

# Supporting Information for Chiral Ammonium Betaines: A Bifunctional Organic Base Catalyst for Asymmetric Mannich-type Reaction of $\alpha$ -Nitrocarboxylates

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**General Information:** Infrared spectra were recorded on a JASCO FT/IR-230 or JASCO FT/IR-300E spectrometer.  $^1\text{H}$  NMR spectra were recorded on a Varian INOVA-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance ( $(\text{CD}_3)_2\text{SO}$ ; 2.50 ppm,  $\text{CD}_3\text{OD}$ ; 3.31 ppm) or  $\text{Me}_4\text{Si}$  resonance (0.0 ppm;  $\text{CDCl}_3$ ,  $(\text{CD}_3)_2\text{CO}$ ) as the internal standard. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broad) and coupling constants (Hz).  $^{13}\text{C}$  NMR spectra were recorded on a Varian INOVA-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance ( $\text{CDCl}_3$ ; 77.16 ppm,  $(\text{CD}_3)_2\text{SO}$ ; 39.5 ppm,  $\text{CD}_3\text{OD}$ ; 49.0 ppm) or  $\text{Me}_4\text{Si}$  resonance (0.0 ppm;  $(\text{CD}_3)_2\text{CO}$ ) as the internal standard. Optical rotations were measured on a JASCO DIP-1000 polarimeter. The high resolution mass spectra were conducted at the Research Center for Materials Science, Graduate School of Science, Nagoya University. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF<sub>254</sub>, 0.25 mm). Flash column chromatography was performed on silica gel 60 (spherical, 40-50  $\mu\text{m}$ ; Kanto Chemical Co., Inc.). Enantiomeric excesses were determined by HPLC analysis using chiral columns ( $\phi$  4.6 mm x 250 mm, DAICEL CHIRALPAK AD-H (AD-H) or CHIRALCEL OD-H (OD-H)).

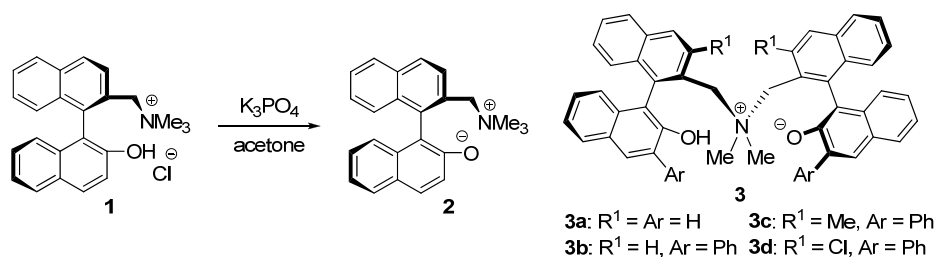
Toluene was supplied from Kanto Chemical Co., Inc. as “Dehydrated solvent system”. Aromatic and heteroaromatic imines,<sup>1</sup> aliphatic imines,<sup>2</sup> and nitroacetates<sup>3</sup> were prepared by following the literature procedure. Other simple chemicals were purchased and used as such.

<sup>1</sup> Wenzel, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 12964.

<sup>2</sup> Song, J.; Wang, Y.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 6048.

<sup>3</sup> Kornblum, N.; Blackwood, R. K. *Org. Synth. Coll. Vol.* **1963**, *4*, 454.

## Experimental Section:



### Characterization of Betaine Precursors:

**1:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.15 (1H, br), 7.87 (1H, d,  $J$  = 8.5 Hz), 7.82-7.1 (3H, m), 7.61 (1H, d,  $J$  = 8.5 Hz), 7.48 (1H, d,  $J$  = 8.5 Hz), 7.44 (1H, t,  $J$  = 8.5 Hz), 7.23 (1H, d,  $J$  = 8.5 Hz), 7.22 (1H, t,  $J$  = 8.5 Hz), 7.10 (1H, t,  $J$  = 8.5 Hz), 7.07 (1H, t,  $J$  = 8.5 Hz), 6.65 (1H, d,  $J$  = 8.5 Hz), 4.43 (1H, d,  $J$  = 13.0 Hz), 4.31 (1H, d,  $J$  = 13.0 Hz), 2.65 (9H, s); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  153.3, 139.2, 134.1, 133.8, 132.8, 130.8, 130.0, 128.7, 128.5, 128.4, 128.1, 127.8, 127.7, 127.3, 127.0, 124.7, 123.7, 123.3, 119.4, 115.2, 67.6, 52.9; IR (KBr): 3384, 3171, 1623, 1508, 1475, 1434, 1344, 1299, 1274, 1233, 974, 878, 825, 763 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>24</sub>H<sub>24</sub>NO<sup>+</sup> ([M-Cl]<sup>+</sup>) 342.1858. Found 342.1871.

**3a·HCl:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.20 (2H, br), 7.74 (2H, d,  $J$  = 8.5 Hz), 7.62 (2H, d,  $J$  = 8.5 Hz), 7.48 (2H, d,  $J$  = 8.5 Hz), 7.43 (2H, t,  $J$  = 8.5 Hz), 7.34 (2H, t,  $J$  = 8.5 Hz), 7.31 (2H, d,  $J$  = 8.5 Hz), 7.30-7.20 (6H, m), 7.13 (2H, t,  $J$  = 8.5 Hz), 7.00 (2H, t,  $J$  = 8.5 Hz), 6.53 (2H, d,  $J$  = 8.5 Hz), 4.66 (2H, d,  $J$  = 12.5 Hz), 3.86 (2H, d,  $J$  = 12.5 Hz), 2.36 (6H, brs); <sup>13</sup>C NMR (175 MHz, (CD<sub>3</sub>)<sub>2</sub>CO)  $\delta$  155.0, 141.0, 134.9, 134.4, 133.7, 130.3, 129.8, 129.6, 129.3, 128.9, 128.6, 128.5, 128.1, 127.6, 127.4, 124.9, 123.4<sub>5</sub>, 123.4<sub>2</sub>, 120.3, 115.8, 66.6, 50.0; IR (KBr): 3165, 3058, 1623, 1507, 1475, 1434, 1344, 1274, 977, 820 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>44</sub>H<sub>36</sub>NO<sub>2</sub><sup>+</sup> ([M-Cl]<sup>+</sup>) 610.2746. Found 610.2736.

