

The Brønsted Acid-Catalyzed Direct Aza-Darzens Synthesis of *N*-Alkyl *cis*-Aziridines

Amie L. Williams and Jeffrey N. Johnston*

Department of Chemistry, Indiana University, Bloomington, IN 47405-7102

General Experimental Details

Flame-dried (under vacuum) glassware was used for all non-aqueous reactions. All reagents and solvents were commercial grade and purified prior to use when necessary. Diethyl ether (Et₂O), tetrahydrofuran (THF), dichloromethane (CH₂Cl₂), and benzene (C₆H₆) were dried by passage through a column of activated alumina as described by Grubbs.¹ Benzene was additionally passed through a column containing activated Q-5 reactant. Solvents other than benzene were degassed using the freeze-pump-thaw method when necessary. All additional solvents were dried by distillation from calcium hydride or Na/benzophenone (hydrocarbon deuterated solvents) when necessary. Magnesium sulfate was used to dry organic solutions unless otherwise noted. Preparation and analytical data has been previously reported for **2c**, **2d**, **2e**.²

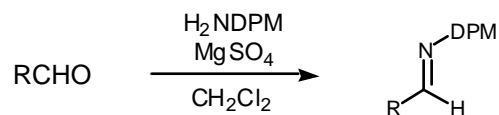
Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μ) plates, and flash chromatography utilized 230–400 mesh silica gel from Scientific Adsorbents. Products were visualized by UV light, iodine, and/or the use of ceric ammonium molybdate, potassium permanganate, ninhydrin, *p*-anisaldehyde, and potassium iodoplatinate solutions.

IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer. Liquids and oils were analyzed as neat films on a salt plate (transmission), whereas solids were applied to a diamond plate (ATR). Nuclear magnetic resonance spectra (NMR) were acquired on either a Varian Inova-400 or VXR-400 instrument. Chemical shifts are measured relative to tetramethylsilane, as judged by the residual partially deuterated solvent peak. Aziridine relative stereochemical

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

² Antilla, J. C.; Wulff, W.D. *Angew. Chem. Int. Ed.* **2000**, *39*, 4518–4521.

assignments were made on the basis of coupling constants typical for *cis*- and *trans*-aziridines. Mass spectra were obtained using a Kratos MS-80 spectrometer using the ionization technique indicated. Combustion analyses were performed by Atlantic Microlab, Norcross, GA.



General Procedure for Aldimine Condensations

To a diethyl ether or dichloromethane solution of the aldehyde (0.5 M) and MgSO_4 or 4 Å MS (1:1 w/w) at 0 °C was added the amine (0.5 M). The solution was allowed to warm to 25 °C and stirred until complete conversion was achieved, as evidenced by ^1H NMR. The mixture was filtered and washed with Et_2O . The solvent was removed *in vacuo* to give the analytically pure aldimine, which was used without further purification.

General Procedure for Acid Catalyzed Aziridinations

To a propionitrile solution of the aldimine (0.3M) at –78 °C, was added triflic acid (0.25 equiv). After 5 min, ethyl diazoacetate (1.2 equiv) was added dropwise to the cold solution. The mixture was stirred at –78 °C for 6 h, and then quenched by the addition of a saturated sodium bicarbonate solution. The layers were separated, and the aqueous layer extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated to give the crude product, which was analyzed by ^1H NMR to determine the ratio of diastereomers. Flash chromatography or recrystallization of the crude mixture provided the analytically pure aziridine.

Benzhydrylimino-acetic acid methyl ester (2a). Following the general procedure, oxo-acetic acid methyl ester (2.88 g, 32 mmol) and 4 Å MS were stirred in dichloromethane (10 mL) and cooled to 0 °C, then diphenylmethyl amine (5.65 mL, 32 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 °C and stirred until ^1H NMR spectroscopy revealed complete aldimine formation. Filtering of the mixture, and removal of the solvent afforded 7.55 g (93%) of the aldimine as white solid. IR (film) 3085, 3061, 3027, 2950, 2849, 1751, 1728, 1494, 1453, 1300, 1211, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) 7.74 (s, 1H), 7.30–7.19 (m, 10H), 5.63 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 163.8, 153.4, 141.6,

141.6, 128.8, 128.8, 127.9, 127.9, 127.5, 127.5, 77.6, 52.8; HRMS (EI): Exact mass calcd for $C_{16}H_{14}NO_2$ $[M-H]^+$ 252.1025. Found 252.1021.

