## Electronic Supplementary Information for

# Vinylogy in Nitronates: Utilization of $\alpha$-Aryl Conjugated Nitroolefins as a Nucleophile for Highly Stereoselective Aza-Henry Reaction 

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General Information: Infrared spectra were recorded on a SHIMADZU IRAffinity-1 spectrometer. ${ }^{1}$ H NMR spectra were recorded on a JEOL JNM-ECS400 $(400 \mathrm{MHz})$ spectrometer. Chemical shifts are reported in ppm from tetramethylsilane ( 0.00 ppm ) resonance as the internal standard. Data are reported as follows: chemical shift, integration, multiplicity ( $\mathrm{s}=$ singlet, $\mathrm{d}=$ doublet, $\mathrm{t}=$ triplet, $\mathrm{q}=$ quartet, $\mathrm{m}=$ multiplet, $\mathrm{br}=$ broad), and coupling constants (Hz). ${ }^{13} \mathrm{C}$ NMR spectra were recorded on a JEOL JNM-ECS400 ( 101 MHz ) spectrometer or JEOL JNM-ECA600 (151 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance $\left(\mathrm{CDCl}_{3}: 77.16 \mathrm{ppm}\right)$. The high resolution mass spectra were conducted on Thermo Fisher Scientific Exactive (ESI). Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel $60 \mathrm{GF}_{254}, 0.25 \mathrm{~mm}$ ). Flash column chromatography was performed on silica gel 60 (spherical, 40-50 $\mu \mathrm{m}$; Kanto Chemical Co., Inc.). Enantiomeric excesses were determined by HPLC analysis using chiral columns [ $\phi 4.6 \mathrm{~mm} \times 250 \mathrm{~mm}$, DAICEL CHIRALPAK IA (IA), CHIRALPAK IC (IC), CHIRALPAK ID-3 (ID-3), CHIRALPAK IF-3 (IF-3), CHIRALPAK AD-3 (AD-3), CHIRALPAK AZ-3 (AZ-3), CHIRALPAK AD-H (AD-H), and CHIRALCEL OD-3 (OD-3) with hexane (H), 2-propanol (IPA), and ethanol (EtOH) as eluent].

Diethyl ether ( $\mathrm{Et}_{2} \mathrm{O}$ ) was supplied from Kanto Chemical Co., Inc. as "Dehydrated" and further purified by passing through neutral alumina under nitrogen atmosphere. Betaines ${ }^{1}$, nitro olefins ${ }^{2}$, and $N$-Boc imines ${ }^{3}$ were prepared by following the literature procedure. Powdered $4 \AA$ molecular sieves (MS 4A) was supplied by NACALAI TESQUE, INC. Other simple chemicals were purchased and used as such.

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## Experimental Section:

## Characterization of Nitroolefins:



2a: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.53-7.43(4 \mathrm{H}, \mathrm{m}), 7.31-7.24(2 \mathrm{H}, \mathrm{m}), 1.83(3 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}) ; Z$ isomer $\delta$ $7.42-7.37(3 \mathrm{H}, \mathrm{m}), 7.36-7.31(2 \mathrm{H}, \mathrm{m}), 6.15(1 \mathrm{H}, \mathrm{q}, J=7.3 \mathrm{~Hz}), 2.00(3 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR (151 MHz, $\mathrm{CDCl}_{3}$ ) $E$ isomer $\delta 152.3,134.0,130.5,129.7,128.7,126.5,14.5 ; Z$ isomer $\delta 129.6_{4}, 129.5_{5}, 129.0$, 123.7, 14.1, two carbon atoms were not found probably due to overlapping; IR (film) 3057, 1667, 1514, 1443, 1327, 1184, 1074, $930 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{9} \mathrm{H}_{9} \mathrm{~N}_{1} \mathrm{O}_{2} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$186.0525. Found 186.0527.


2b: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.44(1 \mathrm{H}, \mathrm{q}, J=7.3 \mathrm{~Hz}), 7.26(2 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.16(2 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz})$, $2.41(3 \mathrm{H}, \mathrm{s}), 1.82(3 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}) ; Z$ isomer $\delta 7.30-7.18(4 \mathrm{H}, \mathrm{m}), 6.09(1 \mathrm{H}, \mathrm{q}, J=7.3 \mathrm{~Hz}), 2.37(3 \mathrm{H}$, s), $1.98(3 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $\left.151 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 152.3,139.8,133.6,130.4,129.4$, 126.6, 21.6, 14.5; $Z$ isomer $\delta 129.6,129.0,126.4,122.7,21.4,14.1$, two carbon atoms were not found probably due to overlapping; IR (film) 2914, 1667, 1514, 1377, 1327, 1180, 1113, 1038, $930 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{10} \mathrm{H}_{11} \mathrm{~N}_{1} \mathrm{O}_{2} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$200.0682. Found 200.0682.


2c: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.50(1 \mathrm{H}, \mathrm{q}, J=7.8 \mathrm{~Hz}), 7.30-7.23(2 \mathrm{H}, \mathrm{m}), 7.15(2 \mathrm{H}, \mathrm{t}, J=8.7 \mathrm{~Hz}), 1.83(3 \mathrm{H}$, $\mathrm{d}, J=7.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(151 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 163.4\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=250.1 \mathrm{~Hz}\right), 151.3,134.5,132.6$ $\left(\mathrm{d}, J_{\mathrm{F}-\mathrm{C}}=8.6 \mathrm{~Hz}\right), 125.5\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=3.0 \mathrm{~Hz}\right), 115.9\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=21.6 \mathrm{~Hz}\right), 14.6$; IR (film) 2922, 1667, 1633, 1504, 1327, 1225, 1159, 1098, $932 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{9} \mathrm{H}_{8} \mathrm{~N}_{1} \mathrm{O}_{2} \mathrm{~F}_{1} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$204.0431. Found 204.0433.