**3b·CF<sub>3</sub>CO<sub>2</sub>H:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.87 (2H, d,  $J$  = 8.5 Hz), 7.71 (2H, d,  $J$  = 8.5 Hz), 7.68 (2H, d,  $J$  = 8.5 Hz), 7.57 (2H, s), 7.51 (2H, d,  $J$  = 8.5 Hz), 7.50 (2H, t,  $J$  = 8.5 Hz), 7.32-7.22 (12H, m), 7.18-7.12 (6H, m), 6.68 (2H, d,  $J$  = 8.5 Hz), 4.56 (2H, d,  $J$  = 13.0 Hz), 4.22 (2H, d,  $J$  = 13.0 Hz), 2.57 (6H, s), O-H protons were not found due to broadening; <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  162.5 (q,  $J_{F-C}$  = 37.2 Hz), 148.4, 137.1, 136.3, 134.4, 132.8, 132.4, 130.8, 130.2, 129.8, 129.5, 129.2, 129.1, 128.9, 128.6<sub>4</sub>, 128.5<sub>9</sub>, 128.2, 128.0, 127.7, 127.2, 127.0, 125.2, 124.5, 123.8, 116.4<sub>5</sub>, 116.3<sub>6</sub> (q,  $J_{F-C}$  = 292.3 Hz), 66.5, 50.0; IR (KBr): 3390, 3059, 1678, 1498, 1476, 1425, 1206, 1138, 1072, 1029, 768, 705 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>56</sub>H<sub>44</sub>NO<sub>2</sub><sup>+</sup> ([M-CF<sub>3</sub>CO<sub>2</sub>]<sup>+</sup>) 762.3372. Found 762.3366.

**3d·HCl:** Although NMR analysis gave broad spectrum at room temperature, it can be improved at 100 °C. <sup>1</sup>H NMR (500 MHz, (CD<sub>3</sub>)<sub>2</sub>SO, 100 °C)  $\delta$  8.63 (2H, brs), 8.28 (2H, s), 8.04 (2H, d,  $J$  = 8.5 Hz), 8.03 (2H, s), 8.00 (2H, d,  $J$  = 8.5 Hz), 7.65 (2H, t,  $J$  = 8.5 Hz), 7.57 (4H, d,  $J$  = 8.5 Hz), 7.47 (4H, t,  $J$  = 8.5 Hz), 7.42 (2H, d,  $J$  = 8.5 Hz), 7.40 (2H, t,  $J$  = 8.5 Hz), 7.30 (2H, t,  $J$  = 8.5 Hz), 7.21 (2H, t,  $J$  = 8.5 Hz), 7.20 (2H, t,  $J$  = 8.5 Hz), 6.62 (2H, d,  $J$  = 8.5 Hz), 4.77 (2H, d,  $J$  = 13.5 Hz), 4.61 (2H, br), 2.66 (6H, brs); <sup>13</sup>C NMR (126 MHz, (CD<sub>3</sub>)<sub>2</sub>SO, 100 °C)  $\delta$  149.7, 141.1, 137.2, 134.3, 132.1, 131.8, 131.7, 131.1, 129.2, 129.0, 128.9, 128.2<sub>5</sub>, 128.1<sub>6</sub>, 128.1, 127.6, 127.1, 127.0, 126.8, 126.6, 123.9, 123.4, 116.8, 65.4, 50.5, two carbons were not found probably due to overlapping; IR (KBr): 3405, 3056, 1619, 1472, 1427, 1259, 1199, 1006, 899, 750 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>56</sub>H<sub>42</sub>Cl<sub>2</sub>NO<sub>2</sub><sup>+</sup> ([M-Cl]<sup>+</sup>) 830.2593. Found 830.2592.

**Preparation of Ammonium betaine 2:** A solution of ammonium chloride **1** in acetone was treated with an excess amount of anhydrous  $K_3PO_4$  and filtered with the aid of ethyl acetate. The filtrate was concentrated by rotary evaporation. The residual solid was dissolved to trifluoroethanol and the solution thus obtained was filtered through a syringe filter (porous size: 0.45  $\mu m$ ). After concentration, the residual solid was washed with  $Et_2O$  on a funnel and dried under vacuum to afford chiral ammonium betaine **2** as a yellowish solid. **2:**  $^1H$  NMR (500 MHz,  $CD_3OD$ )  $\delta$  8.03 (1H, d,  $J = 8.5$  Hz), 7.97 (1H, d,  $J = 8.5$  Hz), 7.80 (1H, d,  $J = 8.5$  Hz), 7.74<sub>2</sub> (1H, d,  $J = 8.5$  Hz), 7.73<sub>6</sub> (1H, d,  $J = 8.5$  Hz), 7.53 (1H, td,  $J = 8.5, 1.0$  Hz), 7.46 (1H, d,  $J = 8.5$  Hz), 7.30 (1H, td,  $J = 8.5, 1.0$  Hz), 7.18 (1H, d,  $J = 8.5$  Hz), 7.08-7.02 (2H, m), 6.59-6.54 (1H, m), 4.53 (1H, d,  $J = 13.0$  Hz), 4.28 (1H, d,  $J = 13.0$  Hz), 2.89 (9H, s);  $^{13}C$  NMR (126 MHz,  $CD_3OD$ )  $\delta$  163.2, 143.6, 136.4, 136.2, 134.9, 131.2, 130.9, 129.4, 129.3, 129.0, 128.9, 128.4, 127.9, 127.5, 127.3, 126.3, 124.9, 123.6, 121.6, 116.8, 69.6, 53.8; IR (KBr): 3398, 1623, 1508, 1475, 1434, 1344, 1274, 1233, 975, 878, 826, 763  $cm^{-1}$ ; HRMS (FAB) Calcd for  $C_{24}H_{24}NO^+$  ( $[M+H]^+$ ) 342.1858. Found 342.1849.

