Stereoselective Enol Tosylation: Preparation of Trisubstituted α,β-Unsaturated Esters

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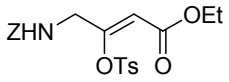
Supporting Information

Experimental: All reactions were run under an atmosphere of nitrogen using anhydrous solvents purchased from Aldrich. All reagents were purchased from Aldrich and used as received. All NMR spectra were recorded on a Bruker 400 MHz instrument in $CDCl_3$ unless otherwise noted. Elemental analyses were performed by QTI, Quantitative Technologies, Inc.

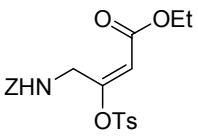


3a

Enol Tosylate **3a**: *n*-BuLi (39.3 mmol, 5.5 mL) was added to a solution of beta-keto ester (36 mmol, 10g) in 100mL THF at -70 °C. After stirring for two hours at -70 °C, Ts_2O (43.0 mmol, 14.0 g) was added in one portion and the solution stirred for 12 hours. 100 mL isopropyl acetate and 20mL H_2O were added and after the phase cut, the aqueous layer was extracted with 2 x 50mL isopropyl acetate. The organic layer was then washed with 2 x 25mL of 1.0 N NaOH, and 2 x 50 mL of brine. The organic layer was dried over $MgSO_4$ and treated with KB-B Darco (1 g), and filtered through Solka Floc. The filtrate was concentrated to approximately 50 mL and then heptane (350 mL) was added slowly. The resulting slurry was cooled to 5 °C, filtered, and washed with chilled 7:1 heptane/isopropyl acetate (2 x 50 mL). A total of 10.0 g was isolated (65 % yield). ^{1}H NMR δ 7.90 (d, 2H, J = 8.0 Hz), 7.33 (m, 7H), 5.76 (s, 1H), 5.40 (s, 1H), 5.10 (s, 2H), 4.05 (m, 4H), 2.44 (s, 3H), 1.19 (t, 3H, J = 7.0 Hz) ppm; ^{13}C NMR δ 14.0, 21.7, 43.6, 60.6, 67.2, 111.2, 128.1, 128.3, 128.5, 128.6, 129.8, 132.6, 136.1, 145.8, 155.0, 156.0, 162.6. Anal. Calcd for $C_{21}H_{23}NSO_7$: C, 58.19; H, 5.35; N, 3.23. Found: C, 58.23; H, 5.13; N, 3.15.

J = 7.0 Hz) ppm; ^{13}C NMR δ 14.0, 21.7, 43.6, 60.6, 67.2, 111.2, 128.1, 128.3, 128.5, 128.6, 129.8, 132.6, 136.1, 145.8, 155.0, 156.0, 162.6. Anal. Calcd for $C_{21}H_{23}NSO_7$: C, 58.19; H, 5.35; N,3.23. Found: C, 58.23; H, 5.13; N, 3.15.

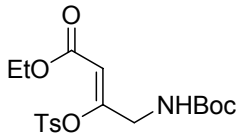
nOe (d_6-acetone): 0.8% nOe from vinyl CH to CH_2, 0.5% nOe from CH_2 to vinyl CH.



4a

Enol Tosylate **4a**: Et_3N (39.4 mmol, 5.5 mL) was added to beta-keto ester **1a** (36 mmol, 10g) in 100mL

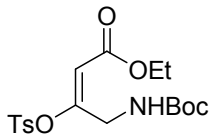
CH_2Cl_2 at 0 °C. After stirring for one hour the solution was warmed to RT and then Ts_2O (39.4 mmol, 12.9 g) added in one portion. The solution was stirred for 12 hours. The solution was then evaporated and 100mL isopropyl acetate and 50mL H_2O added. After the phase cut, the organic layer was washed with 2 x 50mL of 1.0 N NaOH, and 2 x 50 mL of brine. The organic layer was dried over $MgSO_4$ and treated with KB-B Darco (1 g), and filtered through Solka Floc. The filtrate was concentrated to approximately 50 mL and then heptane (350 mL) was added slowly. The resulting slurry was cooled to 5 °C, filtered, and washed with chilled 7:1 heptane/isopropyl acetate (2 x 50 mL). A total of 12.4 g was isolated (83% yield). ^{1}H NMR δ 7.80 (d, 2H, *J* = 8.0 Hz), 7.33 (m, 7H), 5.94 (s, 1H), 5.23 (s, 1H), 5.08 (s, 2H), 4.38 (d, 2H, *J* = 6.4 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 2.44 (s, 3H), 1.28 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 14.1, 21.7, 40.8, 61.0, 66.9, 111.9, 128.0, 128.1, 128.3, 128.5, 130.0, 132.3, 136.3, 146.0, 156.0, 160.1, 164.9. Anal. Calcd for $C_{21}H_{23}NSO_7$: C, 58.19; H, 5.35; N,3.23. Found: C, 58.3; H, 5.17; N, 3.3.



