

# Catalytic, Enantioselective Alkylation of $\alpha$ -Imino Esters: The Synthesis of Nonnatural $\alpha$ -Amino Acid Derivatives

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**General.** Unless otherwise stated, all reactions were carried out under strictly anhydrous, air-free conditions. Formation of all ligand-metal complexes was done in a glove box under N<sub>2</sub>. All solvents were dried and distilled by standard procedures. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were acquired on a Varian Unity 400 MHz Spectrometer. The <sup>1</sup>H (400 MHz) and <sup>13</sup>C chemical shifts (101 MHz) are given in parts per million ( ) with respect to internal TMS standards or residual solvent peaks. The <sup>13</sup>C NMR spectra were acquired with proton decoupling. FTIR spectra were recorded on a Bruker IFS-55 spectrometer and optical rotations were recorded on a Perkin Elmer 120 polarimeter at room temperature. The diastereomeric and enantiomeric ratios were determined by Chiralcel OD chiral HPLC column or the chiral shift reagent praseodymium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate].<sup>1</sup> The title  $\alpha$ -imino ester **1b** was made from ethyl glyoxylate<sup>2</sup> and *N*-toluenesulfonylisocyanate (Aldrich) by Weinreb's procedure.<sup>3</sup> The silylimine **1a** was made by a modification of the reported procedure.<sup>4</sup> The enol silanes **2a-f**,<sup>5</sup> **2g**,<sup>6</sup> **2h-k**,<sup>7</sup> and **17a-c**<sup>8</sup> were made by standard protocols. The olefins **11b**,<sup>9</sup> **11c**,<sup>10</sup> and **11e**,<sup>11</sup> were

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prepared by known methods. Trimethylsilylethanesulfonamide<sup>12</sup> and acetals **9a-h**<sup>13,14</sup> are known so characterization data is excluded. All other starting materials were purchased from Aldrich Chemical Company, except for (*R*)- and (*S*)-Tol-BINAP and (*R*)- and (*S*)-BINAP which were purchased from Strem. Reported optical rotations are corrected to enantiomeric purity.

**Preparation of Ethyl-*N*-*tert*-butyldimethylsilyl imino ester (1a).** To a solution of ethyl glycine hydrochloride (2.8 g, 20 mmol) in THF (10 mL) was added triethylamine (4.5 g, 44 mmol) and 4-*N,N*-dimethylaminopyridine (25 mg, 0.2 mmol). The reaction mixture was cooled to 0 °C and a solution of *tert*-butyldimethylchlorosilane (3.0 g, 20 mmol) in THF (10 mL) was added over a 5 min period. The reaction was stirred for 12 h, diluted with diethyl ether (50 mL), and filtered. The filtrate was concentrated *in vacuo* and the crude residue was distilled under high vacuum yielding 3.7 g (85%) of *N-tert*-butyldimethylsilylglycine. To a stirred solution of this product in THF (30 mL) at 0 °C was added *tert*-butyl hypochlorite<sup>15</sup> over 5 min. The reaction was stirred at 0 °C for 2 h and filtered through a coarse fritted funnel. The filtrate was concentrated *in vacuo*, weighed (4.0 g, 16.2 mmol) and dissolved in 30 mL of diethyl ether. The mixture was cooled to 0 °C and a solution of freshly distilled DBU (2.0 g, 16.2 mmol) in Et<sub>2</sub>O (5 mL) was added over a 5 min period. The reaction was stirred for 1 h at 0 °C and filtered. The filtrate was concentrated and the residue, >98% **1a** by <sup>1</sup>H NMR, was used without further purification.

**(*S*)-Ethyl-3-Benzoyl-2-(tosylamino)propanoate (4a).** White crystalline solid mp = 90-92 °C; [α]<sub>D</sub> = +73.2° (c = 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.86 (d, 2H), 7.76 (d, 2H), 7.58 (t, 1H), 7.42 (t, 2H), 7.22 (d, 2H), 5.79 (d, 1H), 4.22 (m, 1H), 4.03 (q, 2H), 3.60 (m, 2H), 2.39 (s, 3H), 1.08 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 196.9, 170.3, 143.6, 137.0, 135.9, 133.8, 129.7, 128.7, 128.1, 127.2, 62.1, 51.9, 42.1, 21.6, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3354, 1741, 1682; HPLC (10% EtOH/hexane, 1.4 mL/min) (*R*) = 12.44, (*S*) = 14.09 min. Anal. Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>5</sub>S: C, 60.78; H, 5.64; N, 3.73. Found C, 60.53; H, 5.61; N, 3.69.

**Absolute Configuration of 4a.** (*S*)-Ethyl-3-benzoyl-2-(tosylamino)propanoate (**4a**) was made independently by Wessig *et al.* from (*S*)-aspartic acid.<sup>16</sup> This material possessed an almost identical optical rotation to our synthetic material ([α]<sub>D</sub> = +74.1° (c = 1.0, CHCl<sub>3</sub>)). The absolute configuration of the other products was then based on analogy to this case (sign of optical rotation, HPLC elution times were consistent with stereoregularity).

**(*S*)-Ethyl-3-(phenylcarboxy)-2-(tosylamino)propanoate (4b).** White crystalline solid mp = 88-90 °C; [α]<sub>D</sub> = +16.6° (c = 0.03, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.78 (d, 2H), 7.30 (m, 5H), 7.00 (d, 2H), 5.61 (d, 1H), 4.22 (m, 1H), 4.03 (m, 2H), 3.16 (m, 2H), 2.40 (s, 3H), 1.07 (t, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)

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<sup>16</sup> Wessig, P.; Steiner, A.; Posborn, K. *Helv. Chim. Acta* **1996**, 79, 1843.

169.6, 168.8, 150.1, 143.8, 136.5, 129.7, 129.4, 127.2, 126.1, 121.3, 62.4, 52.2, 38.2, 21.5, 13.8; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3283, 2926, 1743, 1493, 1342, 1267, 1164; HPLC (10% i-PrOH/hexane, 0.7 mL/min) (R) = 42.5, (S) = 48.2 min. Anal. Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>6</sub>S: C, 58.3; H, 5.41; N, 3.58. Found C, 58.50; H, 5.44; N, 3.62.