Benzhydrylimino-acetic acid *tert*-butyl ester (2b). Following the general procedure, oxo-acetic acid *tert*-butyl ester (4.01 g, 30.7 mmol) and $MgSO_4$ were stirred in dichloromethane (30 mL) and cooled to 0 °C, then diphenylmethyl amine (5.03 mL, 29.1 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 °C and stirred until 1H NMR spectroscopy revealed complete aldimine formation. Filtering of the mixture, and removal of the solvent afforded 8.5 g (99%) of the aldimine as white solid. IR (film) 3079, 3058, 3034, 2971, 2942, 1862, 1735, 1374, 1234 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) 7.65 (s, 1H), 7.28-7.18 (m, 10H), 5.58 (s, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 162.2, 155.1, 142.1, 142.1, 128.7, 128.7, 127.9, 127.9, 127.5, 127.5, 82.7, 77.5, 28.1; HRMS (EI): Exact mass calcd $C_{15}H_{12}NO_2$ $[M-C_4H_9]^+$ 238.0868. Found 238.0866.

Benzhydrylpyridin-2-ylmethylene amine (2f). Following the general procedure, pyridine-2-carboxaldehyde (0.501 g, 4.67 mmol) and $MgSO_4$ were stirred in dichloromethane (10 mL) and cooled to 0 °C, then diphenylmethyl amine (0.80 mL, 4.67 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 °C and stirred until 1H NMR spectroscopy revealed complete aldimine formation. Filtering of the mixture, and removal of the solvent afforded 1.26 g (99%) of the aldimine as yellow solid. IR (film) 3081, 3048, 3022, 2077, 2868, 1644, 1584, 1493, 1447, 1365, 1274, 1025, 991 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 4.8 Hz, 1H), 8.53 (s, 1H), 8.22 (d, J = 8.1 Hz, 1H), 7.72 (dd, J = 8.3, 7.5 Hz, 1H), 7.40 (d, J = 7.5 Hz, 4H), 7.33 (dd, J = 7.5, 7.5 Hz, 4H), 7.29-7.22 (m, 3H), 5.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 162.0, 154.8, 149.4, 143.4, 143.4, 136.5, 128.6, 128.6, 127.8, 127.8, 127.2, 127.2, 124.9, 121.6, 77.7; HRMS (CI): Exact mass calcd for $C_{19}H_{16}N_2$ $[M]^+$ 272.1313. Found 272.1304.

Benzhydryl-cyclopropylmethylene-amine (2g). Following the general procedure, cyclopropane carboxaldehyde (0.50 mL, 6.69 mmol) and $MgSO_4$ were stirred in dichloromethane (10 mL) and cooled to 0 °C, then diphenylmethyl amine (1.15 mL, 6.69 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 °C and stirred until 1H NMR spectroscopy

revealed complete aldimine formation. Filtering of the mixture, and removal of the solvent afforded 1.52 g (97%) of the aldimine as yellow oil. IR (film) 3084, 3060, 3025, 3005, 2829, 1661, 1493, 1453, 1029 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.25 (m, 8H), 7.24 -7.20 (m, 2H), 7.17 (d, J = 7.8 Hz, 1H), 5.32 (s, 1H), 1.83 (dddd, J = 12.6, 7.8, 7.8, 4.6 Hz, 1H), 0.91 (ddd, J = 7.2, 7.2, 4.3 Hz, 2 H), 0.73 (ddd, J = 7.0, 7.0, 4.3 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) 167.7, 143.9, 143.9, 128.5, 128.5, 127.7, 127.7, 126.9, 126.9, 77.9, 16.6, 6.4, 6.4; HRMS (EI): Exact mass calcd for $\text{C}_{17}\text{H}_{17}\text{N}$ $[\text{M}]^+$ 235.1361. Found 235.1360.

4-Benzhydrylimino-but-2-enoic acid ethyl ester (2g). Following the general procedure, 4-oxo-but-2-enoic acid ethyl ester (0.401 g, 3.13 mmol) and MgSO_4 were stirred in dichloromethane (10 mL) and cooled to 0 $^\circ\text{C}$, then diphenylmethyl amine (0.54 mL, 3.13 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 $^\circ\text{C}$ and stirred until ^1H NMR spectroscopy revealed complete aldimine formation. Filtering of the mixture, and removal of the solvent afforded 0.89 g (97%) of the aldimine as yellow oil. IR (film) 3085, 3062, 3027, 2981, 2937, 2904, 2871, 1722, 1716, 1616, 1493, 1453, 1305, 1258, 1187, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.17 (d, J = 9.0 Hz, 1H), 7.47 (dd, J = 15.8, 9.0 Hz, 1H), 7.35-7.27 (m, 10 H), 6.30 (d, J = 15.8 Hz, 1H), 5.53 (s, 1H), 4.26 (ddd, J = 7.1, 7.1, 7.1 Hz, 2H), 1.33 (dd, J = 7.1, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 165.7, 160.5, 142.9, 142.5, 142.5, 130.8, 128.6, 128.5, 128.4, 127.7, 127.6, 127.3, 78.4, 60.9, 14.2; HRMS (EI): Exact mass calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_2$ $[\text{M}]^+$ 293.1416. Found 293.1424.