3b

Enol Tosylate **3b**: β-keto ester **1b** (203.4 mmol, 50 g) was dissolved in 600 mL of THF and cooled to -50 °C. LDA (2 M solution in THF/ethylbenzene/heptane, 1.05 eq., 101.5 mL) was added via addition funnel keeping the temperature below -48 °C. Reaction aged for 3 hours at -50 °C followed by the addition of Ts_2O (264 mmol, 86.5 g) in one portion. The resulting reaction mixture was stirred at -50 °C for 1 hour and then allowed to warm to room temperature overnight. The reaction mixture was cooled to 5 °C followed by the addition of 500 mL of isopropyl acetate and 500 mL of saturated $NaHCO_3$. The aqueous layer was separated. The organic layers were combined and washed with 2 x 200 mL of 1N NaOH and 2 x 200 mL of brine. The organic layer was dried over $MgSO_4$ and treated with 10 g of KB-B Darco and filtered. The filtrate was concentrated to approximately 250 mL followed by the slow addition of 250 mL of heptane. After about 50 mL of the heptane was added, a significant seed bed was formed. The solution was stirred for 1 hr at room temperature to maximize the seed bed before the remaining 200 mL of heptane was added. The mixture was cooled to 5 °C, stirred for 1 hr, filtered, and rinsed with 2 x 75 ml of 5:1 heptane:isopropyl acetate to afford 55.1 grams of a white solid (68% isolated yield). ^{1}H NMR δ 7.90 (d, 2H, *J* = 8.4 Hz), 7.36 (d, 2H, *J* = 8.4 Hz), 5.74 (s, 1H), 5.02 (s, 1H), 4.04 (q, 2H, *J* = 7.2 Hz), 3.98 (d, 2H, *J* = 6.4 Hz), 2.45 (s, 3H), 1.44 (s, 9H), 1.20 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 14.1, 21.8, 28.4, 43.4, 60.6, 80.3, 110.9, 128.6, 129.8, 132.9, 145.8, 155.6, 162.7. Anal. Calcd for $C_{18}H_{25}NO_7S$: C, 54.12; H, 6.31; N, 3.51. Found: C, 54.28; H, 6.29; N, 3.44.

nOe ($CDCl_3$): 2.3% nOe from vinyl CH to CH_2; 1.7% nOe from CH_2 to vinyl CH; 0.8% nOe from CH_2 to aromatic CH.

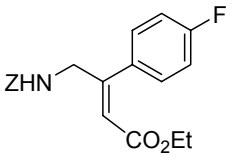


4b

Enol Tosylate **4b**: Et_3N (32.8 mmol, 4.6 mL) was added to beta-keto ester **1b** (32.1 mmol, 7.88g) and Ts_2O (32.8 mmol, 10.71 g) in 100mL CH_2Cl_2 at 0 °C. The solution was warmed to RT and then stirred for 1.5 hours. The solution was then concentrated to 20 mL and 50 mL EtOAc added. The solution was washed with 2 x 50 mL saturated aqueous $NaHCO_3$ solution. After the phase cut, the organic layer was dried over Na_2SO_4, treated with KB-B Darco (1 g), and filtered through Solka Floc. The filtrate was concentrated to approximately 15 mL and then hexane (25 mL) was added slowly. The resulting slurry was cooled to 5 °C, filtered, and washed with chilled 5:1 hexanes:EtOAc. A total of 9.63 g was isolated (75% yield). ^{1}H NMR δ 7.85 (d, 2H, *J* = 8.3 Hz), 7.38 (d, 2H, *J* = 8.2 Hz), 5.89 (s, 1H), 4.95 (s, 1H), 4.32 (d, 2H, *J* = 5.2), 4.18 (q, 2H, *J* = 7.2 Hz), 2.47 (s, 3H), 1.42 (s, 9H), 1.28 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 14.0, 21.6, 28.2, 40.3, 60.9, 111.4, 128.2, 129.9, 132.3, 145.9, 160.5, 164.8. Anal. Calcd for $C_{18}H_{25}NO_7S$: C, 54.12; H, 6.31; N, 3.51. Found: C, 53.97; H, 6.27; N, 3.53

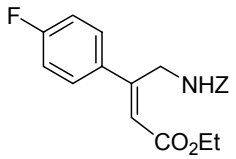
General Procedure for Suzuki Coupling

A Schlenk flask was charged with enol tosylate (0.5 g, 1.15 mmol), aryl boronic acid (1.73 mmol, 1.5 equiv.), and $PdCl_2(PPh_3)_2$ (5 mol%, 0.06 mmol). THF (8 mL) was added followed by 2 M Na_2CO_3 (1.8 mL, 3.68 mmol) and the flask was evacuated and backfilled with N_2 three times. The resulting reaction was stirred overnight at 40 °C under N_2. HPLC of the reaction mixture indicated complete conversion. The mixture was cooled to room temperature and 10 mL of isopropyl acetate was added followed by 5 mL of $NaHCO_3$ (saturated aqueous solution) and 5 mL of water. After the phase cut, the aqueous layer was extracted with 2 x 10 mL of isopropyl acetate. The organic layers were washed with 2 x 10mL of 0.5 N NaOH, and 2 x 10 mL of brine. The organic layer was dried over $MgSO_4$ and treated with KB-B Darco (50 mg), and filtered through Solka Floc. Evaporation and chromatography on silica gel with the indicated solvent system afforded the product.