**(S)-Ethyl-3-(4-Methoxybenzoyl)-2-(tosylamino)propanoate (4c).** White crystalline solid mp = 98-100 °C; [α]<sub>D</sub> = +58.0° (c = 0.147, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.82 (d, 2H), 7.75 (d, 2H), 7.24 (d, 2H), 6.88 (d, 2H), 5.82 (d, 1H), 4.23 (m, 1H), 4.02 (q, 2H), 3.82 (s, 3H), 3.56 (m, 2H), 2.38 (s, 3H), 1.06 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 195.2, 170.3, 163.8, 143.3, 137.0, 130.3, 129.4, 128.8, 127.0, 113.7, 61.8, 55.4, 51.8, 41.6, 21.3, 13.7 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3354, 1741, 1674; HPLC (10% EtOH/hexane, 1.4 mL/min) (R) = 18.63, (S) = 20.76 min. Anal. Calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>6</sub>S: C, 59.24; H, 5.72; N, 3.46. Found C, 59.00; H, 5.70; N, 3.50.

**(S)-Ethyl-3-pivaloyl-2-(tosylamino)propanoate (4d).** Colorless oil; [α]<sub>D</sub> = +60.4° (c = 0.12, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.71 (d, 2H), 7.28 (d, 2H), 5.60 (d, 1H), 4.00 (m, 3H), 3.10 (m, 2H), 2.41 (s, 3H), 1.07 (s, 9H), 1.05 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 213.4, 170.3, 143.5, 136.8, 129.5, 127.1, 61.9, 51.7, 43.7, 40.5, 26.0, 21.4, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3359, 1739, 1705; HPLC (5% i-PrOH/hexane, 1.0 mL/min) (R) = 19.01, (S) = 20.91 min. Anal. Calcd for C<sub>17</sub>H<sub>25</sub>NO<sub>5</sub>S: C, 57.44; H, 7.09; N, 3.94. Found C, 57.31; H, 7.02; N, 3.99.

**(S)-Ethyl-3-(3-nitrobenzoyl)-2-(tosylamino)propanoate (4e).** White crystalline solid mp = 121-123 °C; [α]<sub>D</sub> = +23.5° (c = 0.050, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 8.69 (s, 1H), 8.43 (d, 1H), 8.21 (d, 1H), 7.76 (d, 2H), 7.69 (t, 1H), 7.28 (d, 2H), 5.78 (d, 1H), 4.30 (m, 1H), 4.06 (m, 2H), 3.68 (d, 2H), 2.42 (s, 3H), 1.18 (t, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 194.8, 169.9, 143.7, 137.0, 136.6, 133.6, 130.0, 129.7, 127.9, 127.2, 123.0, 62.3, 51.6, 42.3, 21.5, 13.8 ppm; IR (CDCl<sub>3</sub>): 3359, 1739, 1712; HPLC (10% EtOH/hexane, 1.4 mL/min) (R) = 11.5, (S) = 13.2 min. Anal. Calcd for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>7</sub>S: C, 54.27; H, 4.80; N, 6.67. Found C, 54.45; H, 4.84; N, 6.73.

**(S)-Ethyl-3-(3,4-dichlorobenzoyl)-2-(tosylamino)propanoate (4f).** White crystalline solid mp = 106-108 °C; [α]<sub>D</sub> = +32.9° (c = 0.059, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.85 (s, 1H), 7.70 (d, 2H), 7.65 (d, 1H), 7.50 (d, 1H), 7.23 (d, 2H), 5.68 (d, 1H), 4.21 (m, 1H), 4.03 (m, 2H), 3.56 (m, 2H), 2.39 (s, 3H), 1.09 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 194.7, 170.0, 143.7, 136.7, 135.3, 133.4, 130.8, 130.1, 129.6, 127.2, 127.1, 62.2, 51.6, 42.0, 21.5, 13.8 ppm; IR (CDCl<sub>3</sub>): 3376, 1738, 1685; HPLC (10% EtOH/hexane, 1.4 mL/min) (R) = 13.02, (S) = 17.07 min. Anal. Calcd for C<sub>19</sub>H<sub>19</sub>Cl<sub>2</sub>NO<sub>5</sub>S: C, 51.46; H, 4.32; N, 3.16. Found C, 51.72; H, 4.40; N, 3.19.

**Deprotection of γ-oxo-α-tosylamino ester 4a.** The γ-oxo amino ester (R)-4a (100 mg, 0.27 mmol) was refluxed with phenol (200 mg, 2.1 mmol) in 33% HBr/AcOH (2 mL) for 12 h. Water (2 mL) was added to the mixture which was then heated to 50 °C for 1 h. The reaction mixture was then concentrated *in vacuo* to about 0.5 mL. The product was isolated by ion exchange [Amberlite IR-120 (Plus) resin] and was characterized as (L)-3-(benzoyl)alanine (40 mg, 75%). The optical rotation ([α]<sub>D</sub> = +43.9° (c = 0.10, 6 N HCl) indicated no detectable racemization.

**Oxidation of (S)-BINAP with Cu(ClO<sub>4</sub>)<sub>2</sub>.** A solution of (S)-BINAP (50 mg, 0.080 mmol) was dissolved in THF (0.5 mL) which contained H<sub>2</sub><sup>18</sup>O (100 μL). An excess of Cu(ClO<sub>4</sub>)<sub>2</sub> (209 mg, 0.80 mmol) was added to the solution at room temperature and the reaction was stirred overnight. The reaction was quenched with water (3 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 5 mL). The combined organics were concentrated and chromatographed on silica gel to yield 16 mg (31% yield) of (S)-BINAPO as compared to the literature spectra.<sup>17</sup> An authentic sample of (S)-BINAPO was made by this method in the presence of H<sub>2</sub>O. Mass spectral analysis of the two samples indicate a distinct enrichment in the sample oxidized in the presence of H<sub>2</sub><sup>18</sup>O.

**(2S,3R)-Ethyl-3-benzoyl-2-(tosylamino)butanoate (4g).** White crystalline solid mp = 87-89 °C; [α]<sub>D</sub> = +12.8 ° (c = 0.01, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) (**2S,3R**): 7.90 (d, 2H), 7.80 (d, 2H), 7.58 (t, 1H), 7.43 (t, 2H), 7.26 (d, 2H), 5.93 (d, 1H), 4.23 (m, 1H), 4.13 (m, 1H), 3.84 (q, 2H), 2.40 (s, 3H), 1.37 (d, 3H), 0.94 (t, 3H) ppm (**2S,3S**): 7.90 (d, 2H), 7.80 (d, 2H), 7.58 (t, 1H), 7.43 (t, 2H), 7.26 (d, 2H), 5.70 (d, 1H), 4.19 (m, 1H), 3.85 (m, 3H), 2.40 (s, 3H), 1.34 (d, 3H), 1.00 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) (**2S,3R**): 202.2, 170.2, 143.3, 137.5, 135.4, 133.5, 129.4, 128.7, 128.4, 127.1, 61.7, 58.0, 43.6, 21.5, 14.5, 13.6 ppm; (**2S,3S**): 200.4, 170.5, 143.5, 136.6, 135.2, 133.5, 129.4, 128.6, 128.2, 127.1, 61.8, 57.6, 44.4, 21.4, 14.5, 13.5 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3370, 1737, 1677, 1596, 1339, 1163; Anal. Calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>5</sub>S: C, 61.68; H, 5.96; N, 3.60. Found C, 61.70; H, 5.91; N, 3.64.