2d: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.47(1 \mathrm{H}, \mathrm{q}, J=7.3 \mathrm{~Hz}), 7.37(1 \mathrm{H}, \mathrm{t}, J=8.2 \mathrm{~Hz}), 7.02-6.97(1 \mathrm{H}, \mathrm{m}), 6.88-$ $6.83(1 \mathrm{H}, \mathrm{m}), 6.82-6.79(1 \mathrm{H}, \mathrm{m}), 3.83(3 \mathrm{H}, \mathrm{s}), 1.83(3 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}) ; Z$ isomer $\delta 7.30(1 \mathrm{H}, \mathrm{t}, J=$ $8.2 \mathrm{~Hz}), 6.96-6.91(2 \mathrm{H}, \mathrm{m}), 6.88-6.84(1 \mathrm{H}, \mathrm{m}), 6.14(1 \mathrm{H}, \mathrm{q}, J=7.3 \mathrm{~Hz}), 3.81(3 \mathrm{H}, \mathrm{s}), 1.99(3 \mathrm{H}, \mathrm{d}, J$ $=7.3 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $E$ isomer $\delta 159.7,152.1,134.1,130.7,129.8,122.8,116.1,115.3,55.5$, 14.5; $Z$ isomer $\delta 159.9,133.0,130.0,123.7,118.9,112.1,14.1$, three carbon atoms were not found probably due to overlapping; IR (film) 2959, 2833, 1667, 1580, 1514, 1331, 1240, 1159, 1036, $951 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{10} \mathrm{H}_{11} \mathrm{~N}_{1} \mathrm{O}_{3} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$216.0631. Found 216.0633.


2e: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR ( 400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.47-7.43(3 \mathrm{H}, \mathrm{m}), 7.38(1 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}), 7.30-7.25(2 \mathrm{H}, \mathrm{m}), 2.15(2 \mathrm{H}$, quintet, $J=7.8 \mathrm{~Hz}$ ), $1.09(3 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $E$ isomer $\delta 151.1$, 139.9, 130.5, 129.8, 129.7, 128.7, 22.2, 13.2; IR (film) 2972, 1667, 1547, 1518, 1356, 1331, 1184, 1070, $959 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{10} \mathrm{H}_{11} \mathrm{~N}_{1} \mathrm{O}_{2} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$200.0682. Found 200.0684.
${ }_{3}^{\text {noct }} \quad$ 2f: The synthesis was performed by following the literature procedure. ${ }^{2}$ Yellow oil; ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) E$ isomer $\delta 7.48-7.42(3 \mathrm{H}, \mathrm{m}), 7.39(1 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}), 7.29-7.23(2 \mathrm{H}, \mathrm{m}), 2.12(2 \mathrm{H}, \mathrm{q}, J$
$=7.8 \mathrm{~Hz}), 1.48(2 \mathrm{H}$, quintet, $J=7.8 \mathrm{~Hz}), 1.35-1.15(10 \mathrm{H}, \mathrm{m}), 0.87(3 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \mathrm{NMR}(101 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) E$ isomer $\delta 151.4,139.0,130.5,129.9,129.7,128.6,31.9,29.3,29.2,28.7,28.6,22.8,14.2$, one carbon atom was not found probably due to overlapping; IR (film) 2916, 2855, 1661, 1518, 1360, 1329, 1177, 1028, 964 $\mathrm{cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{16} \mathrm{H}_{23} \mathrm{~N}_{1} \mathrm{O}_{2} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$284.1621. Found 284.1620.


Representative Procedure for Catalytic Asymmetric Aza-Henry Reaction: A magnetic stirrer bar and MS 4A $(100.0 \mathrm{mg})$ were placed in an oven-dried test tube under argon (Ar) atmosphere. The MS 4A was dried with a heat gun under reduced pressure for 5 min and the test tube was refilled with Ar. Chiral ammonium betaine 1f $(3.83 \mathrm{mg}, 0.0050 \mathrm{mmol})$ and $\mathrm{Et}_{2} \mathrm{O}(0.30 \mathrm{~mL})$ were added to the test tube successively under Ar at $25^{\circ} \mathrm{C}$. After the mixture was cooled to $0^{\circ} \mathrm{C}$, nitroolefin $\mathbf{2 a}(17.9 \mathrm{mg}, 0.11 \mathrm{mmol})$ and benzaldehyde-derived $N$-Boc imine $\mathbf{3 a}$ ( 20.5 $\mathrm{mg}, 0.10 \mathrm{mmol}$ ) were introduced to the tube sequentially. The reaction mixture was stirred for 24 h and then, poured into ice-cooled $1 N$ hydrochloric acid. The aqueous phase was extracted with ethyl acetate (EA) twice. The combined organic phases were washed with brine, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, and filtered. All volatiles were removed by evaporation to afford the crude residue, which was analyzed by ${ }^{1} \mathrm{H}$ NMR $(400 \mathrm{MHz})$ to determine the diastereomeric ratio (anti/syn $=>20: 1$ ). Purification of the residue by column chromatography on silica gel $\left(\mathrm{H} / \mathrm{CHCl}_{3}=1: 2\right.$ as eluent) gave $\mathbf{4 a}$ as a mixture of diastereomers ( $33.2 \mathrm{mg}, 0.090 \mathrm{mmol}, 90 \%$ ), whose enantiomeric excesses were determined by HPLC analysis ( $96 \%$ ee for anti isomer). 4a: White solid; HPLC: IA, H/IPA = 98:2, flow rate $=0.3 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 22.0 \mathrm{~min}(1 S, 2 S), 23.2 \mathrm{~min}(1 R, 2 R), 25.5 \mathrm{~min}$ (minor diastereomer), 27.6 $\min$ (minor diastereomer). Absolute and relative configurations were assigned by the derivatization to 7 (see below). ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.60-7.39(3 \mathrm{H}, \mathrm{m}), 7.39-7.30(3 \mathrm{H}, \mathrm{m}), 7.30-7.18$ ( $4 \mathrm{H}, \mathrm{m}$ ), $6.44(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.15(1 \mathrm{H}, \mathrm{dd}, J=17.4,11.0 \mathrm{~Hz}), 5.64(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.37(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.64$ $(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.1,136.7,136.0,135.0,129.0$, $128.8,128.7,127.4,121.4,101.9,80.2,59.3,28.4$, two carbon atoms were not found probably due to overlapping; IR (film) $3447,2976,1713,1547,1479,1366,1312,1294,1159,1057,945 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{24} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$391.1628. Found 391.1626.