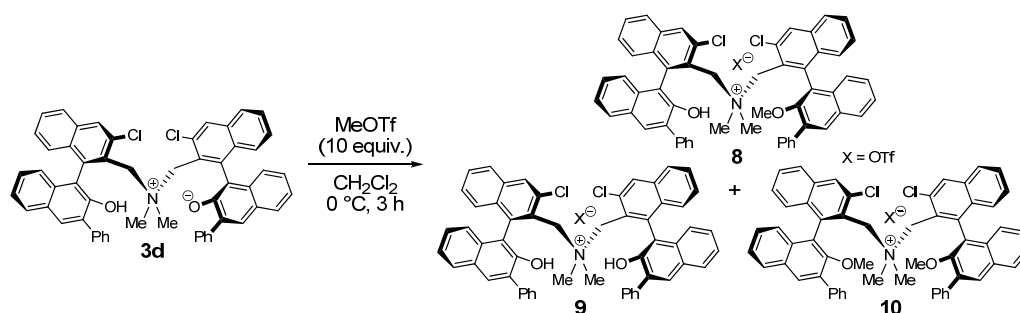
**3a:** Prepared by similar procedure for the preparation of **2**.  $^1H$  NMR (500 MHz,  $(CD_3)_2CO$ )  $\delta$  8.06-7.56 (4H, br), 7.63 (2H, br), 7.56-6.75 (14H, br), 7.47 (2H, br), 6.44 (2H, br), 4.50 (2H, br), 4.04 (2H, br), 2.36 (6H, br), O-H proton was not found probably due to broadening;  $^{13}C$  NMR analysis gave broad spectrum and it was not assignable; IR (KBr): 3057, 2923, 1621, 1473, 1346, 1274, 1146, 869, 820, 749  $cm^{-1}$ ; HRMS (FAB) Calcd for  $C_{44}H_{36}NO_2^+$  ( $[M+H]^+$ ) 610.2736. Found 610.2746.

For the preparation of **3b-d**, the following, rather convenient procedure was also applicable: A solution of ammonium salt **3**·HCl or **3**· $CF_3CO_2H$  in ethyl acetate was treated with 0.1 M aqueous  $NaHCO_3$  and phases were separated. The organic phase was dried over  $Na_2SO_4$  and filtered. All volatiles were removed by evaporation and residual solid was washed with  $Et_2O$  on a funnel. The solid was dried under reduced pressure to afford the ammonium betaine **3** as a yellow solid.

**3b:**  $^1H$  NMR (500 MHz,  $(CD_3)_2CO$ )  $\delta$  7.94 (2H, d,  $J = 8.5$  Hz), 7.79 (2H, d,  $J = 8.5$  Hz), 7.78 (2H, d,  $J = 8.5$  Hz), 7.63 (2H, s), 7.54 (2H, t,  $J = 8.5$  Hz), 7.49 (2H, d,  $J = 8.5$  Hz), 7.36 (2H, d,  $J = 8.5$  Hz), 7.30 (2H, t,  $J = 8.5$  Hz), 7.21 (4H, d,  $J = 8.5$  Hz), 7.09 (2H, t,  $J = 8.5$  Hz), 7.05-6.96 (8H, m), 6.61 (2H, d,  $J = 8.5$  Hz), 4.79 (2H, d,  $J = 13.0$  Hz), 4.38 (2H, d,  $J = 13.0$  Hz), 2.79 (6H, s), O-H proton was not found probably due to broadening;  $^{13}C$  NMR analysis gave broad spectrum and it was not assignable; IR (KBr): 3374, 3052, 1686, 1601, 1421, 1200, 1030, 819, 767, 704  $cm^{-1}$ ; HRMS (FAB) Calcd for  $C_{56}H_{44}NO_2^+$  ( $[M+H]^+$ ) 762.3372. Found 762.3366.