**(1'R,2S)-Ethyl-2-(2'-oxotetralinyl)-2-(tosylamino)acetate (4h).** White crystalline solid mp = 152-154 °C; [α]<sub>D</sub> = +15.1 ° (c = 0.078, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) (**1'R,2S**): 7.92 (d, 1H), 7.72 (d, 2H), 7.46 (t, 1H), 7.22 (m, 4H), 5.42 (d, 1H), 3.92-4.13 (m, 3H), 3.40 (m, 1H), 3.00-3.20 (m, 2H), 2.40 (s, 3H), 2.30 (m, 2H), 1.02 (t, 3H) ppm; (**1'S,2S**): 7.92 (d, 1H), 7.72 (d, 2H), 7.46 (t, 1H), 7.22 (m, 4H), 5.83 (d, 1H), 3.92-4.13 (m, 3H), 3.40 (m, 1H), 3.00-3.20 (m, 2H), 2.40 (s, 3H), 2.30 (m, 2H), 1.20 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) (**1'R,2S**): 198.8, 170.6, 163.7, 143.5, 139.8, 136.6, 130.7, 129.6, 129.5, 128.3, 127.2, 126.3, 61.8, 57.7, 55.4, 44.3, 21.4, 14.8, 13.6 ppm; (**1'S,2S**): 197.4, 170.0, 166.1, 144.1, 138.0, 136.9, 131.9, 129.5, 129.4, 128.6, 127.2, 126.7, 62.3, 56.8, 51.5, 29.0, 26.8, 21.4, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3353, 1741, 1677, 1600, 1339, 1163; Anal. Calcd for C<sub>21</sub>H<sub>23</sub>NO<sub>5</sub>S: C, 62.82; H, 5.78; N, 3.49. Found C, 62.58; H, 5.86; N, 3.48.

**(1'R,2S)-Silyltetralone (4i).** White crystalline solid mp = 132-134 °C; [α]<sub>D</sub> = +35.2 ° (c = 0.035, CDCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) (**1'R,2S**): 7.97 (d, 1H), 7.73 (d, 2H), 7.22 (m, 2H), 6.89 (m, 2H), 5.62 (d, 1H), 4.16 (m, 1H), 3.98 (m, 2H), 3.82 (s, 3H), 3.28 (m, 1H), 2.40 (s, 3H), 1.30 (t, 1H), 1.20 (m, 1H), 1.11 (t, 3H), 0.38 (d, 6H) ppm; (**1'S,2S**): 7.97 (d, 1H), 7.75 (d, 2H), 7.22 (d, 2H), 6.91 (m, 2H), 5.59 (d, 1H), 3.97 (m, 3H), 3.82 (s, 3H), 3.71 (m, 1H), 2.40 (s, 3H), 1.24 (m, 2H), 1.00 (t, 3H), 0.41 (s, 3H), 0.36 (s, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) (**1'R,2S**): 198.3, 162.7, 143.3, 142.8, 137.3, 133.7, 133.6, 131.1, 129.5, 127.2, 117.8, 114.9, 58.9, 55.3, 50.8, 26.8, 21.5, 13.8, 0.97, -2.23, -3.10 ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) (**1'S,2S**): 199.4, 162.8, 143.3, 143.2, 137.6, 133.6, 133.5, 130.9, 129.3, 127.2, 117.9, 115.0, 60.2,

<sup>17</sup> Tayaka, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

55.3, 49.1, 26.9, 21.5, 13.7, 0.92, -2.05, -2.75 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3366, 1737, 1660, 1583, 1231, 1163; Anal. Calcd for C<sub>23</sub>H<sub>29</sub>NO<sub>6</sub>SSi: C, 58.09; H, 6.15; N, 2.95. Found C, 58.14; H, 6.19; N, 2.97.

**(1'R,2S)-Ethyl-2-(2'-oxocyclohexyl)-2-(tosylamino)acetate (4j).** White crystalline solid mp = 125-127 °C; [α]<sub>D</sub> = +38.5 ° (c = 0.050, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) (**1'R,2S**): 7.70 (d, 2H), 7.24 (d, 2H), 5.45 (d, 1H), 3.90 (m, 1H), 3.81 (m, 2H), 3.18 (m, 1H), 2.40 (m, 3H), 1.90-2.35 (m, 5H), 1.60-1.78 (m, 3H), 1.00 (t, 3H) ppm; (**1'S, 2S**): 7.70 (d, 2H), 7.24 (d, 2H), 5.45 (d, 1H), 3.50 (m, 3H), 2.96 (m, 1H), 2.40 (s, 3H), 1.90-2.35 (m, 5H), 1.60-1.78 (m, 3H), 1.19 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) (**1'R,2S**): 211.0, 170.1, 143.3, 137.3, 129.4, 127.2, 61.7, 56.5, 53.4, 41.8, 30.6, 26.9, 24.6, 21.4, 13.6 ppm; (**1'S,2S**): 209.7, 170.3, 143.5, 136.8, 129.5, 127.2, 61.6, 56.4, 55.2, 41.5, 30.7, 26.8, 24.7, 21.4, 13.9 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3361, 1746, 1707, 1596, 1339, 1167; Anal. Calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>5</sub>S: C, 57.77; H, 6.56; N, 3.97. Found C, 57.53; H, 6.61; N, 3.92.