4b: Yellow oil; HPLC: AD-3, H/IPA $=98: 2$, flow rate $=0.3 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 27.1 \mathrm{~min}$ (minor enantiomer of major diastereomer), 29.5 min (major enantiomer of major diastereomer), 32.2 min (minor diastereomer), 37.2 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.44-$ $7.37(3 \mathrm{H}, \mathrm{m}), 7.24-7.19(2 \mathrm{H}, \mathrm{m}), 7.16(2 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 7.13(2 \mathrm{H}, \mathrm{d}, J=9.2 \mathrm{~Hz}), 6.40(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.17$ $(1 \mathrm{H}, \mathrm{dd}, J=17.4,11.0 \mathrm{~Hz}), 5.60(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.36(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.63(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 2.34(3 \mathrm{H}$, s), $1.33(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.1,138.5,136.1,135.1,133.6,129.5,129.0,128.7$,
$128.5,127.4,121.3,102.0,80.1,59.0,28.4,21.3$; IR (film) $3449,2974,1713,1547,1483,1366,1310,1290,1165$, $941 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$405.1785. Found 405.1786.


4c: Yellow oil; HPLC: $\mathrm{ID}-3, \mathrm{H} / \mathrm{IPA}=97: 3$, flow rate $=0.2 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 30.1 \mathrm{~min}$ (minor enantiomer of major diastereomer), 32.2 min (major enantiomer of major diastereomer), 39.6 min (minor diastereomer), 51.2 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.45-7.39$ $(3 \mathrm{H}, \mathrm{m}), 7.26-7.16(4 \mathrm{H}, \mathrm{m}), 7.05\left(2 \mathrm{H}, \mathrm{dd}, J_{\mathrm{H}-\mathrm{H}}=7.6 \mathrm{~Hz}, J_{\mathrm{F}-\mathrm{H}}=7.6 \mathrm{~Hz}\right), 6.39(1 \mathrm{H}, \mathrm{brd}, J=9.8 \mathrm{~Hz}), 6.14(1 \mathrm{H}, \mathrm{dd}, J$ $=17.4,11.0 \mathrm{~Hz}), 5.62(1 \mathrm{H}, \mathrm{d}, J=9.8 \mathrm{~Hz}), 5.40(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.67(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 162.8\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=251.6 \mathrm{~Hz}\right), 155.1,135.7,134.8,132.5,130.4\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=8.7\right.$ Hz ), 129.1, $128.8,127.3,121.7,115.8\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=22.3 \mathrm{~Hz}\right.$ ), 101.8, 80.4, 58.7, 28.4; IR (film) 3449, 2980, 1711, 1605, 1547, 1479, 1366, 1294, 1225, 1161, $849 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{~F}_{1} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 409.1534$. Found 409.1535.


4d: Yellow oil; HPLC: AZ-3, $\mathrm{H} / \mathrm{EtOH}=98: 2$, flow rate $=0.2 \mathrm{~mL} / \mathrm{min}, \lambda=224 \mathrm{~nm}, 31.0 \mathrm{~min}$ (major enantiomer of major diastereomer), 36.0 min (minor enantiomer of major diastereomer), 41.4 min (minor diastereomer), 43.8 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.45-7.39$ $(3 \mathrm{H}, \mathrm{m}), 7.33(2 \mathrm{H}, \mathrm{d}, J=8.7 \mathrm{~Hz}), 7.24-7.15(4 \mathrm{H}, \mathrm{m}), 6.38(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 6.14(1 \mathrm{H}, \mathrm{dd}, J=17.4,11.0 \mathrm{~Hz}), 5.61$ $(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 5.40(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.67(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 155.0,135.6,135.3,134.7,130.0,129.2,129.0,128.8,127.3,121.8,101.7,80.5,58.7,28.4$, one carbon atom was not found probably due to overlapping; IR (film) 3451, 2980, 1713, 1549, 1483, 1344, 1163, 1092, 1015, 947, $849 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{23}{ }^{35} \mathrm{Cl}_{1} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$425.1239. Found 425.1239.


4e: White solid; HPLC: IA, H/IPA $=98: 2$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=221 \mathrm{~nm}, 12.1 \mathrm{~min}$ (major enantiomer of major diastereomer), 15.4 min (minor diastereomer), 16.4 min (minor diastereomer), 17.9 min (minor enantiomer of major diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H} \mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.62(2 \mathrm{H}, \mathrm{d}, J=8.2$ $\mathrm{Hz}), 7.46-7.41(3 \mathrm{H}, \mathrm{m}), 7.39(2 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.24-7.17(2 \mathrm{H}, \mathrm{m}), 6.43(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.13(1 \mathrm{H}, \mathrm{dd}, J=$ $17.4,10.8 \mathrm{~Hz}), 5.70(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.43(1 \mathrm{H}, \mathrm{d}, J=10.8 \mathrm{~Hz}), 4.71(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.35(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.1,140.8,135.4,134.5,130.9\left(\mathrm{q}, J_{\mathrm{F}-\mathrm{C}}=33.2 \mathrm{~Hz}\right), 129.3,129.2,128.9,127.3$, $125.8\left(\mathrm{q}, J_{\mathrm{F}-\mathrm{C}}=3.9 \mathrm{~Hz}\right), 124.0\left(\mathrm{q}, J_{\mathrm{F}-\mathrm{C}}=276.1 \mathrm{~Hz}\right), 122.1,101.5,80.6,59.0,28.4$; IR (film) 3464, 2976, 1711, 1620, 1551, 1479, 1323, 1163, 1125, 1069, 947, $853 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{~F}_{3} \mathrm{Na}^{+}$([M+Na] $)$ 459.1502. Found 459.1501.
 4f: White solid; HPLC: IA, H/IPA/EtOH $=96: 2: 2$, flow rate $=0.2 \mathrm{~mL} / \mathrm{min}, \lambda=214 \mathrm{~nm}, 25.7$ $\min$ (major enantiomer of major diastereomer), 28.2 min (minor enantiomer of major diastereomer), 29.3 min (minor diastereomer), 31.0 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.47(1 \mathrm{H}$, $\mathrm{dt}, J=7.3,1.6 \mathrm{~Hz}), 7.45-7.35(4 \mathrm{H}, \mathrm{m}), 7.23(1 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}), 7.22-7.15(3 \mathrm{H}, \mathrm{m}), 6.38(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.16$ $(1 \mathrm{H}, \mathrm{dd}, J=17.4,10.8 \mathrm{~Hz}), 5.60(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.43(1 \mathrm{H}, \mathrm{d}, J=10.8 \mathrm{~Hz}), 4.69(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.35(9 \mathrm{H}$,
$\mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.0,139.0,135.5,134.7,131.9_{3}, 131.8_{8}, 130.4,129.2,128.8,127.3$, $122.8,122.0,101.6,80.5,58.8,28.4$, one carbon atom was not found probably due to overlapping; IR (film) 3453, 2976, 1713, 1547, 1470, 1410, 1339, 1288, 1161, 1059, 947, $839 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{4}{ }^{79} \mathrm{Br}_{1} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$469.0733. Found 469.0735.