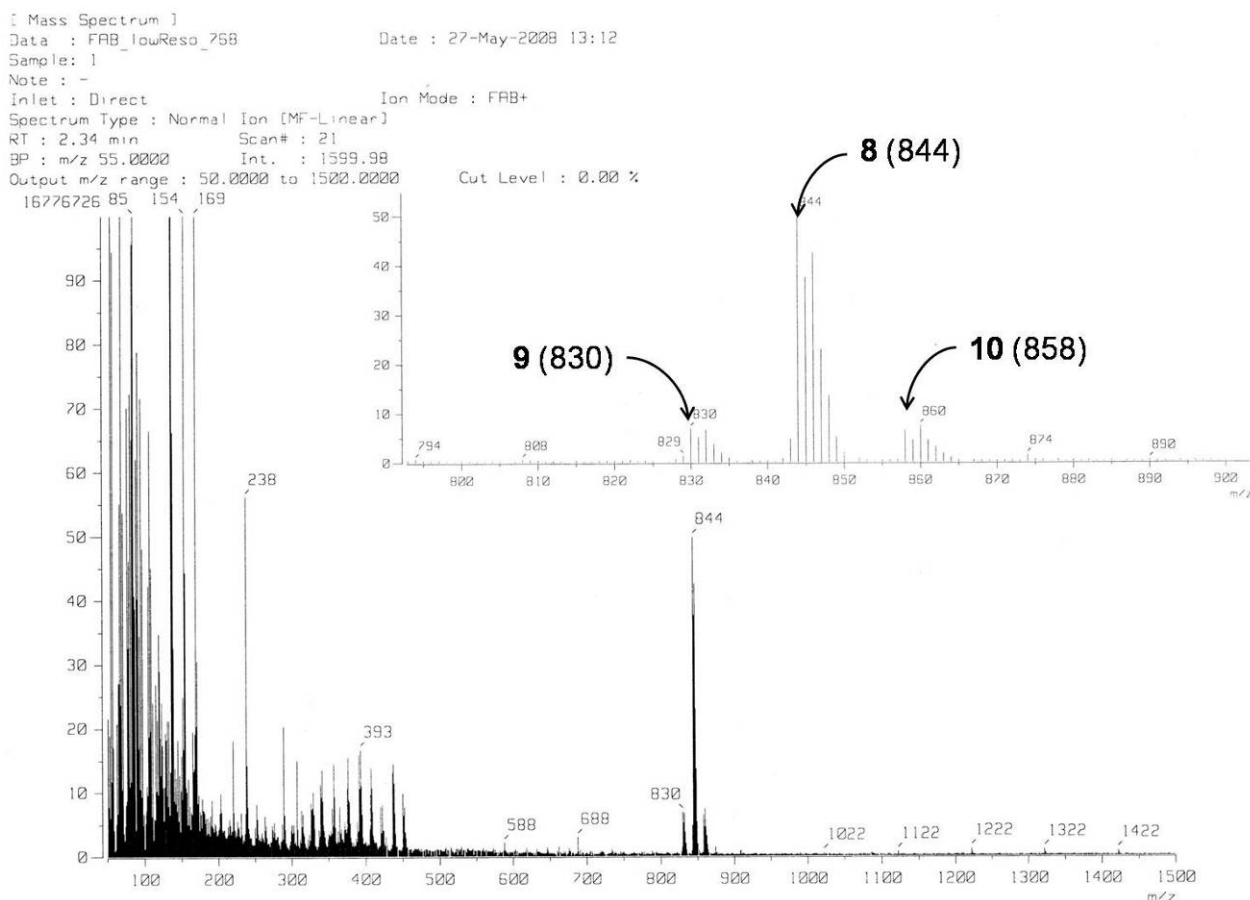
**3d:**  $^1H$  NMR (500 MHz,  $(CD_3)_2CO$ )  $\delta$  8.10 (1H, br), 7.97 (1H, br), 7.95 (1H, brd,  $J = 7.5$  Hz), 7.87 (2H, br), 7.80 (2H, br), 7.69 (1H, br), 7.64 (1H, br), 7.59 (2H, br), 7.45 (3H, br), 7.24 (1H, br), 7.14 (3H, br), 7.03 (5H, br), 6.90 (6H, br), 6.45 (1H, br), 5.18 (1H, br), 4.91 (1H, d,  $J = 13.5$  Hz), 4.71 (1H, br), 4.70 (1H, d,  $J = 13.5$  Hz), 3.15 (3H, brs), 2.35 (3H, s), O-H proton was not found probably due to broadening;  $^{13}C$  NMR analysis gave broad spectrum and it was not assignable; IR (KBr): 3435, 3054, 1611, 1494, 1469, 1424, 1005, 849, 791, 748  $cm^{-1}$ ; HRMS (FAB) Calcd for  $C_{56}H_{42}Cl_2NO_2^+$  ( $[M+H]^+$ ) 830.2593. Found 830.2592.  $[\alpha]_D^{25} -104.1$  ( $c = 0.36$ , MeOH).

In order to obtain compelling evidence to support the betaine structure of **3d**, we performed the direct monomethylation of **3d** as shown below.