**(3S,4R,5R)-4-methyl-5-phenyl-3-(tosylamino)tetrahydrofuranone (7).** To a solution of (2S, 3R)-ethyl-3-benzoyl-2-(tosylamino)butanoate **4g** (160 mg, 0.41 mmol) in 6 mL MeOH/EtOAc (5/1) was added 30 mg of Pd/C. The mixture was placed in a high pressure apparatus under H<sub>2</sub> (15-20 psi) for 2 h or until no starting material was evident by TLC (30% EtOAc/hexane). The reaction was filtered through celite and the filtrate was concentrated to yield a (15:1/anti:syn) mixture of diastereomers. The pure **(3S,4R,5R)-7** was obtained from one recrystallization (Et<sub>2</sub>O) to yield 121 mg (86% yield) of a white crystalline solid mp = 152-154 °C. [α]<sub>D</sub> = +115.0 ° (c = 0.03, CDCl<sub>3</sub>) <sup>1</sup>H NMR (CDCl<sub>3</sub>): 7.72 (d, 2H), 7.37 (m, 3H), 7.22 (d, 2H), 7.20 (d, 2H), 5.28 (bs, 1H), 5.21 (d, 1H), 4.10 (d, 1H), 2.90 (m, 1H), 2.40 (s, 3H), 1.21 (d, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 173.6, 144.1, 137.4, 135.7, 129.8, 128.9, 128.5, 127.0, 124.5, 85.4, 54.2, 41.3, 21.5, 14.2 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3340, 1784, 1351, 1167; Anal. Calcd for C<sub>18</sub>H<sub>19</sub>NO<sub>4</sub>S: C, 62.59; H, 5.55; N, 4.06. Found C, 62.43; H, 5.51; N, 4.10.

**Hydrolysis and protection of 7.** (3S,4R,5R)-4-methyl-5-phenyl-3-(tosylamino)tetrahydrofuranone **6i** (150 mg, 0.44 mmol) was dissolved in HBr/HOAc (30%, 3 mL) followed by addition of phenol (124 mg, 1.32 mmol). The mixture was heated to 70 °C in a sealed tube for 5 h. The reaction was cooled to room temperature, quenched with 3 mL of H<sub>2</sub>O and heated to 50 °C for 30 min. The mixture was concentrated to a brown residue and redissolved in 5 mL of diethyl ether and 5 mL of H<sub>2</sub>O. The aqueous phase was extracted several times with diethyl ether. The remaining aqueous phase was concentrated to yield 64 mg of the crude lactone hydrobromide salt. The salt was suspended in 1 mL of CHCl<sub>3</sub> followed by the successive addition of a solution of 10% NaHCO<sub>3</sub> (0.5 mmol), NaCl (50 mg, 0.86 mmol) and (BOC)<sub>2</sub>O (55 mg, 0.25 mmol). The reaction was stirred at room temperature overnight. The reaction mixture was extracted with CHCl<sub>3</sub> (3 x 3 mL) and the combined organics were dried and concentrated *in vacuo* yielding 52 mg (48% overall) of the protected lactone (3S,4R,5R)-3-[(*tert*-butoxycarbonyl)amino]-4-methyl-5-phenyltetrahydrofuranone. The optical rotation and spectral data were analogous to the known literature compound.<sup>18</sup>

<sup>18</sup> Gair, S.; Jackson, R. F. W.; Brown, P. A. *Tetrahedron Lett.* **1997**, 38, 3059.

**Determination of relative and absolute stereochemistry of 4h.** Crystals of **4h** were obtained by slow evaporation of EtOAc. Crystal data for **4h**: monoclinic,  $P2_1$ ;  $a = 9.3063(4)$ ,  $b = 9.6251(4)$ ,  $c = 11.8917(5)$  Å;  $V = 1002.65(7)$  Å<sup>3</sup>;  $Z = 2$ ;  $d_{\text{calcd}} = 1.330$  Mg/m<sup>3</sup>;  $F(000) = 424$ ;  $\mu(\text{Mo K } \alpha) = 0.193$  mm<sup>-1</sup>;  $\lambda = 0.71073$  Å; 5611 reflections measured; 3393 observed;  $(I > 2\sigma(I)) = 2950$ ; 255 variables;  $R = 0.0436$ ,  $R_W = 0.0538$ , GOF = 1.083.

**General Synthesis of N,O-Acetals 9d-g.** The requisite sulfonamide (5.0 g, 29.2 mmol) was mixed with ethyl glyoxylate (3.0 g, 29.2 mmol) in CHCl<sub>3</sub> and refluxed for several hours depending on the amide or sulfonamide. The reactions were monitored by <sup>1</sup>H NMR and glyoxylate was added when necessary to drive the reaction to completion. The reactions were worked up by removal of the solvent and any excess glyoxylate *in vacuo*. The crystalline residue was recrystallized from EtOAc/hexane, Et<sub>2</sub>O/hexane or chromatographed on florisil to yield analytically pure material.

**(S)-Ethyl-3-(benzoyl)-2-(acetamino)propanoate (10c).** Colorless oil;  $[\alpha]_D = +31.3^\circ$  ( $c = 0.064$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.89 (d, 2H), 7.56 (t, 1H), 7.41 (t, 2H), 6.72 (d, 1H), 4.93 (m, 1H), 4.19 (q, 2H), 3.73 (m, 1H), 3.57 (m, 1H), 2.00 (s, 3H), 1.22 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 197.8, 171.1, 169.9, 135.8, 133.7, 128.7, 128.0, 61.7, 48.2, 40.4, 23.0, 13.9 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3437, 3055, 1741, 1680, 1503, 1265, 1219; HPLC (10% i-PrOH/hexane, 0.4 mL/min) (*R*) = 41.1, (*S*) = 43.4 min. Anal. Calcd for C<sub>14</sub>H<sub>17</sub>NO<sub>4</sub>: C, 63.85; H, 6.51; N, 5.32. Found C, 63.74; H, 6.45; N, 5.26.

**(S)-Ethyl-3-Benzoyl-2-((trimethylsilyl)ethanesulfonylamino)propanoate (10e).** Colorless oil;  $[\alpha]_D = +17.3^\circ$  ( $c = 0.026$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.91 (d, 2H), 7.58 (t, 1H), 7.45 (t, 2H), 5.44 (d, 1H), 4.44 (m, 1H), 4.20 (m, 2H), 3.78 (m, 1H), 3.56 (m, 1H), 3.03 (m, 2H), 1.23 (t, 3H), 1.03 (m, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 197.3, 171.0, 135.7, 133.9, 128.7, 128.1, 62.0, 52.2, 50.0, 42.6, 14.0, 10.3, -2.02 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3206, 2912, 1740, 1676, 1325, 1220, 1152, 1116, 1029; HPLC (10% EtOH/hexane, 1.0 mL/min) (*R*) = 42.44, (*S*) = 50.54 min. Anal. Calcd for C<sub>17</sub>H<sub>27</sub>NO<sub>5</sub>SSi: C, 52.97; H, 7.07; N, 3.64. Found C, 52.72; H, 7.18; N, 3.71.