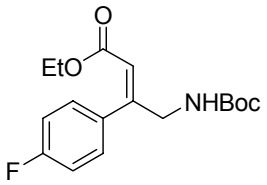


Compound 1-*E*: Isolated in 76% yield after SiO_2 chromatography from 4:1 (hexanes:EtOAc). ^{1}H NMR δ 7.35 (m, 5H), 7.19 (m, 2H), 7.05 (t, 2H, *J*= 8.5 Hz), 6.01 (s, 1H), 5.13 (s, 2H), 5.09 (s, 1H), 4.08 (d, 2H, *J* = 5.8 Hz), 4.01 (q, 2H, *J* = 7.1 Hz), 1.11 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 13.9, 47.8, 60.1, 67.1, 115.0, 115.3, 117.4, 128.1, 128.3, 128.6, 129.3, 129.4, 133.2, 136.2, 153.7, 156.1, 161.4, 163.9, 165.5. ^{19}F NMR δ -114. Anal. Calcd for $C_{20}H_{20}FNO_4$: C, 67.22; H, 5.64; N, 3.92. Found: C, 67.23; H, 5.48; N, 3.79.

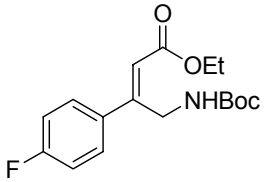
nOe (d6-acetone): 0.5% nOe from vinyl CH to CH2, 1.3% nOe from CH2 to vinyl CH.



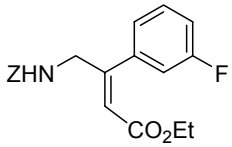
Compound 1-*Z*: Isolated in 72% yield after SiO_2 chromatography from 14:1 (toluene:EtOAc). ^{1}H NMR δ 7.68 (m, 2H), 7.34 (m, 5H), 7.08 (t, 2H, *J*= 8.6 Hz), 6.17 (s, 1H), 5.90 (s, 1H), 5.11 (s, 2H), 4.58 (d, 2H, *J* = 4.6 Hz), 4.23 (q, 2H, *J* = 7.1 Hz), 1.33 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.2, 40.9, 60.6, 66.8, 115.6, 115.8, 119.4, 128.0, 128.1, 128.2, 128.5, 129.3, 135.4, 136.5, 155.6, 156.2, 162.4, 164.8, 166.5. ^{19}F NMR δ -112. Anal. Calcd for $C_{20}H_{20}FNO_4$: C, 67.22; H, 5.64; N, 3.92. Found: C, 67.38; H, 5.52; N, 3.76.
nOe (CDCl3): 1.2 % nOe from vinyl CH to aromatic CH.



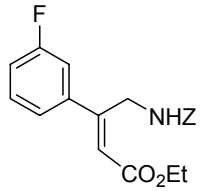
Compound 2-*E*: Isolated in 91% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.18 (m, 2H), 7.05 (m, 2H), 5.99 (s, 1H), 4.83 (s, 1H), 4.01 (m, 4H), 1.44 (s, 9H), 1.10 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 60.0, 114.9, 115.1, 129.2, 129.2, 133.4, 133.4, 154.3, 161.3, 165.5. ^{19}F NMR δ -114.2. Anal. Calcd for $C_{17}H_{22}FNO_4$: C, 63.14; H, 6.86; N, 4.33. Found: C, 63.22; H, 6.87; N, 4.32.
nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



Compound 2-*Z*: Isolated in 61% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.65 (m, 2H), 7.07 (m, 2H), 6.14 (s, 1H), 5.53 (s, 1H), 4.51 (d, 2H, *J* = 6.7 Hz), 4.23 (q, 2H, *J* = 7.1 Hz), 1.41 (s, 9H), 1.32 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 14.1, 28.3, 40.2, 60.4, 79.3, 115.4, 115.6, 119.2, 129.1, 129.2, 155.5, 155.8, 162.2, 166.4. ^{19}F NMR δ -112.9. Anal. Calcd for $C_{17}H_{22}FNO_4$: C, 63.14; H, 6.86; N, 4.33. Found: C, 63.01; H, 6.92; N, 4.28.
nOe ($CDCl_3$): 2% nOe from vinyl CH to aromatic CH.

