9h):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 92 °C; ¹H NMR (C₆D₆, 500 MHz) δ 0.35 (s, 3H), 0.54 (s, 3H), 0.94 (t, J = 7.3 Hz, 3H), 1.57 (AB sys, J = 17.3 Hz, 1H), 1.70 (sep, J = 7.1 Hz, 1H), 1.81-1.89 (m, 1H), 1.85 (AB sys, J = 17.3 Hz, 1H), 1.99 (s, 3H), 2.42 (s, 3H), 3.44 (AB sys, J = 14.3 Hz, 1H), 3.54 (AB sys, J = 14.3 Hz, 1H), 5.23 (dt, J = 6.6, 8.1 Hz), 6.04 (d, J = 8.1 Hz, 1H), 6.60 (s, 2H), 6.99-7.02 (m, 1H), 7.06-7.10 (m, 2H), 7.35 (d, J = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 9.9, 20.0, 21.2, 25.3, 26.2, 27.6, 43.8, 56.4, 60.3, 60.4, 87.7, 125.1, 127.8, 128.6, 128.8, 129.4, 137.4, 137.9, 139.1, 154.1, 166.1, 174.9; HRMS calcd. for C₂₇H₃₃N₃O₃Na⁺ is 470.2414 and Observed = 470.2424.

1-Benzyl-2-[4', 5'-*trans*-dihydro-5-phenyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-5,5-dimethylpyrazolidine-3-one (9i):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 67 °C; ¹H NMR (C₆D₆, 500 MHz) δ 0.33 (s, 3H), 0.49 (s, 3H), 1.46 (AB sys, J = 17.1 Hz, 1H), 1.78 (AB sys, J = 17.1 Hz, 1H), 1.99 (s, 3H), 2.41 (s, 6H), 3.41 (AB sys, J = 14.5 Hz, 1H), 3.51 (AB sys, J = 14.5 Hz, 1H), 6.43-6.45 (m, 2H), 6.60 (s, 2H), 6.98-7.12 (m, 6H), 7.33 (d, J = 7.2 Hz, 2H), 7.51 (d, J = 7.2 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.0, 21.3, 24.9, 26.5, 43.8, 56.1, 60.3, 63.6, 87.6, 124.6, 126.6, 127.8, 128.6, 128.8, 128.9, 129.1, 129.3, 137.2, 137.9, 139.0, 139.3, 154.2, 165.4, 174.7; HRMS calcd. for C₃₁H₃₃N₃O₃Na⁺ is 518.2414 and Observed = 518.2396.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-ethoxycarbonyl-3-(2,4,6-trimethylphenyl)-isoxazol-4-yl]-5,5-dimethylpyrazolidine-3-one (9j):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 51 °C; ¹H NMR (C₆D₆, 500 MHz) δ 0.38 (s, 3H), 0.50 (s, 3H), 0.89 (t, J = 7.1 Hz, 3H), 1.50 (AB sys, J = 17.3 Hz, 1H), 1.83 (AB sys, J = 17.3 Hz, 1H), 1.97 (s, 3H), 2.44 (s, 3H), 3.38 (AB sys, J = 14.3 Hz, 1H), 3.48 (AB sys, J = 14.3 Hz, 1H), 3.93 (t, J = 7.1 Hz, 2H), 5.74 (br s, 1H), 6.59 (s, 2H), 6.71 (br s, 1H), 7.00-7.12 (m, 3H), 7.35 (d, J = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.3, 19.9, 21.3, 25.1, 26.5, 43.5, 56.4, 59.6, 60.6, 62.4, 82.6, 123.7, 127.9, 128.7, 128.8, 129.4, 137.2, 138.1, 139.4, 153.9, 164.4, 169.2, 174.6; HRMS calcd. for C₂₈H₃₃N₃O₅Na⁺ is 514.2312 and Observed = 514.2304.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-methyl-3-phenyl-isoxazol-4-yl]-5,5-dimethylpyrazolidine-3-one (9k):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 149 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.61 (s, 3H), 0.67 (s, 3H), 1.40 (d, J = 6.4 Hz, 3H), 1.91 (AB sys, J = 17.1 Hz, 1H), 2.00 (AB sys, J = 17.1 Hz, 1H), 3.51 (AB sys, J = 14.1 Hz, 1H), 3.57 (AB sys, J = 14.1 Hz, 1H), 4.77-4.82 (m, 1H), 5.46 (d, J = 4.8 Hz), 6.88-7.12 (m, 6H), 7.36 (d, J = 7.5 Hz, 2H), 7.72 (d, J = 6.9 Hz); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.94, 26.0, 26.7, 43.8, 56.9, 59.7, 61.1, 83.3, 126.9, 127.0, 127.9, 128.5, 128.9, 129.2, 130.2, 137.4, 154.9, 166.1, 175.6; HRMS calcd. for $\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_3\text{Na}^+$ is 414.1788 and Observed = 414.1765.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-methyl-3-(2-chlorophenyl)-isoxazol-4-yl]- 5,5-dimethylpyrazolidine-3-one (9l):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1]; mp 45 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.58 (s, 3H), 0.60 (s, 3H), 1.58 (d, J = 6.2 Hz, 3H), 1.82 (AB sys, J = 17.1 Hz, 1H), 1.91 (AB sys, J = 17.1 Hz, 1H), 3.44 (AB sys, J = 14.1 Hz, 1H), 3.53 (AB sys, J = 14.1 Hz, 1H), 4.85 (qn, J = 6.2 Hz, 1H), 5.98 (d, J = 5.6 Hz, 1H), 6.60-6.70 (m, 2H), 6.94-7.15 (m, 5H), 7.94 (dd, J = 1.8, 7.7 Hz, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.2, 25.9, 26.7, 43.6, 56.8, 61.1, 61.5, 83.8, 127.3, 127.9, 128.5, 128.7, 129.4, 130.1, 131.1, 132.2, 132.5, 137.1, 154.9, 165.8, 175.1; HRMS calcd. for $\text{C}_{23}\text{H}_{24}\text{ClN}_3\text{O}_3\text{Na}^+$ is 448.1398 and Observed = 448.1375.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-methyl-3-(4-chlorophenyl)-isoxazol-4-yl]- 5,5-dimethylpyrazolidine-3-one (9m):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 103 °C; ^1H NMR (C_6D_6 , 500