**Deprotection of 10e.**<sup>19,20</sup> A solution of compound **9i** (65 mg, 0.17 mmol) and cesium fluoride (82 mg, 0.54 mmol) were heated together in DMF (1 mL) for 24 h. The reaction mixture was concentrated and the resulting crude residue was partitioned between Et<sub>2</sub>O and 1N HCl. Basification of the acidic layer followed by extraction with EtOAc (3 mL) afforded the crude amine which was transformed to the hydrochloride salt as above (36 mg, 90% yield). The amine was refluxed for 4 h in 6N HCl and concentrated to afford 34 mg (87% overall yield) of (*L*)-benzoylalanine hydrochloride.

**One Pot Synthesis of 4a.** A solution of *p*-toluenesulfonamide (150 mg, 0.88 mmol) and freshly distilled ethyl glyoxylate (90 mg, 0.88 mmol) were mixed together in CH<sub>2</sub>Cl<sub>2</sub> (3 mL). After 1 h, a solution of catalyst **3c** was added and the reaction mixture was stirred at room temperature for 24 h. The enol silane **2a** was then added to the mixture at 0 °C over a 30 min period. After 2 h, the

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<sup>19</sup> Garigipati, R. S.; Tschaen, D. M.; Weinreb, S. M. *J. Am. Chem. Soc.* **1990**, *112*, 3475.

reaction was quenched with H<sub>2</sub>O (3 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 mL). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> and the combined organics were dried with MgSO<sub>4</sub> and concentrated. The crude reaction mixture was triturated with hexane and the resulting crystals were recrystallized from Et<sub>2</sub>O to yield 0.294 g (89%) of compound **4a**. Chiral HPLC analysis revealed that the product was 95% enantiomerically enriched.

**Synthesis of (L)-*m*-Nitrobenzoylalanine (5e).** To solution of *N,O*-acetal **9e** (2.18 g, 6.5 mmol) in THF (20 mL) was added 1-(*m*-nitrophenyl)-1-(trimethylsilyloxy)ethylene (1.7 g, 7.0 mmol) and a solution of catalyst **3d** (100 mg, 0.1 mmol) at room temperature. The reaction was refluxed for 24 h and quenched with water (15 mL). The product was extracted from the THF:H<sub>2</sub>O mixture with CH<sub>2</sub>Cl<sub>2</sub> (2 x 20 mL). The combined organics were dried, concentrated and chromatographed on silica gel (1:5:5 EtOAc::CH<sub>2</sub>Cl<sub>2</sub>) to afford 2.45 g (85% yield, 94% ee) of a yellow crystalline solid. Recrystallization of **10d** from EtOAc/ provided 1.8 g of 99% enantiomerically enriched material mp = 130-131°C [  $\alpha$ ]<sub>D</sub> = +21.9° (c = 0.05, EtOAc); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 8.68 (s, 1H), 8.43 (d, 2H), 8.33 (d, 2H), 8.22 (d, 1H), 8.04 (d, 2H), 7.68 (t, 1H), 6.00 (d, 1H), 4.37 (m, 1H), 4.03 (m, 2H), 3.79 (m, 1H), 3.66 (m, 1H), 1.04 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 194.9, 169.5, 150.1, 148.4, 145.6, 136.7, 133.5, 130.2, 128.5, 128.2, 124.2, 123.0, 62.6, 51.8, 42.5, 13.9 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3355, 3075, 2942, 1742, 1692, 1613, 1535, 1352, 1313, 1221, 1169; HPLC (15% EtOH/hexane, 1.0 mL/min) (*R*) = 41.1, (*S*) = 43.1 min. Anal. Calcd for C<sub>18</sub>H<sub>17</sub>N<sub>3</sub>O<sub>9</sub>S: C, 47.89; H, 3.80; N, 9.31. Found C, 47.75; H, 3.84; N, 9.28. Deprotection of the *N-p*-nitrosulfonyl group was done according to literature methodology.<sup>20</sup> The ethyl ester was cleaved by heating in 6 N HCl (10 mL) to yield 0.703 g (77% overall) of the enantiomerically pure (*L*)-*m*-nitrobenzoylalanine.<sup>21</sup>

**O-Silylation NMR Experiment:** The following 0.5 mL CD<sub>2</sub>Cl<sub>2</sub> solutions were made up A) *N-p*-toluenesulfonylhydroxyglycine ethyl ester **1b** (25 mg, 0.091 mmol) B) CuClO<sub>4</sub>•(CH<sub>3</sub>CN)<sub>4</sub> (30 mg, 0.091 mmol) and (*R*)-Tol-BINAP (62 mg, 0.091 mmol) C) 1-phenyl-1-(trimethylsilyloxy)-ethylene **2a** [35 mg, 0.181 mmol, <sup>1</sup>H NMR: 7.65 (d, 2H), 7.38 (m, 3H), 5.00 (s, 1H), 4.51 (s, 1H), 0.38 (s, 9H) ppm]. Solutions A and B were mixed together. No detectable peak shifts were observed. A solution of C (0.125 mL) is added to the solution of A and B. The spectra contained peaks corresponding to both the enol silane (see above) and acetophenone [<sup>1</sup>H NMR: 8.01 (d, 2H), 7.58 (t, 1H), 7.50 (t, 2H), 2.62 (s, 3H) ppm]. The amide peak of **9d** ( 5.95 ppm) maintained its relative integration. The alcohol proton of **9d**, however, ( 3.78 ppm) decreased its relative integration and the presence of a new silyl group ( 0.18 ppm). Another 0.130 mL of C was added to A/B and the spectra taken at 5 min and 1 h after the addition. After 1 h new peaks attributed to the product **4a** were visible. The rest of C was added to A/B and the proton spectra collected at 5 min, 1 h, 2 h, 4 h and 18 h. During this period the smooth conversion to product was

<sup>20</sup> Golubev, A. S.; Sewald, N.; Burger, K. *Tetrahedron* **1996**, *52*, 14757

<sup>21</sup> Pellicciari, R.; Natalini, B.; Constantino, G. *J. Med. Chem.* **1994**, *37*, 647.

observed. As indicated in the text, peaks corresponding to the silylated product *N*-TMS-4 are not observed during the reaction, and peaks corresponding to the imine **1b** are not observed.

In a separate experiment, *N*-*p*-toluenesulfonylhydroxyglycine ethyl ester **9d** (25 mg, 0.091 mmol) and 1-phenyl-1-(trimethylsilyloxy)ethylene **4a** (70 mg, 0.364 mmol) were dissolved in CD<sub>2</sub>Cl<sub>2</sub> (0.75 mL) and a <sup>1</sup>H NMR spectra was obtained. There is no evidence for any product formation under these conditions even after several days of stirring.