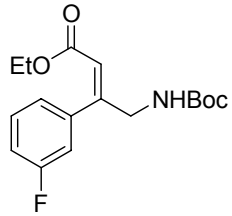


Compound 3-*E*: Isolated in 72% yield after SiO_2 chromatography from 10:1 (toluene:EtOAc). ^{1}H NMR δ 7.35 (m, 6H), 7.0 (m, 3H), 6.02 (s, 1H), 5.13 (s, 2H), 5.09 (s, 1H), 4.08 (d, 2H, J = 5.7 Hz), 4.0 (q, 2H, J = 7.0 Hz), 1.09 (t, 3H, J = 7.0 Hz) ppm; ^{13}C NMR (13.9, 47.6, 60.2, 67.1, 114.5, 114.8, 115.0, 115.2, 117.7, 123.1, 123.2, 128.1, 128.3, 128.6, 129.7, 129.8, 136.2, 139.7, 153.2, 156.1, 161.2, 163.7, 165.3. 19F NMR δ -114 Anal. Calcd for $C_{20}H_{20}FNO_4$: C, 67.22; H, 5.64; N, 3.92. Found: C, 67.07; H, 5.55; N, 3.77. nOe(d6-acetone): 0.5% nOe from vinyl CH to CH_2, 1.4% nOe from CH_2 to vinyl CH.



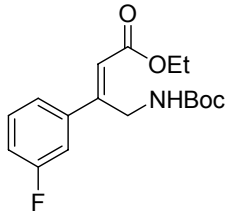
Compound 3-*Z*: Isolated in 50% yield after SiO_2 chromatography from 20:1 to 10:1 (toluene:EtOAc). ^{1}H NMR δ 7.54 (d, 1H, J = 6.7 Hz), 7.34 (m, 7H), 7.09 (t, 1H, J = 6.6 Hz), 6.21 (s, 1H), 5.86 (s, 1H), 5.11 (s, 2H), 4.58 (d, 2H, J = 6.7 Hz), 4.24 (q, 2H, J = 7.0 Hz), 1.34 (t, 3H, J = 7.2 Hz) ppm; ^{13}C NMR δ 14.1, 40.7, 60.6, 66.7, 114.1, 114.3, 116.2, 116.4, 120.5, 122.9, 127.9, 128.0, 128.4, 130.1, 130.2, 136.4, 141.5, 141.6, 155.1, 156.1, 161.5, 164.0, 166.3. ^{19}F NMR δ -113. Anal. Calcd for $C_{20}H_{20}FNO_4$: C, 67.22; H, 5.64; N, 3.92. Found: C, 67.07; H, 5.6; N, 3.9.

nOe($CDCl_3$): 1.0% nOe from vinyl CH to aromatic CH; 1.4% nOe from vinyl CH to aromatic CH.



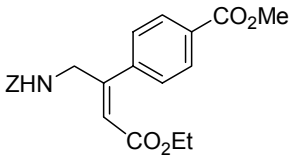
Compound 4-*E*: Isolated in 95% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.32 (m, 1H), 7.00 (m, 3H), 6.00 (s, 1H), 4.83 (s, 1H), 4.00 (m, 4H), 1.45 (s, 9H), 1.09 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 47.1, 60.0, 79.9, 114.4, 114.6, 114.7, 114.9, 117.2, 123.0, 123.1, 129.5, 129.6, 139.9, 139.9, 153.8, 155.4, 161.1, 163.5, 165.3. ^{19}F NMR δ -113.8. Anal. Calcd for $C_{17}H_{22}FNO_4$: C, 63.14; H, 6.86; N, 4.33. Found: C, 63.08; H, 6.83; N, 4.27.

nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



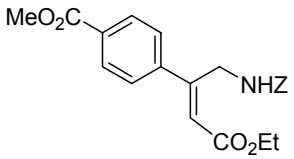
Compound 4-*Z*: Isolated in 81% yield after SiO_2 chromatography from 5:1 (hexanes:EtOAc). ^{1}H NMR δ7.44 (d, 1H, *J* = 7.5 Hz), 7.35 (m, 2H), 7.07 (m, 1H), 6.18 (s, 1H), 5.46 (s, 1H), 4.53 (d, 2H, *J* = 6.7 Hz), 4.25 (q, 2H, *J* = 7.2 Hz), 1.42 (s, 9H), 1.33 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 14.1, 28.2, 40.1, 60.5, 114.0, 114.2, 116.0, 116.2, 120.3, 122.9, 130.0, 130.1, 155.4, 161.5, 163.9. ^{19}F NMR δ -112.9. Anal. Calcd for $C_{17}H_{22}FNO_4$: C, 63.14; H, 6.86; N, 4.33. Found: C, 63.21; H, 6.94; N, 4.31.

nOe ($CDCl_3$): 1.6% nOe from vinyl CH to aromatic CH; 0.8% nOe from vinyl CH to aromatic CH.