Benzhydryl-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-amine (2i). Following the general procedure, 2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde (1.04 g, 7.96 mmol) and 4 Å MS were stirred in diethyl ether (10 mL) and cooled to 0 $^\circ\text{C}$, then diphenylmethyl amine (1.14 mL, 6.64 mmol) was added dropwise to the cold mixture. The mixture was allowed to warm to 25 $^\circ\text{C}$ and stirred until ^1H NMR spectroscopy revealed complete aldimine formation. Filtering of the mixture through Celite, and removal of the solvent afforded 1.90 g (81%) of the aldimine as viscous clear oil. IR (film) 3086, 3062, 3027, 2986, 2935, 2870, 1669, 1494, 1380, 1371, 1215, 1062, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, J = 4.8 Hz, 1H), 7.29-7.17 (m, 10 H),

5.40 (s, 1H), 4.68 (ddd, $J = 6.4, 6.4, 6.4$ Hz, 1H), 4.19 (dd, $J = 8.5, 6.9$ Hz, 1H), 3.97 (dd, $J = 8.5, 6.0$ Hz, 1H), 1.39 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 163.3, 142.8, 142.7, 128.3, 128.1, 127.4, 127.2, 126.92, 126.89, 110.0, 77.2, 76.8, 67.2, 26.3, 25.2; HRMS (EI): Exact mass calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_2$ $[\text{M}]^+$ 295.1572. Found 295.1572.

1-Benzhydrylaziridine-2,3-dicarboxylic acid 2-ethyl ester 3-methyl ester (4a). Following the general procedure, benzhydryliminoacetic acid methyl ester (**2a**) (0.110 g, 0.395 mmol) and triflic acid (11 μL , 98.7 μmol) were stirred in propionitrile (1.3 mL) at -78°C , then ethyl diazoacetate (51 μL , 0.478 mmol) was added dropwise to the cold solution. After stirring at -78°C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (10-30 % ethyl acetate/hexanes) afforded 115 mg (86%) of **4a** as a white solid. $R_f = 0.11$ (10% ethyl acetate/hexanes); IR (film) 3086, 3062, 2987, 2952, 1751, 1752, 1457, 1450, 1223, 1172, 1072 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.755-7.52 (m, 4H), 7.33 (dd, $J = 15.6, 15.6$ Hz, 4H), 7.25 (dd, $J = 7.5, 7.1$ Hz, 2H), 4.20 (dddd, $J = 17.9, 17.9, 10.7, 7.1$ Hz, 2H), 3.88 (s, 1H), 3.73 (s, 3H), 2.71 (d, $J = 6.7$ Hz, 1H), 2.69 (d, $J = 6.7$ Hz, 1H), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 167.7, 167.1, 141.5, 141.5, 128.6, 128.5, 127.6, 127.5, 127.4, 127.4, 77.1, 61.4, 52.4, 43.9, 14.1; HRMS (EI): Exact mass calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_4$ $[\text{M}-\text{H}]^+$ 338.1392. Found 338.1393. *Anal.* Calcd. for $\text{C}_{20}\text{H}_{21}\text{NO}_4$: C, 70.78; H, 6.24; N, 4.13. Found C, 71.03; H, 6.22; N, 4.14.