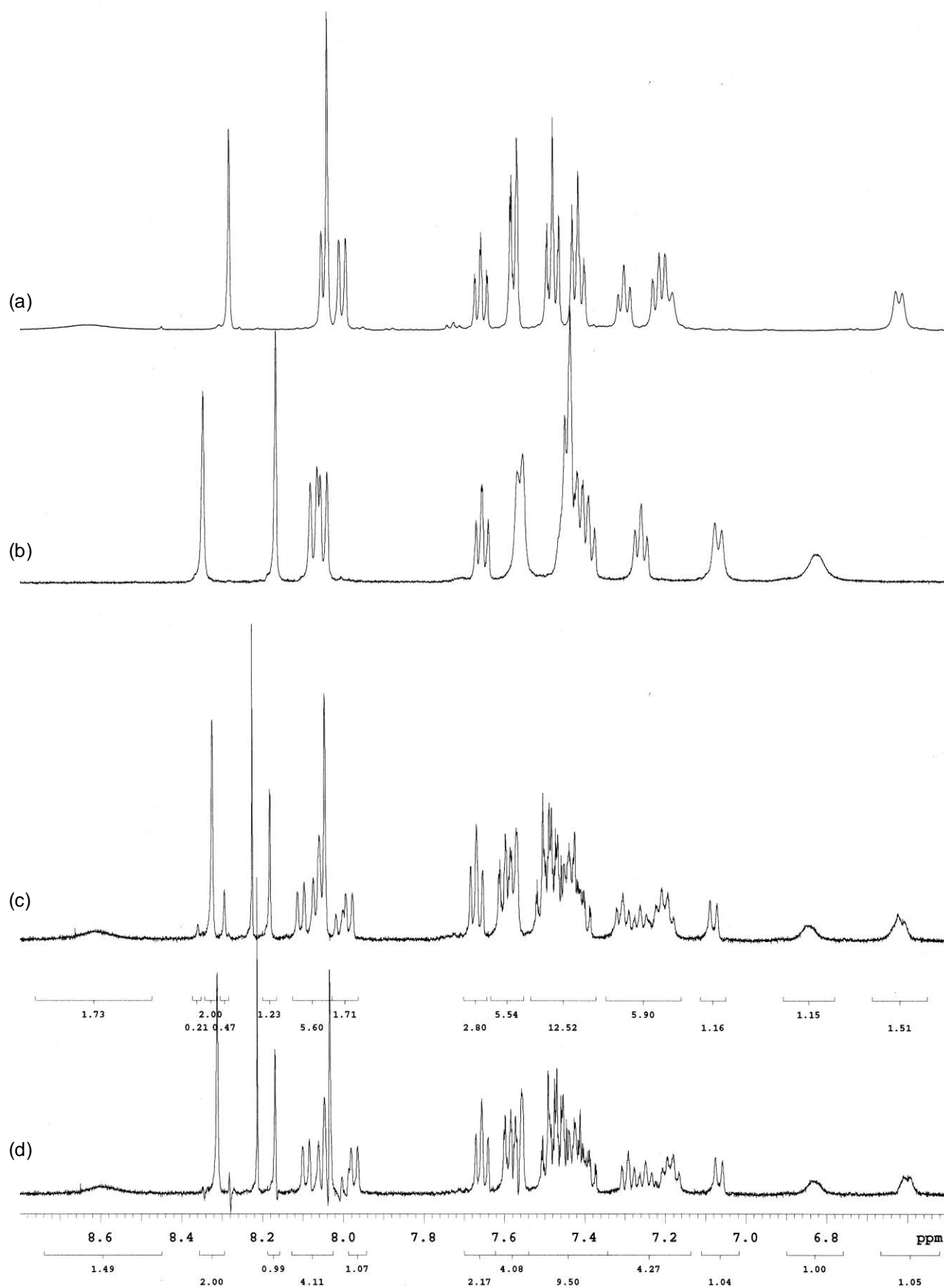


**Direct Monomethylation of Ammonium Betaine **3d**:** To a solution of methyl trifluoromethanesulfonate (17  $\mu\text{L}$ , 0.15 mmol) in 100  $\mu\text{L}$  of  $\text{CH}_2\text{Cl}_2$  was added a solution of **3d** (11.0 mg, 0.013 mmol) in 400  $\mu\text{L}$  of  $\text{CH}_2\text{Cl}_2$  dropwise at  $0^\circ\text{C}$ . The reaction mixture was stirred for 3 h and poured into ice-cooled water. Extractive workup was performed with chloroform and the organic phase was dried over  $\text{Na}_2\text{SO}_4$ . Purification on silica gel column chromatography gave a mixture of ammonium salts (10.9 mg).

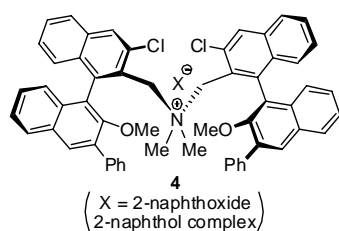
FAB-MS spectrum (Chart S1) of the mixture showed one major peak corresponding to **8** ( $m/z = 844$ ) and two minor peaks corresponding to **9** ( $m/z = 830$ ), **10** ( $m/z = 858$ ), respectively. This result clearly indicated the predominant presence of ammonium betaine **3d** in the solution used for the reaction. Further information was obtained from  $^1\text{H}$  NMR spectra taking at  $100^\circ\text{C}$  (Chart S2) and the ratio of ammonium salts was assigned to be **8/9/10** = 75/17/8. **8**:  $^1\text{H}$  NMR (500 MHz,  $(\text{CD}_3)_2\text{SO}$ ,  $100^\circ\text{C}$ )  $\delta$  8.60 (1H, br), 8.31 (2H, s), 8.17 (1H, s), 8.09 (1H, d,  $J = 8.5$  Hz), 8.05 (1H, d,  $J = 8.5$  Hz), 8.04 (1H, d,  $J = 8.5$  Hz), 8.03 (1H, s), 7.97 (1H, d,  $J = 8.5$  Hz), 7.66 (2H, t,  $J = 8.5$  Hz), 7.60-7.56 (4H, m), 7.51-7.37 (9H, m), 7.29 (1H, t,  $J = 8.5$  Hz), 7.25 (1H, t,  $J = 8.5$  Hz), 7.22-7.16 (2H, m), 7.07 (1H, d,  $J = 8.5$  Hz), 6.84 (1H, br), 6.61 (1H, br), 4.82-4.68 (2H, m), 4.60 (2H, br), 2.79 (6H, s), 2.64 (3H, s).



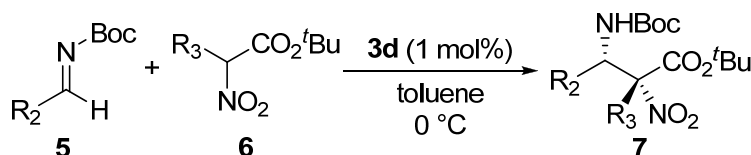
**Chart S1.** FAB-MS (NBA) spectrum.



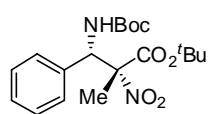
**Chart S2.** Expansion of aromatic region of  $^1\text{H}$  NMR (500 MHz,  $(\text{CD}_3)_2\text{SO}$ ,  $100^\circ\text{C}$ ) spectra of ammonium salts. (a)  $^1\text{H}$  NMR spectrum of **9**. (b)  $^1\text{H}$  NMR spectrum of **10**. (c)  $^1\text{H}$  NMR spectrum of a mixture of **8**, **9**, and **10**. (d) Expecting  $^1\text{H}$  NMR spectrum of **8**, which was made by subtraction of spectrum  $\{(c)-(a)-(b)\}$ .