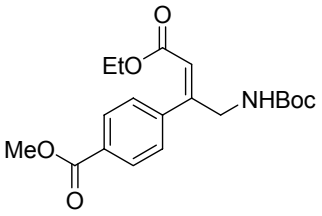
Compound 5-*E*: Isolated in 76 % yield after SiO_2 chromatography from 9:1 to 4:1 (toluene:EtOAc). ^{1}H NMR δ 8.01 (d, 2H, *J* = 8.0 Hz), 7.33 (m, 7H), 6.04 (s, 1H), 5.12 (s, 2H), 5.01 (s, 1H), 4.11 (d, 2H, *J* = 6.0 Hz), 3.99 (q, 2H, *J* = 7.0 Hz), 3.93 (s, 3H), 1.07 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 13.9, 47.6, 52.2, 60.3, 67.2, 117.9, 127.6, 128.2, 128.3, 128.6, 129.5, 129.9, 136.3, 142.6, 156.2, 165.3, 166.8. Anal. Calcd for $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.28; H, 5.77; N, 3.27.

nOe($CDCl_3$): 1.0 % nOe from vinyl CH to CH_2, 1.7 % nOe from CH_2 to vinyl CH.



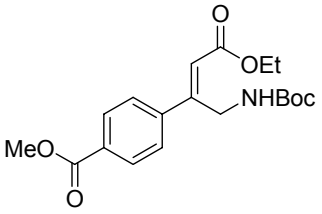
Compound 5-*Z*: Isolated in 74 % yield after SiO_2 chromatography from 4:1 to 2:1 (hexanes:EtOAc). ^{1}H NMR δ 8.05 (d, 2H, *J* = 8.3 Hz), 7.71 (d, 2H, *J* = 8.3 Hz), 7.33 (m, 5H), 6.24 (s, 1H), 5.83 (s, 1H), 5.09 (s, 2H), 4.61 (d, 2H, *J* = 6.7 Hz), 4.24 (q, 2H, *J* = 7.1 Hz), 3.94 (s, 3H), 1.34 (t, 3H, *J*= 7.2 Hz) ppm; ^{13}C NMR δ 13.9, 47.6, 52.2, 60.3, 67.2, 117.9, 127.6, 128.2, 128.3, 128.6, 129.5, 129.9, 136.3, 142.6, 156.2, 165.3, 166.8. Anal. Calcd for $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.0; H, 5.76; N, 3.42.

nOe ($CDCl_3$): 1.4 % nOe from vinyl CH to aromatic CH.



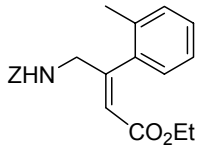
Compound 6-*E*: Isolated in 81% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.98 (d, 2H, *J* = 8.1 Hz), 7.22 (d, 2H, *J* = 7.7 Hz), 5.99 (s, 1H), 5.14 (s, 1H), 3.93 (m, 4H), 3.86 (s, 1H), 1.39 (s, 9H), 1.01 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 47.1, 52.0, 60.0, 79.7, 117.2, 127.4, 129.2, 129.5, 142.8, 154.6, 165.2, 166.2. Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.79; H, 7.02; N, 3.72.

nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



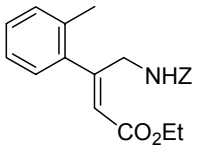
Compound 6-*Z*: Isolated in 84% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.98 (d, 2H, *J* = 8.2 Hz), 7.63 (d, 2H, *J* = 7.4 Hz), 6.16 (s, 1H), 5.47 (s, 1H), 4.51 (d, 2H, *J* = 6.6 Hz), 4.19 (q, 2H, *J* = 7.1 Hz), 3.86 (s, 3H), 1.34 (s, 9H), 1.27 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.2, 28.3, 40.1 52.1, 60.6, 79.4, 121.0, 127.2, 129.8, 130.2, 130.7, 143.9, 144.3, 155.7, 166.2, 166.5. Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.98; H, 6.86; N, 3.72.

nOe ($CDCl_3$): 4% nOe from vinyl CH to aromatic CH.



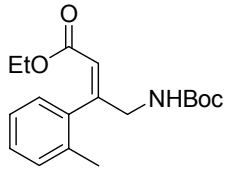
Compound 7-*E*: Isolated in 80% yield after SiO_2 chromatography from 10:1 (tol:EtOAc). ^{1}H NMR δ 7.37 (m, 5H), 7.22 (m, 3H), 6.98 (d, 1H, *J* = 7 Hz), 6.08 (s, 2H), 5.15 (m, 3H), 3.79 (m, 4H), 2.25 (s, 3H), 1.04 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 13.9, 19.1, 47.5, 59.9, 67.1, 117.2, 125.6, 126.7, 127.8, 128.2, 128.6, 129.8, 134.7, 136.3, 137.6, 155.3, 156.2, 165.2. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.10; H, 6.58; N, 4.0.

nOe($CDCl_3$): 0.4 % from vinyl CH to CH_2; 0.4% from CH_2 to vinyl CH.



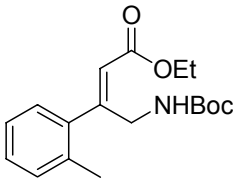
Compound 7-*Z*: Isolated in 75% yield after SiO_2 chromatography from 4:1 (hexanes:EtOAc). ^{1}H NMR δ 7.2 (m, 9H), 5.87 (s, 1H), 5.45 (s, 1H), 5.03 (s, 2H), 4.59 (d, 2H, *J* = 6.5 Hz), 4.24 (q, 2H, *J* = 7.1 Hz), 2.29 (s, 3H), 1.33 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.1, 19.8, 42.3, 60.4, 66.5, 121.3, 125.7, 127.9, 128.1, 128.3, 130.3, 134.5, 136.5, 140.0, 156.0, 157.8, 166.1. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.44; H, 6.45; N, 3.86.

nOe ($CDCl_3$): 0.2% nOe from vinyl CH to ortho-CH_3 group and 0.4 % nOe from vinyl CH to ortho-CH.group.