**(2S)-4-Phenyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (12a).** White crystalline solid recrystallized from Et<sub>2</sub>O mp = 91-93 °C; [α]<sub>D</sub> = +17.4° (c = 0.0245, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.63 (d, 2H), 7.26 (m, 5H), 7.21 (d, 2H), 5.32 (s, 1H), 5.11 (s, 1H), 5.09 (s, 1H), 3.98 (m, 1H), 3.70 (m, 2H), 2.91 (m, 3H), 2.38 (s, 3H), 1.02 (t, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 170.9, 143.5, 142.5, 139.4, 136.6, 129.5, 128.3, 127.8, 127.2, 126.3, 117.2, 61.5, 54.5, 39.3, 21.5, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3353, 2958, 2932, 1735, 1345, 1183, 1092; HPLC (6.25% i-PrOH/hexane, 1.0 mL/min) (R) = 22.03, (S) = 24.02 min. Anal. Calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>4</sub>S: C, 64.32; H, 6.21; N, 3.75. Found C, 64.06; H, 6.24; N, 3.90.

**(2S)-2-(Toluene-4-sulfonylamino)-3-(3,4-dehydronaphthalen-1-yl)-propionic Acid Ethyl Ester (12b).** White crystalline solid recrystallized from Et<sub>2</sub>O mp = 132-134 °C; [α]<sub>D</sub> = +33.2° (c = 0.010, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.60 (d, 2H), 7.15 (m, 6H), 5.87 (t, 1H), 5.03 (d, 1H), 4.04 (q, 1H), 3.84 (q, 2H), 2.83 (m, 2H), 2.62 (t, 2H), 2.35 (s, 3H), 2.19 (q, 2H), 1.06 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 171.5, 143.4, 136.6, 136.5, 133.2, 130.9, 129.5, 129.4, 127.7, 127.0, 126.4, 122.2, 61.5, 54.7, 36.8, 29.7, 28.0, 23.0, 21.4, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3342, 2927, 2853, 1737, 1344, 1266, 1161, 1092; HPLC (5.0% i-PrOH/hexane, 1.0 mL/min) (R) = 46.55, (S) = 56.28 min. Anal. Calcd for C<sub>22</sub>H<sub>25</sub>NO<sub>4</sub>S: C, 66.14; H, 6.28; N, 3.51. Found C, 65.67; H, 6.33; N, 3.52.

**(2S)-2-(Toluene-4-sulfonylamino)-3-(1-(toluene-4-sulfonyl)-1H-indol-3-yl)-propionic Acid Ethyl Ester (12c).** White crystalline solid recrystallized from EtOAc/ mp = 179-182 °C; [α]<sub>D</sub> = +5.91° (c = 0.01045, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 7.92(d, 1H), 7.73 (d, 2H), 7.56 (d, 2H), 7.41 (d, 2H), 7.28-7.14 (m, 6H), 5.17 (d, 1H), 4.21 (m, 1H), 3.88 (t, 2H), 3.08 (qd, 2H), 2.37 (s, 3H), 2.33 (s, 3H), 1.00 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 170.7, 144.9, 143.7, 136.3, 135.1, 134.2, 130.4, 129.9, 129.5, 127.0, 126.8, 124.8, 123.2, 119.3, 116.3, 113.6, 61.9, 55.5, 29.7, 29.1, 21.5, 21.4, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3342, 2932, 2858, 1737, 1597, 1366, 1166, 1092; Anal. Calcd for C<sub>27</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub>: C, 59.98; H, 5.22; N, 5.18. Found C, 59.78; H, 5.02; N, 5.67.

**(2S)-2-(Toluene-4-sulfonylamino)-3-furan-3-yl-propionic Acid Ethyl Ester (12d).** White crystalline solid recrystallized from Et<sub>2</sub>O mp = 78-80 °C; [α]<sub>D</sub> = +13.5° (c = 0.010, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.68 (d, 2H), 7.29 (m, 3H), 7.18 (s, 1H), 6.18 (s, 1H), 5.17 (d, 1H), 4.09 (m, 1H), 3.88 (q, 2H), 2.86 (d, 2H), 2.38 (s, 3H), 1.02 (t, 3H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 170.6, 143.7, 143.0, 140.6, 136.7, 129.6, 127.2, 118.1, 111.2, 61.8, 55.7, 28.9, 21.5, 13.9 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3339, 2928, 1732, 1344, 1260, 1159; HPLC (10.0% i-PrOH/hexane, 1.0 mL/min) (R) = 13.38, (S) = 14.17 min. Anal. Calcd for C<sub>16</sub>H<sub>19</sub>NO<sub>5</sub>S: C, 56.96; H, 5.68; N, 4.15. Found C, 56.77; H, 5.69; N, 4.28.

**(2S,3R)-3-Methyl-4-Phenyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (12e).** The standard procedure (see above) was followed but the reaction time extended over 3 days at room temperature. White crystalline solid recrystallized to diastereomeric purity (*syn*) from Et<sub>2</sub>O mp = 91-93 °C; [α]<sub>D</sub> = +17.4° (c = 0.0245, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.63 (d, 2H), 7.26 (m, 5H), 7.21 (d, 2H), 5.32 (s, 1H), 5.11 (s, 1H), 5.09 (s, 1H), 3.98 (m, 1H), 3.70 (m, 2H), 2.91 (m, 3H), 2.38 (s, 3H), 1.02 (t, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 170.9, 143.5, 142.5, 139.4, 136.6, 129.5, 128.3, 127.8, 127.2, 126.3, 117.2, 61.5, 54.5, 39.3, 21.5, 13.8 ppm; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3353, 2958, 2932, 1735, 1345, 1183, 1092; HPLC (6.25% i-PrOH/hexane, 1.0 mL/min) (*R*) = 22.03, (*S*) = 24.02 min. Anal. Calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>4</sub>S: C, 64.32; H, 6.21; N, 3.75. Found C, 64.06; H, 6.24; N, 3.90.