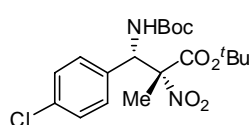
**4:** Prepared from the corresponding ammonium hydroxide according to the literature procedure.<sup>4</sup> Although NMR analysis gave broad spectrum at room temperature, it can be improved at 100 °C. <sup>1</sup>H NMR (500 MHz, (CD<sub>3</sub>)<sub>2</sub>SO, 100 °C)  $\delta$  8.34 (2H, s), 8.16 (2H, s), 8.07 (2H, d,  $J$  = 8.5 Hz), 8.05 (2H, d,  $J$  = 8.5 Hz), 7.69 (2H, d,  $J$  = 8.5 Hz), 7.66 (2H, d,  $J$  = 8.5 Hz), 7.65<sub>5</sub> (2H, t,  $J$  = 8.5 Hz), 7.61-7.54 (6H, m), 7.47-7.37 (10H, m), 7.32 (2H, t,  $J$  = 8.5 Hz), 7.26 (2H, t,  $J$  = 8.5 Hz), 7.17 (2H, t,  $J$  = 8.5 Hz), 7.08 (2H, d,  $J$  = 8.5 Hz), 7.05 (2H, d,  $J$  = 8.5 Hz), 7.04 (2H, s), 6.83 (2H, br), 4.88 (2H, b), 4.74 (2H, d,  $J$  = 13.5 Hz), 2.81 (6H, s), 2.59 (6H, s); <sup>13</sup>C NMR (126 MHz, (CD<sub>3</sub>)<sub>2</sub>SO, 100 °C)  $\delta$  137.0, 133.9, 132.0<sub>3</sub>, 131.9<sub>7</sub>, 130.9, 130.1, 129.9, 129.4, 128.5<sub>3</sub>, 128.4<sub>5</sub>, 128.3<sub>8</sub>, 128.3<sub>1</sub>, 127.8, 127.2, 127.0, 126.8<sub>8</sub>, 126.8<sub>2</sub>, 126.6, 126.1, 125.8, 125.7, 125.4, 125.1, 124.6, 124.3, 123.3, 121.9, 118.1, 108.3, 65.2, 59.5, 50.8, five carbons were not found; IR (KBr): 3056, 1627, 1496, 1459, 1402, 1220, 901, 849, 750 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>58</sub>H<sub>46</sub>Cl<sub>2</sub>NO<sub>2</sub><sup>+</sup> ([M-(2-naphthoxide·2-naphthol)]<sup>+</sup>) 858.2906. Found 858.2911.



**Representative Procedure for Catalytic Asymmetric Mannich-type Reaction of  $\alpha$ -Nitrocarboxylates:** To a dried test tube was weighed betaine **3d** (0.01 equiv., 2  $\mu$ mol) under an argon atmosphere. The catalyst was dissolved into 400  $\mu$ L of toluene at room temperature. *tert*-Butyl 2-nitropropionate (**6a**, 1.0 equiv., 0.2 mmol) was added at 0 °C. Benzaldehyde-derived *N*-Boc imine **5a** (1.1 equiv., 0.22 mmol) was introduced dropwise and the stirring was continued for the indicated time under the conditions. The reaction mixture was poured into ice-cooled 1 N aqueous HCl and the aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and filtered. All volatiles were removed by evaporation and the diastereomeric ratio was determined by <sup>1</sup>H NMR analysis of the crude residue. Purification of the residue by column chromatography on silica gel gave **7a** as a mixture of diastereomers (97%, *syn:anti* = 3.9:1), whose enantiomeric excesses were determined by HPLC analysis (*syn/anti* = 99% ee/93% ee).



**7a:** AD-H, Hexane (H)/Isopropyl alcohol (IPA) = 10:1, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 11.8 min (major *anti* isomer; (2*S*,3*S*)), 13.2 min (major *syn* isomer; (2*R*,3*S*)), 18.5 min (minor *syn* isomer; (2*S*,3*R*)), 19.3 min (minor *anti* isomer; (2*R*,3*R*)). Absolute and relative configurations were determined by comparison with literature data after derivatization.<sup>5</sup> <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.38-7.28 (3H, m), 7.26-7.22 (2H, m), 6.57 (1H, d,  $J$  = 10.5 Hz), 5.38 (1H, d,  $J$  = 10.5 Hz), 1.71 (3H, s), 1.53 (9H, s), 1.41 (9H, s); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  165.5, 154.7, 135.5, 128.8, 128.4, 96.6, 85.3, 80.2, 59.0, 28.5, 27.8, 21.7, one carbon was not found probably due to overlapping; IR (KBr): 3452, 2978, 1742, 1583, 1556, 1370, 1352, 1314, 754, 704 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>19</sub>H<sub>29</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup> ([M+H]<sup>+</sup>) 381.2026. Found 381.2042.

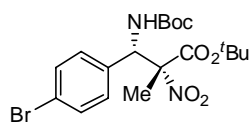


**7b:** AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 14.4 min (major *anti* isomer), 15.5 min (major *syn* isomer), 28.0 min (minor *anti* isomer), 29.7 min (minor *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.31 (2H, d,  $J$  = 8.5 Hz), 7.19 (2H, d,  $J$  = 8.5 Hz), 6.54 (1H, d,  $J$  = 10.0 Hz), 5.35 (1H, d,

<sup>4</sup> Tozawa, T.; Nagao, H.; Yamane, Y.; Mukaiyama, T. *Chem. Asian J.* **2007**, *2*, 123.

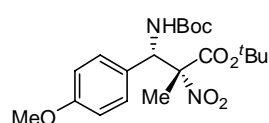
<sup>5</sup> Chen, Z.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 2170.

$J = 10.0$  Hz), 1.71 (3H, s), 1.52 (9H, s), 1.41 (9H, s);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.3, 154.6, 134.9, 134.0, 129.8, 129.0, 96.4, 85.6, 80.5, 58.4, 28.4, 27.8, 21.6; IR (liq. film): 3453, 2980, 2934, 1746, 1714, 1596, 1557, 1370, 1346, 844,  $759\text{ cm}^{-1}$ ; HRMS (FAB) Calcd for  $\text{C}_{19}\text{H}_{28}\text{ClN}_2\text{O}_6^+$  ( $[\text{M}+\text{H}]^+$ ) 415.1636. Found 415.1653.