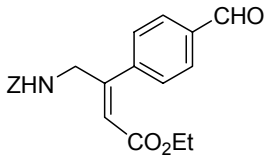
Compound 8-*E*: Isolated in 76% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.16 (m, 3H), 6.97 (d, 1H, *J* = 7.02 Hz), 6.47 (s, 1H), 6.02 (s, 1H), 3.89 (m, 4H), 2.22 (s, 3H), 1.44 (s, 9H), 0.97 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.7, 19.1, 28.3, 47.1, 59.8, 79.7, 116.8, 125.4, 126.6, 127.6, 129.6, 134.5, 137.7, 155.5, 155.8, 165.3. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.71; H, 7.98; N, 4.35.

nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



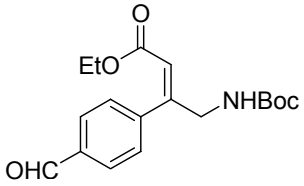
Compound 8-*Z*: Isolated in 86% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.19 (m, 3H), 7.09 (d, 1H, *J* = 7.2 Hz), 5.83 (s, 1H), 5.06 (s, 1H), 4.51 (d, 2H, *J* = 6.11 Hz), 4.23 (q, 2H, J = 7.1 Hz), 2.29 (s, 3H), 1.32 (s, 9H), 1.32 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 14.1, 19.7, 28.2, 41.7, 60.3, 79.0, 121.0, 125.5, 127.9, 130.2, 134.5, 140.1, 155.4, 158.5, 166.1. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.78; H, 7.79; N, 4.28.

nOe ($CDCl_3$): 1.9% nOe from vinyl CH to aromatic CH and 0.55% nOe from vinyl CH to CH_3.



Compound 9-*E*: Isolated in 67 % yield after SiO_2 chromatography with 10:1 to 6:1 (toluene:EtOAc). ^1H NMR δ 9.94 (s, 1H), 7.81 (d, 2H, *J* = 7.5 Hz), 7.30 (m, 7H), 6.05 (s, 1H), 5.67 (s, 1H), 5.09 (s, 2H), 4.05 (d, 2H, *J* = 5.6 Hz), 3.96 (q, 2H, *J* = 7.0 Hz), 1.05 (t, 3H, *J* = 6.9 Hz) ppm; ^{13}C NMR δ 13.8, 47.4, 60.2, 66.9, 117.8, 128.0, 128.1, 128.2, 128.5, 129.4, 135.7, 136.2, 144.3, 154.1, 156.2, 165.1, 191.8. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.61; H, 5.63; N, 3.66.

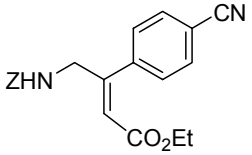
nOe($CDCl_3$): 1.4 % from vinyl CH to CH_2, 1.1% from CH_2 to vinyl CH.



Compound 10-*E*: Isolated in 97% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^1H NMR δ 10.03 (s, 1H), 7.89 (d, 2H, *J* = 8.41 Hz), 7.37 (d, 2H, *J* = 8.01 Hz), 6.06 (s, 1H), 4.81 (s, 1H), 4.05 (d, 2H, *J* = 5.02 Hz), 4.00 (q, 2H, *J* = 6.8 Hz), 1.45 (s, 9H), 1.08 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 47.1, 60.1, 107.3, 128.0, 129.4, 135.7, 144.4, 154.4, 165.1, 191.7.

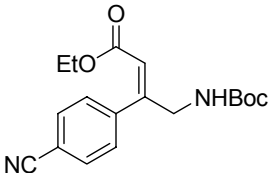
Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 65.02; H, 6.95; N, 4.09.

nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



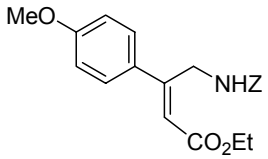
Compound 11-*E*: Isolated in 86 % yield after SiO_2 chromatography with 4:1 (hexanes:EtOAc). ^1H NMR δ 7.63 (d, 2H, *J* = 7.9 Hz), 7.34 (m, 7H), 6.06 (s, 1H), 5.12 (s, 3H), 4.08 (d, 2H, *J* = 5.9 Hz), 4.01 (q, 2H, *J* = 7.2 Hz), 1.1 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.9, 47.4, 60.4, 67.2, 111.9, 118.4, 118.6, 128.2, 128.3, 128.4, 128.6, 131.9, 136.1, 142.7, 153.2, 156.1, 164.9. Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.22; H, 5.53; N, 7.69. Found: C, 69.02; H, 5.48; N, 7.57.

nOe(d_6-acetone): 1.0 % nOe from vinyl CH to CH_2, 1.8% nOe from CH_2 to vinyl CH.