1-Benzhydrylaziridine-2,3-dicarboxylic acid 2- t -butyl ester 3-ethyl ester (4b). Following the general procedure, benzhydryliminoacetic acid t -butyl ester (**2b**) (0.110 g, 0.338 mmol) and triflic acid (10 μL , 84.6 μmol) were stirred in propionitrile (1.1 mL) at -78°C , then ethyl diazoacetate (44 μL , 0.406 mmol) was added dropwise to the cold solution. After stirring at -78°C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (10-30 % ethyl acetate/hexanes) afforded 115 mg (89%) of **4b** as a white solid. $R_f = 0.22$ (10% ethyl acetate/hexanes); IR (film) 3064, 3030, 2980, 2934, 1743, 1733, 1455, 1368,

1236, 1200, 1155, 1101 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.56-7.54 (m, 4H), 7.32 (ddd, J = 7.1, 7.1, 2.0 Hz, 4H), 7.26-7.23 (m, 2H), 4.27-4.12 (m, 2H), 3.85 (s, 1H), 2.61 (d, J = 6.6 Hz, 1H), 2.57 (d, J = 6.8 Hz, 1H), 1.46 (s, 9H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 167.4, 166.2, 141.9, 141.9, 128.6, 128.5, 127.6, 127.6, 127.5, 127.5, 81.9, 76.9, 61.3, 44.7, 43.7, 28.0, 14.2; HRMS (EI): Exact mass calcd for $\text{C}_{19}\text{H}_{18}\text{NO}_4$ $[\text{M}-\text{C}_4\text{H}_9]^+$ 324.1236. Found 324.1232. *Anal.* Calcd. for $\text{C}_{23}\text{H}_{27}\text{NO}_4$: C, 72.42; H, 7.13; N, 3.67. Found C, 72.38; H, 7.13; N, 3.77.

1-Benzhydryl-3-cyclohexyl-aziridine-2-carboxylic acid ethyl ester (4c). Following the general procedure benzhydryl-cyclohexylidene-amine (**2c**) (0.204 mg, 0.735 mmol) and triflic acid (21 μL , 0.184 mmol) were stirred in propionitrile (2.5 mL) at 25 $^\circ\text{C}$, then ethyl diazoacetate (95.0 μL , 0.882 mmol) was added dropwise to the cold solution. After stirring at 25 $^\circ\text{C}$ for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. ^1H NMR Analysis of the crude reaction mixture showed a 1:2:12 ratio of enamide:*trans*-aziridine:*cis*-aziridine. Purification by column chromatography on silica gel (3-5-20% ether/hexanes) afforded 0.113 g (42%) of **4c** as a white solid. ^1H NMR data was consistent with that reported previously.²

1-Benzhydryl-3-tert-butyl-aziridine-2-carboxylic acid ethyl ester (4d). Following the general procedure, benzhydryl-(2,2-dimethyl-propylidene)-amine (**2d**) (0.201 g, 0.796 mmol) and triflic acid (22 μL , 0.19 mmol) were stirred in propionitrile (2.5 mL) at 25 $^\circ\text{C}$, then ethyl diazoacetate (0.103 mL, 0.955 mmol) was added dropwise to the cold solution. After stirring at 25 $^\circ\text{C}$ for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. ^1H NMR Analysis of the crude reaction mixture showed a 1:5:7.5 ratio of enamide:*trans*-aziridine:*cis*-aziridine. Purification by column chromatography on silica gel (3-5-20% ether/hexanes) afforded 0.121 g (45%) of **4d** as a white solid. ^1H NMR data matched the analytical data reported in the literature.

1-Benzhydryl-3-phenylaziridine-2-carboxylic acid ethyl ester (4e). Following the general procedure, benzhydrylbenzylidene-amine (**2e**) (0.201 g, 0.736 mmol) and triflic acid (21 μL ,

0.184 mmol) were stirred in propionitrile (2.5 mL) at 0 °C, then ethyl diazoacetate (95 µL, 0.884 mmol) was added dropwise to the cold solution. After stirring at 0 °C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. ¹H NMR Analysis of the crude reaction mixture showed a 2:1:4.5 ratio of enamide:*trans*-aziridine:*cis*-aziridine. Purification by column chromatography on silica gel (10-30 % ethyl acetate/hexanes) afforded 122 mg (42%) of **4e** as a white solid. ¹H NMR data matched the analytical data reported in the literature.