MHz) δ 0.62 (s, 3H), 0.66 (s, 3H), 1.38 (d, J = 6.4 Hz, 3H), 1.90 (AB sys, J = 17.3 Hz, 1H), 2.00 (AB sys, J = 17.3 Hz, 1H), 3.51 (AB sys, J = 14.1 Hz, 1H), 3.56 (AB sys, J = 14.1 Hz, 1H), 4.73-4.77 (m, 1H), 5.28 (d, J = 4.6 Hz, 1H), 6.88-7.08 (m, 5H), 7.35 (d, J = 7.1 Hz, 2H), 7.41-7.42 (m, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.9, 26.0, 26.7, 43.8, 57.0, 59.6, 61.2, 83.6, 127.9, 128.2, 128.6, 129.2, 129.3, 129.9, 136.2, 137.2, 154.0, 165.9, 175.6; HRMS calcd. for $\text{C}_{23}\text{H}_{24}\text{ClN}_3\text{O}_3\text{Na}^+$ is 448.1398 and Observed = 448.1398.

1-Benzyl-2-[4', 5'-*trans*-dihydro-5-methyl-3-(4-methoxyphenyl)-isoxazol-4-yl]- 5,5-dimethylpyrazolidine-3-one (9n):

General procedure for the enantioselective 1,3-dipolar cycloadditions under a base free condition was used. Slow addition rate = 35 min/3.5 mL. Total reaction time = 10.5 h. Pale yellow solid [silica gel column chromatography eluted by

hexane/ethyl acetate = 2/1 (v/v)]; mp 56 °C; ^1H NMR (C_6D_6 , 500 MHz) δ 0.63 (s, 3H), 0.69 (s, 3H), 1.42 (d, J = 6.4 Hz, 3H), 1.94 (AB sys, J = 17.3 Hz, 1H), 2.02 (AB sys, J = 17.3 Hz, 1H), 3.13 (s, 3H), 3.55 (AB sys, J = 13.9 Hz, 1H), 3.61 (AB sys, J = 13.9 Hz, 1H), 4.79-4.84 (m, 1H), 5.49 (d, J = 4.8 Hz, 1H), 6.61 (d, J = 8.9 Hz, 2H), 6.98-7.08 (m, 5H), 7.38 (d, J = 7.3 Hz, 2H), 7.68-7.70 (m, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 21.0, 26.1, 26.7, 43.8, 55.6, 56.9, 59.9, 61.1, 83.0, 114.4, 121.9, 127.8, 128.5, 128.5, 129.2, 137.5, 154.5, 161.2, 166.1, 175.5; HRMS calcd. for $\text{C}_{24}\text{H}_{27}\text{N}_3\text{O}_4\text{Na}^+$ is 444.1893 and Observed = 444.1887.