**(2S)-3-Benzoyl-2-(toluene-4-sulfonylamino)-propionic Acid Ethyl Ester (4a)** was generated by a modification of the method of Viski et al.<sup>22</sup> To a solution of (2S)-4-phenyl-2-(toluene-4-sulfonylamino)-pent-4-enoic acid ethyl ester **12a** (70 mg, 0.19 mmol) in 1.5 mL THF was added 52 mg of KMnO<sub>4</sub> in 1 mL of water over 30 min. The mixture was heated to 45 °C for 30 min. The brown precipitate was filtered and the filtrate was extracted with diethyl ether. The organic phase was concentrated and chromatographed (25% EtOAc/hexane) to yield pure **(2S)-4a** in 30% yield (20 mg). The optical rotation and spectral data were analogous to the known literature compound.<sup>11</sup>

**Kinetic Isotope Experiments.** The previously reported<sup>23</sup> -methyl-*d*<sub>3</sub>-styrene (**11a-d**<sub>3</sub>) was prepared by Tebbe methylenation of acetophenone-methyl-*d*<sub>3</sub> with freshly prepared reagent in dichloromethane solvent according to the procedure of Pine.<sup>24</sup> The **11a-d**<sub>3</sub> thus generated was found to be >98% D by <sup>1</sup>H NMR. Furthermore, <sup>2</sup>H NMR indicated none of the vinylic deuterium isomer. The KIE experiments were conducted by using 2 mmol of a 1:1 mixture of **11a:11a-d**<sub>3</sub> in our general procedure in BTF and THF, but the reactions were quenched with methanol after approximately 5% conversion. Following a standard workup and purification by preparative thin layer chromatography, the product which contained a mixture of **12a** and **12a-d**<sub>2</sub> was analyzed by CI-MS with ammonia as the carrier gas. The pure sample of **12a** under these conditions was found to cleanly produce an M+18 peak with no attendant M+17 peak visible. The ratio of **12a:12a-d**<sub>2</sub> produced in both trials was determined to be 80:20 by the method of Biemann,<sup>25</sup> which leads to a k<sub>H</sub>/k<sub>D</sub> = 4.4 in both solvents after extrapolation to zero time.

**Determination of Rate Constant.** -Methylstyrene **11a** (5 M), imine **1b** (0.2 M), and 2 mg of biphenyl were mixed together in 2 mL of CH<sub>2</sub>Cl<sub>2</sub> and cooled to 0 °C. Addition of 2.5 mol% **3d** to each of the solutions followed. Aliquots of the reaction mixture were assayed directly via GC at

<sup>22</sup> Viski, P.; Szeverényi, Z.; Simándi, L. *J. Org. Chem.* **1986**, *51*, 3213.

<sup>23</sup> Volger, H. C. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 677.

<sup>24</sup> Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212.

<sup>25</sup> Biemann, K. *Mass Spectrometry: Organic Chemical Applications*; McGraw-Hill: New York, 1962, Chapter 5.

45, 120, 200, and 280 min. The rate of imine **1b** depletion and product **12a** formation were nearly identical. The observed rate of reaction  $k'$  was determined to be  $6.8 \times 10^{-3} \text{ M}^2$  as derived from equation 12. Factoring out the concentrations of styrene and catalyst, the rate constant  $k$  was  $3.4 \times 10^{-2} \text{ min}^{-1}\text{M}^{-2}$ .

**Determination of the Effect of Catalyst Loading.** Three reaction mixtures (2 mL) containing the imine (0.2 M), styrene (0.2 M) and 2 mg of biphenyl in  $\text{CH}_2\text{Cl}_2$  were cooled to  $0^\circ\text{C}$  and various amounts of a stock solution of catalyst **3d** (1 mL of a 0.5 M solution) were added to the three reactions (10, 20 and  $40\mu\text{L}$ ). Aliquots from each of these reactions were measured by GC over a 3 h period to determine the effect of catalyst concentration.

**Product Inhibition Experiments.** Solutions (1 mL) of  $\alpha$ -methylstyrene **12a** (5 M), imine **1b** (0.2 M) and 2 mg of biphenyl were subjected to 5 mol% **3d** at  $0^\circ\text{C}$  in  $\text{CH}_2\text{Cl}_2$ . Aliquots of the reaction mixture were assayed directly via GC over a 24 h period. Once again, the rate of imine **1b** depletion and product **13a** formation were nearly identical. After several hours, the rate of the reaction was no longer pseudo first order as shown in Figure 5.

Three reaction mixtures (2 mL) were made consisting of imine **1b** (0.2 M),  $\alpha$ -methylstyrene **12a** (0.2 M), and 2 mg biphenyl. To one of these reaction mixtures was added 0.1 mmol of product (S)-**13a** and to another one was added 0.1 mmol of (R)-**13a**. All three reactions were cooled to  $-78^\circ\text{C}$  followed by addition of 5 mol% **3c**.

**(S)-Ethyl-3-Allyl-2-(tosylamino)propanoate (12h).** White crystalline solid recrystallized from  $\text{Et}_2\text{O}$  mp =  $87\text{--}89^\circ\text{C}$ ;  $[\alpha]_{\text{D}} = +7.4^\circ$  ( $c = 0.030$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ) 7.68 (d, 2H), 7.24 (d, 2H), 5.70–5.56 (m, 1H), 5.19–5.01 (m, 3H), 4.09–4.04 (m, 1H), 3.96–3.88 (m, 2H), 2.50–2.38 (m, 5H), 1.11 (t, 3H) ppm;  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ) 171.9, 144.7, 137.9, 132.4, 130.7, 128.3, 120.8, 62.8, 56.2, 38.7, 22.6, 15.0; IR ( $\text{CH}_2\text{Cl}_2$ ): 3400, 1760, 1670, 1470, 1310, 1170, 1100; HPLC (10% i-PrOH/hexane, 0.9 mL/min) (R) = 29.2, (S) = 32.7 min.; Anal. Calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{S}$ : C, 56.55; H, 6.45; N, 4.71. Found C, 56.70; H, 6.52; N, 4.75.

**N-p-Tosylstyrylalanine Ethyl Ester (12i).** White crystalline solid recrystallized from  $\text{Et}_2\text{O}$  mp =  $94\text{--}96^\circ\text{C}$ ;  $[\alpha]_{\text{D}} = +8.4^\circ$  ( $c = 0.050$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ) 7.73 (d, 2H), 7.25 (m, 7H), 6.38 (d, 1H), 5.97 (m, 1H), 5.27 (d, 1H), 4.10 (m, 1H), 3.98 (m, 2H), 2.60 (m, 2H), 2.39 (s, 3H), 1.10 (t, 3H) ppm;  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ) 170.9, 143.6, 136.7, 134.4, 129.6, 128.5, 127.6, 127.2, 126.2, 122.6, 61.7, 55.5, 36.9, 29.7, 21.5, 14.0 ppm; IR ( $\text{CH}_2\text{Cl}_2$ ): 3400, 1760, 1670; HPLC (6.25% i-PrOH/hexane, 1.0 mL/min) (R) = 12.03, (S) = 14.02 min. Anal. Calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_4\text{S}$ : C, 64.32; H, 6.21; N, 3.75. Found C, 64.56; H, 6.25; N, 3.77.