4g: Yellow oil; HPLC: IA, H/IPA $=98: 2$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 15.6 \mathrm{~min}$ (major enantiomer of major diastereomer), 17.4 min (minor enantiomer of major diastereomer), 18.9 min (minor diastereomer), 35.0 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta$ 7.47$7.37(3 \mathrm{H}, \mathrm{m}), 7.26(1 \mathrm{H}, \mathrm{t}, J=8.0 \mathrm{~Hz}), 7.24-7.17(2 \mathrm{H}, \mathrm{m}), 6.89-6.82(2 \mathrm{H}, \mathrm{m}), 6.79(1 \mathrm{H}, \mathrm{s}), 6.40(1 \mathrm{H}, \mathrm{d}, J=10.1$ $\mathrm{Hz}), 6.20(1 \mathrm{H}, \mathrm{dd}, J=17.4,11.0 \mathrm{~Hz}), 5.61(1 \mathrm{H}, \mathrm{d}, J=10.1 \mathrm{~Hz}), 5.37(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.64(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz})$, $3.79(3 \mathrm{H}, \mathrm{s}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 159.7,155.1,138.1,136.0,135.0,129.8$, $129.0,128.7,127.4,121.4,120.9,114.7,113.9,101.8,80.2,59.2,55.4,28.4$; IR (film) $3431,2976,1711,1601$, 1547, 1479, 1342, 1256, 1157, 1038, 947, $862 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{5} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 421.1734$. Found 421.1729.


4h: Yellow oil; HPLC: ID-3, $\mathrm{H} / \mathrm{EtOH}=95: 5$, flow rate $=0.1 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 46.6 \mathrm{~min}$ (minor enantiomer of major diastereomer), 50.4 min (major enantiomer of major diastereomer), 53.6 min (minor diastereomer), 56.2 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.47-7.38(3 \mathrm{H}, \mathrm{m})$, $7.38-7.29(1 \mathrm{H}, \mathrm{m}), 7.29-7.19(3 \mathrm{H}, \mathrm{m}), 7.16(1 \mathrm{H}, \mathrm{t}, J=7.1 \mathrm{~Hz}), 7.09\left(1 \mathrm{H}, \mathrm{t}, J_{\mathrm{H}-\mathrm{H}}=7.1 \mathrm{~Hz}, J_{\mathrm{F}-\mathrm{H}}=11.4 \mathrm{~Hz}\right), 6.43(1 \mathrm{H}$, $\mathrm{d}, J=9.6 \mathrm{~Hz}), 6.10(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.06(1 \mathrm{H}, \mathrm{ddd}, J=17.2,10.7,3.0 \mathrm{~Hz}), 5.40(1 \mathrm{H}, \mathrm{d}, J=10.7 \mathrm{~Hz}), 4.64(1 \mathrm{H}, \mathrm{d}$, $J=17.2 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 160.2\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=251.6 \mathrm{~Hz}\right), 155.0,134.7(\mathrm{~d}$, $\left.J_{\mathrm{F}-\mathrm{C}}=5.8 \mathrm{~Hz}\right), 130.5\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=8.7 \mathrm{~Hz}\right), 129.1,128.8,128.7,127.5,125.1,124.5\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=12.6 \mathrm{~Hz}\right), 122.4,115.8(\mathrm{~d}$, $J_{\mathrm{F}-\mathrm{C}}=23.2 \mathrm{~Hz}$ ), 102.1, $80.4,51.9,28.4$, one carbon atom was not found probably due to overlapping; IR (film) 3449 , 2932, 1713, 1549, 1481, 1344, 1298, 1229, 1157, 1057, $839 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{~F}_{1} \mathrm{Na}^{+}$ $\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$409.1534. Found 409.1535.


4i: Yellow oil; HPLC: OD-3, H/IPA $=98: 2$, flow rate $=0.3 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 18.9 \mathrm{~min}$ (major enantiomer of major diastereomer), 35.2 min (minor enantiomer of major diastereomer), minor diastereomers were not assigned. Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 8.20(1 \mathrm{H}, \mathrm{d}, J=8.5 \mathrm{~Hz}), 7.87(2 \mathrm{H}, \mathrm{t}, J=8.5 \mathrm{~Hz})$, $7.57-7.40(7 \mathrm{H}, \mathrm{m}), 7.38-7.35(2 \mathrm{H}, \mathrm{m}), 6.72(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 6.69(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.79(1 \mathrm{H}, \mathrm{dd}, J=17.4$, $10.8 \mathrm{~Hz}), 5.22(1 \mathrm{H}, \mathrm{d}, J=10.8 \mathrm{~Hz}), 4.58(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.32(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 155.2,136.2,135.0,133.8,133.7,131.7,129.5,129.1_{2}, 129.0_{7}, 128.8,127.6,126.8,126.0,125.9,125.4$, $123.7,122.0,103.1,80.0,52.4,28.4$; IR (film) 2926, 1713, 1549, 1487, 1368, 1325, 1165, $1067 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{25} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$441.1785. Found 441.1783.