1-Benzyl-2-[4', 5'-*trans*-dihydro-5-methyl-3-(*tert*-butyl)-isoxazol-4-yl]- 5,5-dimethylpyrazolidine-3-one (9o):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 65 °C; ^1H NMR (C_6D_6 , 500 MHz)

□ 0.67 (s, 3H), 0.76 (s, 3H), 1.15 (s, 9H), 1.42 (d, J = 6.2 Hz, 3H), 1.96 (AB sys, J = 17.1 Hz, 1H), 2.10 (AB sys, J = 17.1 Hz, 1H), 3.60 (AB sys, J = 13.9 Hz, 1H), 3.69 (AB sys, J = 13.9 Hz, 1H), 4.57 (dq, J = 6.2, 3.8 Hz, 1H), 5.02 (d, J = 3.8 Hz, 1H), 5.01-7.13 (m, 3H), 7.47-7.48 (m, 2H), 7.68-7.70 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) □ 20.8, 25.7, 27.1, 28.5, 43.9, 56.9, 59.1, 61.1, 82.3, 127.9, 128.6, 129.3, 129.8, 137.4, 163.5, 166.4, 175.4; HRMS calcd. for C₂₁H₂₉N₃O₃Na⁺ is 394.2101 and Observed = 394.2081.

1-Benzyl-2-[4', 5'-*trans*-Dihydro-5-methyl-3-(*iso*-butyl)-isoxazol-4-yl]- 5,5-dimethyl-pyrazolidine-3-one (9p):

Pale yellow oil [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; ¹H NMR (C₆D₆, 500 MHz) □ 0.69 (s, 3H), 0.75 (s, 3H), 0.81-0.86 (m, 6H), 1.37 (d, J = 6.2 Hz, 3H), 1.91 (m, 1H), 1.97 (AB sys, J = 17.3 Hz, 1H), 2.05 (AB sys, J = 17.3 Hz), 2.89 (dd, J = 5.4, 15.3 Hz, 1H), 2.24 (dd, J = 8.7, 15.3 Hz, 1H), 3.60 (AB sys, J = 13.9 Hz, 1H), 3.65 (AB sys, J = 13.9 Hz, 1H), 4.71-4.76 (m, 1H), 4.95 (d, J = 6.0 Hz, 1H), 7.03-7.13 (m, 3H), 7.44 (d, J = 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) □ 20.4, 22.3, 23.2, 25.9, 26.2, 26.6, 36.0, 43.6, 57.0, 61.1, 61.5, 81.7, 127.9, 128.6, 129.4, 137.1, 155.9, 166.2, 175.3; HRMS calcd. for C₂₁H₂₉N₃O₃Na⁺ is 394.2101 and Observed = 394.2126.

VI. Reductive conversion of isoxazolidines to known alcohols; Determination of absolute configuration

The structure and enantioselectivity of isoxazolidines, pictured in Table 1 were confirmed by ¹H NMR and chiral HPLC after reductive conversion of those to known alcohols **10** and **11**.^{13, 14, 15} **8i** was also transformed to known alcohol **14** by reduction. The selective cleavage of template bearing **8j** was carried out by using of L-Selectride® as a hydride source to give alcohol **16**.¹⁶ The absolute configuration of one of the prototypical

cycloadduct **8k** was established by converting it to known compound **15**. The optical rotation data was compared.¹⁷

***trans*-4-Methyl-3-(2,4,6-trimethylphenyl)-2-isoxazolidine-5-methanol (**10**):**

Colorless oil [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; $[\alpha]_D^{25} = +280.0$ (c 0.58, CHCl₃)

[97% ee estimated by chiral HPLC analysis on Daicel Chiral Cell OJ-OJ doubly connected column, hexane / 2-propanol (19:1 v/v), 0.5 mL/min, t_r (minor) = 70.9 min, t_r (major) = 78.7 min]; ¹H NMR (CDCl₃, 500 MHz) δ 1.13 (d, J = 7.3 Hz, 3H), 2.00 (br s, 1H), 2.25 (s, 6H), 2.29 (s, 3H), 3.54 (qn, J = 7.3 Hz, 1H), 3.73 (dd, J = 4.4, 12.1 Hz, 1H), 3.93 (dd, J = 3.0, 12.1 Hz, 1H), 4.36-4.39 (m, 1H), 6.89 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 15.9, 20.3, 21.3, 47.6, 63.0, 87.9, 125.4, 128.9, 137.2, 138.9, 162.34; HRMS calcd. for C₁₄H₁₉NO₂Na⁺ is 256.1307 and Observed = 256.1304.