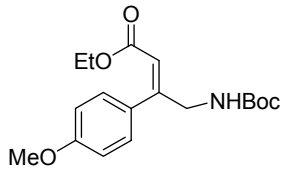
Compound 12-*E*: Isolated in 87% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.65 (d, 2H, *J* = 8.3 Hz), 7.31 (d, 2H, *J* = 7.9 Hz), 6.05 (s, 1H), 4.84 (s, 1H), 4.00 (m, 4H), 1.43 (s, 9H), 1.09 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 47.0, 60.2, 80.2, 111.8, 117.9, 118.5, 128.2, 131.8, 142.8, 153.8, 155.3, 164.9. Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.37; H, 6.69; N, 8.39.

nOe ($CDCl_3$): 2% nOe from vinyl CH to CH_2.



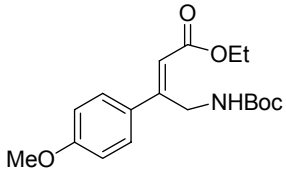
Compound 13-*Z*: Isolated in 70 % yield after SiO_2 chromatography with 20:1 (toluene:EtOAc). ^{1}H NMR δ 7.67 (d, 2H, *J* = 8.7 Hz), 7.32 (m, 5H), 6.93 (d, 2H, *J*= 8.7 Hz), 6.18 (s, 1H), 5.91 (s, 1H), 5.11 (s, 2H), 4.59 (d, 2H, *J* = 6.7 Hz), 4.23 (q, 2H, *J* = 7.0 Hz), 3.84 (s, 3H), 1.31 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 14.3, 40.7, 55.3, 60.4, 66.7, 114.1, 117.5, 128.0, 128.5, 128.8, 131.5, 136.6, 156.0, 156.2, 160.9, 166.8. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.27; H, 6.18; N, 3.71.

nOe($CDCl_3$): 1.4% nOe from vinyl CH to aromatic CH.



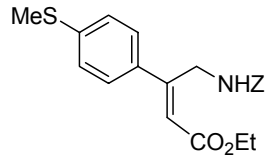
Compound 14-*E*: Isolated in 93% after SiO_2 chromatography from 1:4 to 1:2 (EtOAc:hexanes). ^{1}H NMR δ 7.17 (d, 2H, *J* = 8.4 Hz), 6.89 (m, 2H), 5.96 (s, 1H), 4.75 (s, 1H), 4.03 (m, 4H), 3.82 (s, 3H), 1.45 (s, 9H), 1.12 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR δ 13.9, 28.2, 47.3, 55.1, 59.9, 79.8, 113.4, 116.1, 128.8, 129.5, 154.8, 155.4, 159.5, 165.8. Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.43; H, 7.55; N, 4.04.

nOe ($CDCl_3$): 2.2% nOe from vinyl CH to CH_2.



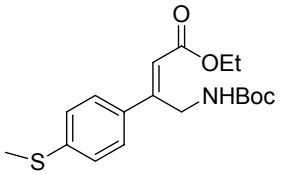
Compound 14-*Z*: Isolated in 65% yield after SiO_2 chromatography from 10:10:1 (hexanes:toluene: EtOAc).^{1}H-NMR δ 7.61(d, 2H, *J* = 8.5 Hz), 6.87 (m, 2H), 6.12 (s, 1H), 5.56 (s, 1H), 4.50 (d, 2H, *J* = 6.4 Hz), 4.19 (q, 2H, J = 7.1 Hz), 3.78 (s, 3H), 1.39 (s, 9H), 1.29 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C-NMR δ 14.1, 28.3, 39.9, 55.1, 60.2, 79.0, 113.9, 117.2, 128.6, 131.4, 155.5, 156.2, 160.7, 166.7. Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.25; H, 7.62; N, 4.04.

nOe ($CDCl_3$): 3.6% nOe from vinyl CH to aromatic CH.



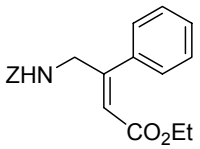
Compound 15-*Z*: Isolated in 73 % yield after SiO_2 chromatography with 20:1 to 10:1 (toluene:EtOAc). ^{1}H NMR δ 7.62 (d, 2H, *J* = 8.4 Hz), 7.30 (m, 5H), 7.25 (d, 2H, *J* = 8.4 Hz), 6.21 (s, 1H), 5.89 (s, 1H), 5.11 (s, 2H), 4.59 (d, 2H, *J* = 6.7 Hz), 4.23 (q, 2H, *J* = 7.1 Hz), 2.50 (s, 3H), 1.33 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.2, 15.2, 40.2, 60.5, 66.7, 118.6, 126.0, 127.6, 128.0, 128.5, 135.5, 136.6, 141.1, 155.8, 156.1, 166.7. Anal. Calcd for $C_{21}H_{23}NSO_5$: C, 65.43; H, 6.01; N, 3.63. Found: C, 65.36; H, 5.98; N, 3.55.

nOe($CDCl_3$): 1.0 % nOe from vinyl CH to aromatic CH.