4j: Yellow oil; HPLC: $\mathrm{AD}-3, \mathrm{H} / \mathrm{EtOH}=98: 2$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 12.7 \mathrm{~min}$ (major enantiomer of major diastereomer), 13.9 min (minor diastereomer), 15.7 min (minor
diastereomer), 17.7 min (minor enantiomer of major diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.45-7.31(5 \mathrm{H}, \mathrm{m}), 7.24-7.15(2 \mathrm{H}, \mathrm{m})$, $6.40-6.26(3 H, m), 6.06(1 H, d, J=10.5 \mathrm{~Hz}), 5.84(1 \mathrm{H}, \mathrm{d}, J=10.5 \mathrm{~Hz}), 5.46(1 \mathrm{H}, \mathrm{d}, J=10.5 \mathrm{~Hz}), 4.87(1 \mathrm{H}, \mathrm{d}, J=$ $17.4 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.0,150.3,142.7,134.9,134.5,129.0,128.7$, $127.1,122.0,110.7,109.5,101.1,80.4,53.6,28.3$; IR (film) $3431,2976,1713,1551,1485,1366,1329,1231,1155$, 1013, $949,870 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{19} \mathrm{H}_{22} \mathrm{~N}_{2} \mathrm{O}_{5} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$381.1421. Found 381.1420.


4k: White solid; HPLC: IA, H/IPA $=95: 5$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 10.3 \mathrm{~min}$ (major enantiomer of major diastereomer), 10.9 min (minor enantiomer of major diastereomer), 11.6 min (minor diastereomer), 12.7 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.38-7.29(3 \mathrm{H}, \mathrm{m})$, $7.27-7.22(2 \mathrm{H}, \mathrm{m}), 7.21(2 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.10(2 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 6.43(1 \mathrm{H}, \mathrm{d}, J=9.9 \mathrm{~Hz}), 6.14$ $(1 \mathrm{H}, \mathrm{dd}, J=17.3,10.9 \mathrm{~Hz}), 5.60(1 \mathrm{H}, \mathrm{d}, J=9.9 \mathrm{~Hz}), 5.36(1 \mathrm{H}, \mathrm{d}, J=10.9 \mathrm{~Hz}), 4.66(1 \mathrm{H}, \mathrm{d}, J=17.3 \mathrm{~Hz}), 2.38(3 \mathrm{H}$, s), $1.35(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.1,139.0,136.8,136.2,132.1,129.4,128.8,128.7$, $127.3,121.3,101.7,80.2,59.2,28.4,21.2$, one carbon atom was not found probably due to overlapping; IR (film) $3447,2970,1713,1547,1483,1366,1310,1292,1169,1057,843 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}$ $\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$405.1785. Found 405.1787.


41: White solid; HPLC: IC, H/IPA $=97: 3$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 10.5 \mathrm{~min}$ (major enantiomer of major diastereomer), 13.0 min (minor diastereomer), 14.0 min (minor diastereomer), 18.7 min (minor enantiomer of major diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.39-7.31(3 \mathrm{H}, \mathrm{m})$, $7.26-7.18(4 \mathrm{H}, \mathrm{m}), 7.10\left(2 \mathrm{H}, \mathrm{t}, J_{\mathrm{H}-\mathrm{H}}=8.7 \mathrm{~Hz}, J_{\mathrm{F}-\mathrm{H}}=8.7 \mathrm{~Hz}\right), 6.38(1 \mathrm{H}, \mathrm{d}, J=9.8 \mathrm{~Hz}), 6.16(1 \mathrm{H}, \mathrm{dd}$, $J=17.2,11.0 \mathrm{~Hz}), 5.60(1 \mathrm{H}, \mathrm{d}, J=9.8 \mathrm{~Hz}), 5.39(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 4.65(1 \mathrm{H}, \mathrm{d}, J=17.2 \mathrm{~Hz}), 1.35(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 162.8\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=253.5 \mathrm{~Hz}\right), 155.1,136.4,136.0,130.9\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=2.9 \mathrm{~Hz}\right)$, $129.5\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=8.7 \mathrm{~Hz}\right), 128.9,128.8,128.6,128.5,121.5,115.7\left(\mathrm{~d}, J_{\mathrm{F}-\mathrm{C}}=22.3 \mathrm{~Hz}\right), 101.4,80.4,59.3,28.4$; IR (film) 3453, 2978, 1709, 1605, 1549, 1514, 1485, 1312, 1236, 1169, 1055, 943, $837 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{~F}_{1} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$409.1534. Found 409.1535.


4m: White solid; HPLC: IF-3, H/IPA/EtOH $=94: 2: 4$, flow rate $=0.5 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}$, 11.0 min (minor enantiomer of major diastereomer), 12.1 min (major enantiomer of major diastereomer), 13.2 min (minor diastereomer), 13.8 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a}$. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.38-7.29(4 \mathrm{H}, \mathrm{m}), 7.27-7.22(2 \mathrm{H}, \mathrm{m}), 6.94(1 \mathrm{H}, \mathrm{dd}, J=8.2,2.3 \mathrm{~Hz}), 6.83-6.74(2 \mathrm{H}, \mathrm{m}), 6.44(1 \mathrm{H}, \mathrm{d}, J=$ $9.6 \mathrm{~Hz}), 6.13(1 \mathrm{H}, \mathrm{dd}, J=17.3,10.9 \mathrm{~Hz}), 5.62(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.38(1 \mathrm{H}, \mathrm{d}, J=10.9 \mathrm{~Hz}), 4.73(1 \mathrm{H}, \mathrm{d}, J=17.3$ Hz ), $3.81(3 \mathrm{H}, \mathrm{s}), 1.34(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) anti isomer $\delta 159.8,155.1,136.7,136.3,135.8,129.7$, $128.8,128.7,121.4,119.6,114.8,113.1,101.8,80.2,59.2,55.5,28.4$, one carbon atom was not found probably due to overlapping; IR (film) 3443, 2978, 1703, 1601, 1547, 1487, 1352, 1288, 1227, 1167, 1030, $949 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{5} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$421.1734. Found 421.1733.