**(2S)-4- $\beta$ -Naphthyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (12j).** White crystalline solid recrystallized from  $\text{Et}_2\text{O}$ : mp =  $90\text{--}91^\circ\text{C}$ ;  $[\alpha]_{\text{D}} = +23.3^\circ$  ( $c = 0.055$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ) 7.80–7.66 (m, 4H), 7.56 (d, 2H), 7.48–7.38 (m, 3H), 7.09 (d, 2H), 5.46 (s, 1H), 5.22–5.16 (m, 2H), 4.01 (qt, 1H), 3.74–3.63 (m, 2H), 3.08–2.94 (m, 2H), 2.24 (s, 3H), 0.9 (t, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ) 172.2, 144.6, 143.4, 137.6, 137.6, 134.3, 133.9, 130.5, 129.3, 129.1, 128.6, 128.2, 127.3, 127.2, 126.1, 125.6, 118.7, 62.6, 55.7, 40.5, 22.5, 14.9; IR ( $\text{CH}_2\text{Cl}_2$ ): 3620, 3260, 1740, 1620, 1480, 1300, 1130, 1090;

HPLC (10% i-PrOH/hexane, 0.8 mL/min) (*R*) = 22.2, (*S*) = 24.8 min. Anal. Calcd for C<sub>24</sub>H<sub>25</sub>NO<sub>4</sub>S: C, 68.06; H, 5.95; N, 3.31. Found C, 68.24; H, 6.01; N, 3.34.

**(2*S*, 3*R*) 3-Methyl-4-Phenyl-2-(toluene-4-sulfonylamino)-pent-4-enoic Acid Ethyl Ester (anti-12k).** White crystalline solid recrystallized from Et<sub>2</sub>O mp = 82-84 °C; [*α*]<sub>D</sub> = +16.4° (c = 0.075, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.61 (d, 2H), 7.31-7.17 (m, 7H), 5.31 (s, 1H), 5.13 (s, 1H), 5.11 (s, 1H), 3.85 (qt, 1H), 3.49-3.31 (m, 3H), 2.41-2.30 (bs, 4H), 1.28 (d, 3H), 0.87 (t, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 171.1, 149.4, 144.5, 142.7, 137.6, 130.6, 129.2, 128.7, 128.3, 128.0, 116.8, 62.4, 59.4, 41.6, 22.6, 17.5, 14.7; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3400, 1620; HPLC (10% i-PrOH/hexane, 0.7 mL/min) (*R*) = 42.5, (*S*) = 48.2 min. Anal. Calcd for C<sub>21</sub>H<sub>25</sub>NO<sub>4</sub>S: C, 65.09; H, 6.51; N, 3.62. Found C, 64.95; H, 6.55; N, 3.66.

**(1'*R*, 2*S*)-Ethyl-2-(2'-tetralenyl)-2-(tosylamino)acetate (anti-12l).** White crystalline solid recrystallized from Et<sub>2</sub>O mp = 145-146 °C; [*α*]<sub>D</sub> = +14.3° (c = 0.03, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.61 (d, 2H), 7.41 (d, 1H), 7.22-7.09 (m, 5H), 5.34 (s, 1H), 5.10 (d, 1H), 4.81 (s, 1H), 3.81 (t, 1H), 3.74-3.62 (m, 1H), 3.58-3.48 (m, 1H), 3.06-2.91 (m, 1H), 2.75 (dd, 1H), 2.65 (dt, 1H), 2.41-2.30 (bs, 4H), 1.90 (m, 1H), 1.58 (s, 1H), 0.90 (t, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 172.8, 144.7, 143.4, 137.5, 136.9, 134.1, 130.6, 130.4, 129.2, 128.5, 127.2, 125.9, 112.4, 61.9, 57.4, 46.8, 25.6, 24.9, 22.5, 14.8; IR (CH<sub>2</sub>Cl<sub>2</sub>): 3260, 1630; (72% yield) HPLC (10% i-PrOH/hexane, 0.8 mL/min) anti[(*R*) = 25.8.5, (*S*) = 32.5 min] syn[35.5 min, 37.3 min]. Anal. Calcd for C<sub>20</sub>H<sub>25</sub>NO<sub>4</sub>S: C, 63.97; H, 6.72; N, 3.73. Found C, 63.94; H, 6.65; N, 3.77.

**Synthesis of Trimethyl(2-phenyl-2-propenyl)silane (17d).** This material was generated by a modification of a known route to the corresponding stannane.<sup>26</sup> A flask was loaded with potassium *tert*-butoxide (4.52 g, 40.27 mmol) and *p*-methylstyrene (4.73 g, 40.0 mmol). The reagents were dissolved in THF (120 mL) and the resultant pale yellow solution cooled to -78 °C. To this solution was added a 1.29 M solution of butyllithium in hexanes (31 mL, 40.0 mmol) over 5 min causing color change to dark red. The solution was warmed and allowed to stir for 5 h at -50 °C. This solution was then added to rapidly stirring -78 °C solution of chlorotrimethylsilane (11 mL, 86.7 mmol) in THF (30 mL). During the addition, the solution of silane becomes very thick and cloudy. The solution is then allowed to warm and stir at room temperature overnight. The THF was removed and the residue taken up in *n*-pentane. The solution was filtered through celite, the solvent removed and the residue purified by column chromatography on florisil (5x13 cm petroleum ether to 1% Et<sub>2</sub>O/petroleum ether) to give 79% yield of a clear colorless oil (6.06 g, 31.7 mmol) identical to that reported previously in the literature.

**Synthesis of Trimethyl(3-phenyl-3-propenyl)silane (17e).** This material was prepared by modification of a known procedure by Smith et al.<sup>27</sup> To a solution of hexamethyldisilane (2.5 mmol) in HMPA (3 mL) at 0 °C under nitrogen was added methyllithium (2.5 mmol of Aldrich methyllithium-lithium bromide complex in ether) dropwise. After being stirred for 3 min, the

<sup>26</sup> Desponds, O.; Schlosser, M. *J. Organomet. Chem.* **1991**, 409, 93.

<sup>27</sup> Smith, J. G.; Drozda, S. E.; Petraglia, S. P.; Quinn, N. R.; Rice, E. M.; Taylor, B. S.; Viswanathan, M. *J. Org. Chem.* **1984**, 49, 4112.

resulting red solution was treated with copper(I) cyanide (2.5 mmol), and the black reaction mixture was stirred for 3 min. THF (10 mL) was added and the reaction mixture was cooled to -60 °C and stirred for 5 min. A solution of the allylic halide (1 mmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 1 h at -60 °C. The cold solution was poured into 50 mL of petroleum ether, and the combined organic extracts were dried over magnesium sulfate, filtered and concentrated. The crude product was purified by silica gel column chromatography using petroleum ether as eluent to afford the desired allyltrimethylsilane.