***trans*-5-Methyl-3-(2,4,6-trimethylphenyl)-2-isoxazolidine-4-methanol (**11**):**

Colorless oil [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; Chiral HPLC analysis on Daicel Chiral Cell OJ-OJ

doubly connected column, hexane / 2-propanol (19:1 v/v), 0.5 mL/min, t_r (minor) = 99.9 min, t_r (major) = 117.4 min; ¹H NMR (CDCl₃, 500 MHz) δ 1.48 (d, J = 6.2 Hz, 3H), 1.72 (br s, 1H), 2.24 (s, 6H), 2.28 (s, 3H), 3.30-3.33 (m, 1H), 3.59-3.65 (m, 1H), 4.68-4.73 (m,

1H), 6.88 (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.3, 21.0, 21.3, 60.9, 61.6, 80.5, 125.7, 129.0, 137.1, 139.0, 158.1; HRMS calcd. for C₁₄H₁₉NO₂Na⁺ is 256.1307 and Observed = 256.1307.

***trans*-4-Phenyl-3-(2,4,6-trimethylphenyl)-2-isoxazolidine-5-methanol (14):**

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v) – 2/1 (v/v)]; mp 131 °C; 99% ee:

$[\alpha]_D^{25} = +273.0$ (*c* 0.76, CHCl₃); ¹H NMR (CDCl₃, 500 MHz) δ

2.09 (s, 6H), 2.21 (s, 3H), 2.31 (br s, 1H), 3.81 (dd, *J* = 4.8, 7.5 Hz, 1H), 3.98 (dd, *J* = 3.4, 7.5 Hz, 1H), 4.59 (1H, *J* = 6.2 Hz, 1H), 6.75 (s, 2H), 7.14-7.28 (m, 5H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.4, 21.2, 59.2, 63.6, 88.0, 124.9, 128.0, 128.2, 128.8, 129.1, 137.2, 137.3, 138.8, 160.1; HRMS calcd. for C₁₉H₂₁NO₂Na⁺ is 318.1464 and Observed = 318.1459.

(4*S*, 5*S*)-*trans*-4-Methyl-3-phenyl-2-isoxazolidine-5-methanol (15):

Colorless solid [silica gel column chromatography eluted by hexane/ethyl acetate = 4/1 (v/v)]; mp 68 °C; 98% ee: $[\alpha]_D^{25} = +130.6$

(*c* 0.50, MeOH); (4*R*, 5*R*)-enantiomer: Lit. 98% ee: $[\alpha]_D^{25} = -124$ (*c* 0.14, MeOH)¹⁷, 91% ee: $[\alpha]_D^{25} = -113$ (*c* 0.50, MeOH)¹⁸; ¹H NMR (CDCl₃, 500 MHz) δ 1.34 (d, *J* = 7.3 Hz, 3H), 2.15 (br s, 1H), 3.62 (dq, *J* = 5.2, 7.3 Hz, 1H), 3.67 (dd, *J* = 5.2, 11.9 Hz, 1H), 3.77 (dd, *J* = 3.0, 11.9 Hz, 1H), 4.44 (dq, *J* = 4.0, 5.2 Hz, 1H), 7.38-7.42 (m, 3H), 7.64-7.67 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 17.8, 43.8, 63.6, 88.9, 127.3, 128.7, 129.0, 130.3, 161.5; HRMS calcd. for C₁₁H₁₃NO₂H⁺ is 192.1019 and Observed = 192.1020.

VII. Reductive conversion of **8j** to alcohol **16** by using of L-Selectride® as a hydride source

Under nitrogen atmosphere, a 1 M solution of L-Selectride® in THF (0.44 mL) was added dropwise to a solution of **8j** (0.11 mmol) in THF (2.2 mL) at $-78\text{ }^{\circ}\text{C}$ and stirred for 2 h. After completion, the reaction mixture was poured into ice-cooled 1M HCl and the mixture was extracted with ethyl acetate (5 mL x 3). The combined extracts were washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under reduced pressure to give the crude product. The crude product was purified by flash chromatography on silica gel eluted by hexane/diethyl ether = 1/1 (v/v) to give analytically pure alcohol **16** in 72% yield (23 mg).

***trans*-4-Ethoxycarbonyl-3-(2,4,6-trimethylphenyl)-2-isoxazolidine-5-methanol (**16**):**

The *trans* stereochemistry was confirmed by NOE analysis (no NOE between H-4 and H-5) Colorless oil; 99% ee: $[\alpha]_{\text{D}}^{25} = +290.4$ (c 0.52, CHCl_3); ^1H NMR (CDCl_3 , 500 MHz) δ 0.96 (t, $J = 7.1$ Hz, 3H), 1.98 (br s, 1H), 2.24 (s, 3H), 2.28 (s, 3H), 3.70-3.75 (m, 1H), 3.94-4.00 (m, 1H), 4.02-4.09 (m, 2H), 4.52 (d, $J = 8.9$ Hz, 1H), 5.18 (dt, $J = 3.0, 8.9$ Hz, 1H), 6.87 (s, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.8, 20.2, 21.3, 57.7, 62.0, 62.5, 84.3, 124.8, 128.7, 137.3, 139.2, 155.2, 168.3.

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