4n: White solid; HPLC: AZ-3, $\mathrm{H} / \mathrm{IPA}=98: 2$, flow rate $=0.3 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 21.5 \mathrm{~min}$ (minor enantiomer of major diastereomer), 25.3 min (major enantiomer of major diastereomer), 29.4 min (minor diastereomer), 31.6 min (minor diastereomer). Absolute and relative configurations were assigned on the analogy of $\mathbf{4 a} .{ }^{1} \mathrm{H} \mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 7.44-7.30(6 \mathrm{H}, \mathrm{m})$, $7.28-7.16(4 \mathrm{H}, \mathrm{m}), 6.42(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.78(1 \mathrm{H}, \mathrm{dd}, J=15.8,3.2 \mathrm{~Hz}), 5.61(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.03(1 \mathrm{H}$, sextet, $J=9.0 \mathrm{~Hz}$ ), $1.67(3 \mathrm{H}, \mathrm{d}, J=6.4 \mathrm{~Hz}), 1.33(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \mathrm{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ anti isomer $\delta 155.1,136.9$, $135.9,133.5,129.4,128.8,128.7_{4}, 128.69,128.6_{0}, 127.4,101.9,80.1,59.5,28.4,18.3$, one carbon atom was not found probably due to overlapping; IR (film) 3451, 2972, 1713, 1547, 1479, 1366, 1292, 1161, 1047, 970,843 $\mathrm{cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$405.1785. Found 405.1785.


40: HPLC analysis was performed after reduction of the nitro group to give the corresponding amine S1. Absolute and relative configurations were assigned on the analogy of 4a. White solid; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.44-7.37(3 \mathrm{H}, \mathrm{m}), 7.37-7.30(3 \mathrm{H}, \mathrm{m}), 7.28-$ $7.16(4 \mathrm{H}, \mathrm{m}), 6.43(1 \mathrm{H}, \mathrm{d}, J=10.1 \mathrm{~Hz}), 5.75(1 \mathrm{H}, \mathrm{d}, J=16.0 \mathrm{~Hz}), 5.61(1 \mathrm{H}, \mathrm{d}, J=10.1 \mathrm{~Hz}), 5.02(1 \mathrm{H}, \mathrm{dt}, J=16.0$, $6.8 \mathrm{~Hz}), 1.98(2 \mathrm{H}, \mathrm{q}, J=6.8 \mathrm{~Hz}), 1.34(9 \mathrm{H}, \mathrm{s}), 1.31-1.17(10 \mathrm{H}, \mathrm{m}), 0.87(3 \mathrm{H}, \mathrm{t}, J=6.9 \mathrm{~Hz}),{ }^{13} \mathrm{C}$ NMR ( 101 MHz , $\mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.1,138.6,136.9,135.9,128.7,128.6,128.3,127.4,102.0,80.1,59.6,32.5,31.9,29.1$, $28.6,28.4,22.8,14.2$, four carbon atoms were not found probably due to overlapping; IR (film) 3453, 2922, 1713, 1547, 1483, 1425, 1391, 1256, 1161, $972 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{28} \mathrm{H}_{38} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 489.2724$ Found 489.2725. S1: The synthesis was performed by following the procedure for amine $\mathbf{S 2}$ (shown below). White solid; HPLC: IA, H/IPA $=98: 2$, flow rate $=0.3 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 35.6 \mathrm{~min}$ (minor enantiomer of major diastereomer), 42.2 min (minor diastereomer), 47.6 min (minor diastereomer), 56.7 min (major enantiomer of major diastereomer). ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 7.49(2 \mathrm{H}, \mathrm{d}, J=7.8 \mathrm{~Hz}), 7.33(2 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz})$, $7.29-7.20(4 \mathrm{H}, \mathrm{m}), 7.18(2 \mathrm{H}, \mathrm{br}), 5.95(1 \mathrm{H}, \mathrm{d}, J=15.6 \mathrm{~Hz}), 5.64(1 \mathrm{H}, \mathrm{brd}, J=7.5 \mathrm{~Hz}), 5.27(1 \mathrm{H}, \mathrm{dt}, J=15.6,6.8$ $\mathrm{Hz}), 5.03(1 \mathrm{H}, \mathrm{d}, J=7.5 \mathrm{~Hz}), 1.95(2 \mathrm{H}, \mathrm{q}, J=6.8 \mathrm{~Hz}), 1.36-1.07(19 \mathrm{H}, \mathrm{m}), 0.87(3 \mathrm{H}, \mathrm{t}, J=6.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR (101 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) anti isomer $\delta 155.4,144.5,139.1,136.4,129.6,128.5,128.3,127.7,127.3,126.8,126.2,79.2,62.2$, $32.4,31.9,29.3,29.2,28.3,22.8,14.3$, two carbon atoms were not found probably due to overlapping; IR (film) $3362,2965,2924,1703,1514,1366,1248,1163,1011 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{28} \mathrm{H}_{41} \mathrm{~N}_{2} \mathrm{O}_{2}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$ 437.3163. Found 437.3157.