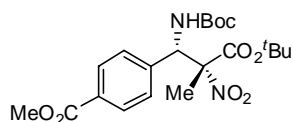
**7c:** AD-H, H/Ethanol (EtOH) = 30:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 12.8 min (major *anti* isomer), 15.3 min (major *syn* isomer), 22.9 min (minor *anti* isomer), 37.6 min (minor *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (2H, d,  $J = 8.5$  Hz), 7.13 (2H, d,  $J = 8.5$  Hz), 6.53 (1H, d,  $J = 10.0$  Hz), 5.33 (1H, d,  $J = 10.0$  Hz), 1.70 (3H, s), 1.52 (9H, s), 1.40 (9H, s);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.2, 154.6, 134.6, 132.0, 130.1, 123.1, 96.4, 85.6, 80.5, 58.5, 28.4, 27.8, 21.6; IR (liq. film): 3454, 2979, 2933, 1746, 1715, 1557, 1487, 1369, 1346, 1166, 1011,  $843\text{ cm}^{-1}$ ; HRMS (FAB) Calcd for  $\text{C}_{19}\text{H}_{28}\text{BrN}_2\text{O}_6^+$  ( $[\text{M}+\text{H}]^+$ ) 459.1131. Found 459.1122.



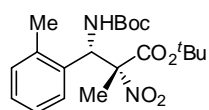
**7d:** AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 14.7 min (major *anti* isomer), 16.2 min (major *syn* isomer), 28.4 min (minor *anti* isomer), 30.7 min (minor *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.16 (2H, d,  $J = 9.0$  Hz), 6.84 (2H, d,  $J = 9.0$  Hz), 6.51 (1H, d,  $J = 10.0$  Hz), 5.32 (1H, d,  $J = 10.0$  Hz), 3.78 (3H, s), 1.69 (3H, s), 1.52 (9H, s), 1.40 (9H, s);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.2, 160.4, 155.2, 130.1, 128.0, 114.7, 97.4, 85.8, 80.7, 59.1, 55.9, 29.0, 28.3, 22.2; IR (liq. film): 3458, 2979, 2935, 1745, 1721, 1584, 1557, 1486, 1254, 1166,  $845\text{ cm}^{-1}$ ; HRMS (FAB) Calcd for  $\text{C}_{20}\text{H}_{31}\text{N}_2\text{O}_7^+$  ( $[\text{M}+\text{H}]^+$ ) 411.2131. Found 411.2124.



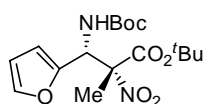
**7e:** AD-H, H/IPA = 3:1, flow rate = 1.0 mL/min,  $\lambda = 210$  nm, 5.8 min (major *anti* isomer), 8.3 min (major *syn* isomer), 13.9 min (minor *syn* isomer), 24.8 min (minor *anti* isomer). Absolute and relative configurations were assigned on the analogy of **7a**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (2H, d,  $J = 9.0$  Hz), 7.34 (2H, d,  $J = 9.0$  Hz), 6.58 (1H, d,  $J = 10.0$  Hz), 5.44 (1H, d,  $J = 10.0$  Hz), 3.91 (3H, s), 1.72 (3H, s), 1.53 (9H, s), 1.40 (9H, s);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 165.2, 154.6, 140.4, 130.7, 130.0, 128.5, 96.3, 85.6, 80.5, 58.8, 52.3, 28.4, 27.8, 21.6; IR (liq. film): 3454, 2980, 1726, 1558, 1486, 1370, 1347, 1283, 1166, 843,  $734\text{ cm}^{-1}$ ; HRMS (FAB) Calcd for  $\text{C}_{21}\text{H}_{31}\text{N}_2\text{O}_8^+$  ( $[\text{M}+\text{H}]^+$ ) 439.2080. Found 439.2080.



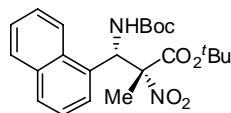
**7f:** AD-H, H/IPA/EtOH = 98:1:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 11.5 min (major *anti* isomer), 14.1 min (minor *anti* isomer), 14.8 min (minor *syn* isomer), 16.3 min (major *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23-7.12 (3H, m), 7.08 (1H, d,  $J = 7.5$  Hz), 6.54 (1H, d,  $J = 10.0$  Hz), 5.84 (1H, d,  $J = 10.0$  Hz), 2.52 (3H, s), 1.63 (3H, s), 1.53 (9H, s), 1.40 (9H, s);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.6, 154.8, 136.9, 134.9, 130.9, 128.5, 127.2, 126.3, 97.2, 85.2, 80.0, 53.6, 28.5, 27.7, 20.5, 20.2; IR (liq. film): 3457, 2979, 2933, 1746, 1717, 1558, 1486, 1369, 1256, 842,  $734\text{ cm}^{-1}$ ; HRMS (FAB) Calcd for  $\text{C}_{20}\text{H}_{31}\text{N}_2\text{O}_6^+$  ( $[\text{M}+\text{H}]^+$ ) 395.2182. Found 395.2184.



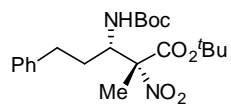
**7g:** AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 10.2 min (major *anti* isomer), 11.2 min (major *syn* isomer), 12.8 min (minor *anti* isomer), 15.3 min (minor *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**.