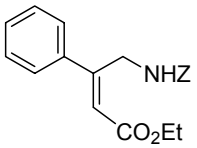
Compound 16-*Z*: Isolated in 72% yield after SiO_2 chromatography from 1:5 (EtOAc:hexanes). ^{1}H NMR δ 7.61 (d, 2H, *J* = 8.0 Hz), 7.25 (d, 2H, *J* = 8.6 Hz), 6.19 (s, 1H), 5.53 (s, 1H), 4.53 (d, 2H, *J* = 6.7 Hz), 4.24 (q, 2H, *J* = 7.1 Hz), 2.50 (s, 3H), 1.43 (s, 9H), 1.34 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.2, 15.1, 28.3, 39.9, 60.3, 79.2, 118.3, 125.9, 127.5, 135.6, 155.5, 156.0, 166.6. Anal. Calcd for $C_{18}H_{25}NO_4S$: C, 61.51; H, 7.17; N, 3.99. Found: C, 61.40; H, 7.15; N, 4.12.

nOe ($CDCl_3$): 4% nOe from vinyl CH to aromatic CH.



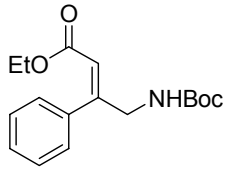
Compound 17-*E*: Isolated in 72% yield after SiO_2 chromatography from 10:1 (tol:EtOAc). ^{1}H NMR δ 7.35 (m, 8H), 7.20 (d, 2H, *J* = 5.2 Hz), 6.0 (s, 1H), 5.13 (s, 3H), 4.12 (d, 2H, *J* = 5.7 Hz), 4.0 (q, 3H, *J* = 7.2 Hz), 1.08 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 47.7, 60.0, 67.0, 116.9, 127.3, 128.0, 128.1, 128.5, 136.2, 137.5, 154.6, 156.1, 165.6. Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.64; H, 6.06; N, 3.93.

nOe(d_6-acetone): 1 % nOe from vinyl CH to CH_2, 0.6 % nOe from CH_2 to vinyl CH.



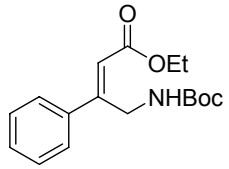
Compound 17-*Z*: Isolated in 75% yield after SiO_2 chromatography from 13:1 (tol:EtOAc). ^{1}H NMR δ 7.67 (m, 2H), 7.40 (m, 4H), 7.34 (m, 5H), 6.23 (s, 1H), 5.91 (s, 1H), 5.12 (s, 2H), 4.64 (d, 2H, *J* = 6.6 Hz), 4.24 (q, 2H, *J* = 7.0 Hz), 1.34 (t, 3H, *J* = 7.0 Hz) ppm; ^{13}C NMR δ 14.2, 40.8, 60.5, 66.6, 119.6, 127.2, 127.9, 128.0, 128.4, 128.7, 129.5, 136.2, 139.3, 156.1, 156.4, 166.5 ppm. Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.69; H, 6.14; N, 3.98.

nOe($CDCl_3$): 0.85 % nOe from vinyl CH to aromatic CH.



Compound 18-*E*: Isolated in 90% yield after SiO_2 chromatography from 5:1 to 3:1 (hexanes:EtOAc). ^{1}H NMR δ 7.35 (m, 3H), 7.20 (d, 2H, *J* = 6.2 Hz), 5.99 (s, 1H), 4.81 (s, 1H), 4.04 (d, 2H, *J* = 5.4), 2.87 (q, 2H, *J* = 7.1 Hz), 1.45 (s, 9H), 1.06 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 13.8, 28.2, 47.3, 59.9, 79.8, 107.3, 116.5, 127.3, 127.9, 128.0, 137.7, 155.2, 165.7. Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.80; H, 7.58; N, 4.51.

nOe ($CDCl_3$): 1% nOe from CH_2 to aromatic CH; 1% nOe from CH_2 to vinyl CH; 2% nOe from vinyl CH to CH_2.



Compound 18-*E*: Isolated in 50% yield after SiO_2 chromatography from 5:2 (hexanes:EtOAc). ^{1}H NMR δ 7.64 (d, 2H, *J* = 5.2), 7.38 (m, 3H), 6.20 (s, 1H), 5.50 (s, 1H), 4.56 (d, 2H, *J* = 6.6 Hz), 4.24 (q, 2H, *J* = 7.1 Hz), 1.42 (s, 9H), 1.34 (t, 3H, *J* = 7.1 Hz) ppm; ^{13}C NMR δ 14.1, 28.3, 40.2, 60.4, 79.2, 119.4, 127.1, 128.6, 129.3, 139.3, 156.7, 166.5. Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.99; H, 7.67; N, 4.55.

nOe ($CDCl_3$): 2% nOe from vinyl CH to aromatic CH.