## Derivatization of 4a:



4a
5

Conversion of Nitroalkene 4a to Differentially Protected Diamine 5: 4a ( $36.8 \mathrm{mg}, 0.10 \mathrm{mmol}$ ) was taken in $\mathrm{HCl} / \mathrm{EtOH} / \mathrm{H}_{2} \mathrm{O}\left(666.7 \mu \mathrm{~L}, 3.0 \mathrm{M}, 2.0 \mathrm{mmol}, \mathrm{EtOH} / \mathrm{H}_{2} \mathrm{O}=1: 2\right)$ and Zn powder ( $130.8 \mathrm{mg}, 2.0 \mathrm{mmol}$ ) was introduced to the solution portionwise. The mixture was stirred for 12 h at ambient temperature. The reaction mixture was diluted
with water and the aqueous phase was extracted with EA twice. The combined organic extracts were washed with brine and dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$. After concentration, the resulting residue was purified by column chromatography on silica gel $\left(\mathrm{H} / \mathrm{EA}=1: 1\right.$ as eluent) to afford the corresponding amine $\mathbf{S} 2 \mathrm{in} 90 \%$ yield ( $30.5 \mathrm{mg}, 0.090 \mathrm{mmol}$ ). S2: White solid; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.50(2 \mathrm{H}, \mathrm{d}, J=7.8 \mathrm{~Hz}), 7.34(2 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz}), 7.30-7.22(4 \mathrm{H}, \mathrm{m}), 7.19(2 \mathrm{H}, \mathrm{brd}, J=$ $6.9 \mathrm{~Hz}), \quad 6.42(1 \mathrm{H}, \mathrm{dd}, J=17.4,10.8 \mathrm{~Hz}), 5.66(1 \mathrm{H}, \operatorname{brd}, J=6.9 \mathrm{~Hz}), 5.09(1 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 5.04(1 \mathrm{H}, \mathrm{d}, J=$ $10.8 \mathrm{~Hz}), 4.93(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.23(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 155.4,144.4,143.7,138.9,128.4_{4}$, $128.3_{7}, 127.8,127.4,127.0,126.2,113.4,79.3,62.9,62.0,28.3$; IR (film) $3318,2976,1703,1585,1514,1366$, 1248, 1169, $995 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{21} \mathrm{H}_{27} \mathrm{~N}_{2} \mathrm{O}_{4}{ }^{+}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$339.2067. Found 339.2065.

The amine $\mathbf{S} 2(30.5 \mathrm{mg}, 0.090 \mathrm{mmol})$ was dissolved into $\mathrm{CH}_{2} \mathrm{Cl}_{2}(0.90 \mathrm{~mL})$ and ${ }^{i} \operatorname{Pr}_{2} \mathrm{EtN}(39.6 \mu \mathrm{~L}, 0.23 \mathrm{mmol})$ and benzyl chloroformate ( $19.3 \mu \mathrm{~L}, 0.14 \mathrm{mmol}$ ) were added sequentially. The reaction mixture was stirred for 24 h and poured to water. The mixture was then extracted with $\mathrm{CHCl}_{3}$ twice and the combined organic extracts were washed with brine. Organic extracts were dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$ and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography $(\mathrm{H} / \mathrm{EA}=5 / 1$ as eluent) to afford $\mathbf{5}$ in $56 \%$ yield ( $23.6 \mathrm{mg}, 0.050 \mathrm{mmol}$ ). 5: White solid; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , acetone) $\delta 7.48(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}$ ), $7.42-7.38$ ( $3 \mathrm{H}, \mathrm{m}$ ), $7.38-7.28$ ( $5 \mathrm{H}, \mathrm{m}$ ), $7.28-7.21(1 \mathrm{H}, \mathrm{m}), 7.21-7.11(5 \mathrm{H}, \mathrm{m}), 6.67(1 \mathrm{H}, \mathrm{s}), 6.08(1 \mathrm{H}, \mathrm{dd}, J=17.4,10.5 \mathrm{~Hz}), 5.38(1 \mathrm{H}, \mathrm{d}, J=8.7 \mathrm{~Hz})$, 5.19-5.09 (3H, m), $5.03(1 \mathrm{H}, \mathrm{d}, J=12.4 \mathrm{~Hz}), 4.84(1 \mathrm{H}, \mathrm{d}, J=17.4 \mathrm{~Hz}), 1.30(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta 156.1,155.4,140.6,137.8,137.5,136.6,128.7,128.5,128.4_{1}, 128.3_{6}, 127.7,127.6,127.5,126.7,116.4,80.1$, $66.9,66.5,62.3,28.5$, one carbon atom was not found probably due to overlapping; IR (film) 3354, 2970, 1715, 1699, 1489, 1456, 1364, 1246, $1165 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{29} \mathrm{H}_{32} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 495.2254$. Found 495.2248.


Ozonolysis of the Double Bond in 5: Ozone $\left(\mathrm{O}_{3}\right)$ gas was generated from pure oxygen by using OZM-300SW (Blowerman co. jp.) and was passed through a solution of $5(23.6 \mathrm{mg}, 0.050 \mathrm{mmol})$ in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(0.50 \mathrm{~mL})$ at $-78{ }^{\circ} \mathrm{C}$ for 1 h . Consumption of 5 was monitored by TLC and then, the passing $\mathrm{O}_{3}$ gas was exchanged with pure oxygen. After a while, dimethyl sulfide ( $36.7 \mu \mathrm{~L}$ ) was added to the solution and the mixture was allowed to warm up to room temperature. All volatiles were removed by evaporation to afford the crude residue, which was purified by column chromatography on silica gel $(\mathrm{H} / \mathrm{EA}=5: 1$ as eluent) to give $\mathbf{6}(19.0 \mathrm{mg}, 0.040 \mathrm{mmol}, 80 \%)$. 6: White solid; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 9.40(1 \mathrm{H}, \mathrm{s}), 7.48-7.31(11 \mathrm{H}, \mathrm{m}), 7.27-7.18(3 \mathrm{H}, \mathrm{m}), 7.09(2 \mathrm{H}, \mathrm{d}, J=7.8 \mathrm{~Hz})$, $6.14(1 \mathrm{H}, \mathrm{s}), 5.96(1 \mathrm{H}, \mathrm{d}, J=9.6 \mathrm{~Hz}), 5.24(1 \mathrm{H}, \mathrm{d}, J=12.6 \mathrm{~Hz}), 5.08(1 \mathrm{H}, \mathrm{d}, J=12.6 \mathrm{~Hz}), 1.37(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 190.8,156.5,156.2,137.7,136.2,132.5,129.5,129.0,128.9,128.8,128.5,128.3,128.2$, $127.5,127.1,79.8,74.4,67.5,56.7,28.5$; IR (film) 3372, 2978, 1711, 1697, 1506, 1456, 1365, 1248, 1165, 1067 $\mathrm{cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{28} \mathrm{H}_{30} \mathrm{~N}_{2} \mathrm{O}_{5} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$497.2047. Found 497.2047.