CDCl<sub>3</sub>)  $\delta$  7.33 (1H, brd,  $J$  = 2.0 Hz), 6.32 (1H, dd,  $J$  = 3.5, 2.0 Hz), 6.30 (1H, brd,  $J$  = 3.5 Hz), 6.23 (1H, d,  $J$  = 10.5 Hz), 5.56 (1H, d,  $J$  = 10.5 Hz), 1.79 (3H, s), 1.50 (9H, s), 1.43 (9H, s); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  164.9, 154.7, 149.5, 142.9, 110.7, 109.4, 95.8, 85.4, 80.5, 53.3, 28.4, 27.7, 21.0; IR (KBr): 3449, 2982, 2938, 1721, 1561, 1491, 1394, 1369, 1302, 1234, 1143, 840 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>17</sub>H<sub>27</sub>N<sub>2</sub>O<sub>7</sub><sup>+</sup> ([M+H]<sup>+</sup>) 371.1818. Found 371.1828.



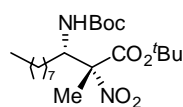
**7h:** OD-H, H/EtOH = 49:1, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 8.8 min (minor *anti* isomer), 9.3 min (major *syn* isomer), 10.0 min (minor *syn* isomer), 10.8 min (major *anti* isomer). Absolute and relative configurations were assigned on the analogy of **7a**. <sup>1</sup>H

NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.28 (1H, d,  $J$  = 8.0 Hz), 7.86 (1H, d,  $J$  = 8.0 Hz), 7.82 (1H, d,  $J$  = 8.0 Hz), 7.59 (1H, t,  $J$  = 8.0 Hz), 7.50 (1H, t,  $J$  = 8.0 Hz), 7.43 (1H, t,  $J$  = 8.0 Hz), 7.38 (1H, d,  $J$  = 8.0 Hz), 6.75 (1H, d,  $J$  = 9.5 Hz), 6.54 (1H, d,  $J$  = 9.5 Hz), 1.56 (9H, s), 1.44 (3H, s), 1.39 (9H, s); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 154.8, 133.7, 132.7, 132.1, 129.4, 129.2, 127.1, 126.0, 125.8, 124.9, 123.0, 97.8, 85.4, 80.2, 52.3, 28.5, 27.8, 21.6; IR (liq. film): 3455, 2979, 2933, 1746, 1714, 1557, 1486, 1370, 1258, 1166, 846 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>23</sub>H<sub>30</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup> ([M]<sup>+</sup>) 430.2104. Found 430.2105.



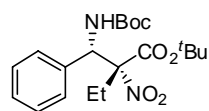
**7i:** AD-H, H/EtOH = 30:1, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 10.0 min (major *syn* isomer), 11.5 min (major *anti* isomer), 12.1 min (minor *anti* isomer), 14.6 min (minor *syn* isomer).

Absolute and relative configurations were assigned on the analogy of **7a**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.32-7.27 (2H, m), 7.22-7.16 (3H, m), 5.53 (1H, d,  $J$  = 11.0 Hz), 4.35 (1H, td,  $J$  = 11.0, 2.5 Hz), 2.79-2.73 (1H, m), 2.68-2.61 (1H, m), 1.91-1.83 (1H, m), 1.75 (3H, s), 1.67-1.59 (1H, m), 1.47 (9H, s), 1.46 (9H, s); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  165.5, 155.6, 141.1, 128.6, 128.5, 126.3, 96.8, 85.0, 80.0, 55.1, 33.1, 32.4, 28.5, 27.7, 21.1; IR (liq. film): 3453, 2979, 2933, 1745, 1721, 1604, 1556, 1495, 1369, 1346, 1167, 842 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>21</sub>H<sub>33</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup> ([M+H]<sup>+</sup>) 409.2339. Found 409.2321.



**7j:** AD-H, H/IPA = 49:1, flow rate = 0.5 mL/min,  $\lambda$  = 254 nm, 9.4min (major *syn* isomer), 12.8 min (major *anti* isomer), 19.2 min (minor *anti* isomer), 23.9 min (minor *syn* isomer). Absolute and relative configurations were assigned on the analogy of **7a**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$

5.38 (1H, d,  $J$  = 11.0 Hz), 4.27 (1H, td,  $J$  = 11.0, 2.5 Hz), 1.80 (3H, s), 1.70-1.62 (1H, m), 1.61-1.53 (1H, m), 1.48 (9H, s), 1.44 (9H, s), 1.41-1.20 (12H, m), 0.87 (3H, t,  $J$  = 7.0 Hz); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 155.5, 97.0, 84.8, 79.7, 55.3, 31.9, 30.7, 29.5, 29.3, 29.2, 28.4, 27.7, 26.0, 22.7, 21.2, 14.2; IR (liq. film): 3453, 2927, 2856, 1747, 1722, 1556, 1493, 1369, 1345, 1169, 843 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>21</sub>H<sub>41</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup> ([M+H]<sup>+</sup>) 417.2965. Found 417.2974.



**7k:** AD-H, H/EtOH = 30:1, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 9.0 min (major *syn* isomer), 9.7 min (major *anti* isomer), 10.9 min (minor *anti* isomer), 12.7 min (minor *syn* isomer).

Absolute and relative configurations were assigned on the analogy of **7a**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.37-7.28 (3H, m), 7.23-7.16 (2H, m), 6.55 (1H, d,  $J$  = 10.5 Hz), 5.39 (1H, d,  $J$  = 10.5 Hz), 2.08 (1H, quin,  $J$  = 7.5 Hz), 1.95 (1H, quin,  $J$  = 7.5 Hz), 1.56 (9H, s), 1.42 (9H, s), 1.07 (3H, t,  $J$  = 7.5 Hz); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  164.3, 154.7, 135.7, 128.9, 127.9, 100.4, 85.3, 80.2, 59.1, 28.6, 28.5, 28.0, 9.1, one carbon was not found probably due to overlapping; IR (liq. film): 3454, 2979, 2936, 1746, 1721, 1556, 1486, 1369, 1252, 1167, 843 cm<sup>-1</sup>; HRMS (FAB) Calcd for C<sub>20</sub>H<sub>31</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup> ([M+H]<sup>+</sup>) 395.2182. Found 395.2184.



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