Pinnick Oxidation of 6: To a solution of $\mathbf{6}(19.0 \mathrm{mg}, 0.040 \mathrm{mmol})$ in ${ }^{t} \mathrm{BuOH} / \mathrm{H}_{2} \mathrm{O}(0.45 / 0.35 \mathrm{~mL})$ were added $\mathrm{NaClO}_{2}(10.9 \mathrm{mg}, 0.12 \mathrm{mmol}), \mathrm{NaH}_{2} \mathrm{PO}_{4}(24.0 \mathrm{mg}, 0.20 \mathrm{mmol})$, and 2-methyl-2-butene ( $42.5 \mu \mathrm{~L}, 0.40 \mathrm{mmol}$ ) at room temperature with stirring. After being stirred for 1 h , the reaction mixture was diluted with brine and the aqueous phase was extracted with EA twice. Organic phases were dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. The residual material was purified by column chromatography on silica gel $\left(\mathrm{CHCl}_{3} / \mathrm{MeOH}=5: 1\right.$ as eluent $)$ to give 7 $(12.0 \mathrm{mg}, 0.024 \mathrm{mmol}, 61 \%)$, whose enantiomeric excess was determined by HPLC analysis after derivatizing to the corresponding methyl ester ( $97 \%$ ee). ${ }^{\text {1a }} \quad 7$ : White solid; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.69(1 \mathrm{H}, \mathrm{br}), 7.50(2 \mathrm{H}$, brd, $J=6.4 \mathrm{~Hz}), 7.42-7.20(11 \mathrm{H}, \mathrm{m}), 7.15(2 \mathrm{H}, \mathrm{t}, J=7.3 \mathrm{~Hz}), 6.57(1 \mathrm{H}, \mathrm{br}), 6.31(1 \mathrm{H}, \mathrm{br}), 5.21(1 \mathrm{H}, \mathrm{d}, J=12.4$ $\mathrm{Hz}), 5.05(1 \mathrm{H}, \mathrm{d}, J=12.4 \mathrm{~Hz}), 1.32(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 171.2,157.1,156.6,138.0,136.4$, $136.2,128.7,128.6,128.5,128.4,128.3,128.1,127.9,127.3,80.8,67.3,28.5$, three carbon atoms were not found probably due to overlapping; IR (film) 3368, 2926, 1713, 1667, 1497, 1368, 1248, 1163, 1051, $885 \mathrm{~cm}^{-1}$; HRMS (ESI) Calcd for $\mathrm{C}_{28} \mathrm{H}_{30} \mathrm{~N}_{2} \mathrm{O}_{6} \mathrm{Na}^{+}\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$513.1996. Found 513.2009. HPLC (methyl ester): AD-H, $\mathrm{H} / \mathrm{EtOH}=$ 95:5, flow rate $=1.0 \mathrm{~mL} / \mathrm{min}, \lambda=210 \mathrm{~nm}, 7.4 \mathrm{~min}(1 S, 2 S), 8.6 \mathrm{~min}(1 R, 2 R), 27.2 \mathrm{~min}$ (minor diastereomer), 40.5 $\min$ (minor diastereomer). Absolute and relative configurations were assigned by comparison with the literature data. ${ }^{\text {1a }}$

## Copies of ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR Spectra:



4a




11.0













11.0



[^1]





[^2]
$4 i$


[^3]








$11.0 \quad 10.0 \quad 9.0 \quad 8.0$


11.0 5.0











[^4]


4a


1 PDA Mutit $1 / 210$ m $4 n m$


## $4 c$



1．PDA Multi $1 / 210 \mathrm{~nm} 4 \mathrm{~nm}$


PDA Multi $1 / 210 \mathrm{~nm} 4 \mathrm{n}$
PDA Ch1 210 nm
ビーク\＃
ピーク\＃

4b



4d


$4 e$



4g


$4 f$




1 PDA Multi $1 / 218 \mathrm{~nm} 4 \mathrm{~nm}$


 1DetA Ch1／210nn
検出器ACh12

ビーク\＃ | 210 nm |
| ---: | ---: |\(| \begin{array}{r}1 <br>

2 <br>
2 <br>
合計\end{array}\)

保持時間 | 18.882 |
| :--- |
| 35.188 |




1 PDA Muti 1 ／ 210 nm 4 nm

$4 j$






4m



## 40



1 PDA Multi $1 / 210 \mathrm{~nm} 4 \mathrm{~nm}$


4n


PDA Multi 1 / $210 \mathrm{~nm} 4 n \mathrm{~nm}$


## 7 (methyl ester)



1 DetA Ch1/210nm



[^0]:    (1) (a) D. Uraguchi, K. Koshimoto, T. Ooi, Chem. Commun. 2010, 46, 300. (b) D. Uraguchi, K. Oyaizu, T. Ooi, Chem. Eur. J. 2012, 18, 8306.
    (2) F. Asaro, G. Pitacco, E. Valentin, Tetrahedron 1987, 43, 3279.
    (3) A. G. Wenzel, E. N. Jacobsen, J. Am. Chem. Soc. 2002, 124, 12964.

[^1]:    $\begin{array}{llllllllllllll}210.0 & 200.0 & 190.0 & 180.0 & 170.0 & 160.0 & 150.0 & 140.0 & 130.0 & 120.0 & 110.0 & 100.0 & 90.0 & 80.0 \\ 70.0\end{array}$

[^2]:    $\begin{array}{lllllllllllllllllllllllllll}210.0 & 200.0 & 190.0 & 180.0 & 170.0 & 160.0 & 150.0 & 140.0 & 130.0 & 120.0 & 110.0 & 100.0 & 90.0 & 80.0 & 70.0 & 60.0 & 50.0 & 40.0 & 30.0 & 20.0 & 10.0 & 0 & -10.0 & -20.0 & \end{array}$

[^3]:    $210.0 \quad 20$
    $\begin{array}{lllllllllllll}200.0 & 190.0 & 180.0 & 170.0 & 160.0 & 150.0 & 140.0 & 130.0 & 120.0 & 110.0 & 100.0 & 90.0 & 80.0 \\ 70.0\end{array}$

[^4]:    $\begin{array}{llllll}11.0 & 10.0 & \mathbf{9 . 0} & \mathbf{8 . 0} & \mathbf{7 . 0}\end{array}$
    6.0