1-Benzhydryl-3-pyridin-2-yl-aziridine-2-carboxylic acid ethyl ester (4f). Following the general procedure, Benzhydryl-pyridin-2-ylmethylene-amine (**2f**) (0.101 g, 0.367 mmol) and triflic acid (10 µL, 91.8 µmol) were stirred in propionitrile (1.2 mL) at 0°C, then ethyl diazoacetate (47 µL, 0.440 mmol) was added dropwise to the cold solution. After stirring at -78 °C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (10-20-40 % ether/hexanes) afforded 96 mg (73%) of **4f** as a white foam. *R_f* = 0.06 (20% ether/hexanes). IR (film) 3062, 3027, 2981, 2937, 1743, 1590, 1454, 1436, 1209, 1182, 1068 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.45 (dd, *J* = 4.9, 4.8 Hz, 1H), 7.65-7.60 (m, 4H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.36 (dd, *J* = 7.7, 7.4 Hz, 2H), 7.29-7.26 (m, 3H), 7.25-7.12 (m, 2H), 4.03 (s, 1H), 3.97 (ddd, *J* = 7.1, 7.1, 7.1 Hz, 2H), 3.42 (d, *J* = 6.8 Hz, 1H), 2.80 (d, *J* = 6.8 Hz, 1H), 1.03 (dd, *J* = 7.1, 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 167.6, 155.2, 148.7, 142.4, 142.2, 136.1, 128.6, 128.6, 127.6, 127.5, 127.3, 127.2, 122.8, 122.5, 77.5, 60.8, 49.3, 46.1, 14.0; HRMS (EI): Exact mass calcd for C₂₃H₂₂N₂O₂ [M]⁺ 358.1681. Found 358.1676.

Anal. Calcd. for C₂₃H₂₂N₂O₂: C, 77.07; H, 6.19; N, 7.82. Found C, 76.95; H, 6.09; N, 7.77.

1-Benzhydryl-3-cyclopropyl-aziridine-2-carboxylic acid ethyl ester (4g). Following the general procedure, benzhydryl-cyclopropylmethylene-amine (**2g**) (0.250 g, 1.06 mmol) and triflic acid (30 µL, 0.26 mmol) were stirred in propionitrile (3.5 mL) at 25 °C, then ethyl

diazoacetate (0.137 μ L, 1.28 mmol) was added dropwise to the cold solution. After stirring at 25 °C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (5-15% ethyl acetate/hexanes) afforded 0.136 g (40%) of **4g** as a white solid. R_f = 0.34 (10% ethyl acetate/hexanes). IR (film) 3085, 3063, 3027, 2982, 2826, 1744, 1453, 1300, 1189, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.49 (d, J = 7.3 Hz, 2H), 7.37 (d, J = 7.3 Hz, 2H), 7.30-7.26 (m, 3H), 7.24-7.15 (m, 3H), 4.24-4.15 (m, 2H), 3.63 (s, 1H), 2.30 (d, J = 6.7 Hz, 1H), 1.62 (dd, J = 6.7, 6.7 Hz, 1H), 1.26 (dd, J = 7.0, 7.0 Hz, 3H), 0.98-0.89 (m, 1H), 0.44-0.33 (m, 2H), 0.17-0.01 (m, 1H), -0.01- -0.07 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) 169.5, 142.8, 142.5, 128.5, 128.4, 127.9, 127.5, 127.4, 127.2, 77.7, 60.9, 49.7, 43.8, 14.4, 8.5, 3.5, 3.1; HRMS (EI): Exact mass calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_2$ $[\text{M}]^+$ 321.1729. Found 321.1726.

Anal. Calcd. for $\text{C}_{21}\text{H}_{23}\text{NO}_2$: C, 78.47; H, 7.21; N, 4.36. Found C, 78.44; H, 7.20; N, 4.37.

1-Benzhydryl-3-(2-ethoxycarbonyl-vinyl)-aziridine-2-carboxylic acid ethyl ester (4h).

Following the general procedure, 4-benzhydrylimino-but-2-enoic acid ethyl ester (**2h**) (50.1 mg, 0.170 mmol) and triflic acid (5 μ L, 42.6 μ mol) were stirred in propionitrile (0.60 mL) at -78 °C, then ethyl diazoacetate (22 μ L, 0.204 mmol) was added dropwise to the cold solution. After stirring at -78 °C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (10-30-50% ethyl acetate/hexanes) afforded 35 mg (53%) of **4h** as a white solid. R_f = 0.19 (10% ethyl acetate/hexanes). IR (film) 3061, 3027, 2983, 2937, 2905, 1716, 1454, 1305, 1264, 1189 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.48 (d, J = 7.3 Hz, 2H), 7.40 (d, J = 7.3 Hz, 2H), 7.43-7.21 (m, 6H), 6.92 (dd, J = 15.8, 7.1 Hz, 1H), 6.07 (d, J = 15.8 Hz, 1H), 4.20-4.15 (m, 4H), 3.85 (s, 1H), 2.70-2.65 (m, 2H), 1.27 (dd, J = 7.1, 7.1 Hz, 3H), 1.25 (dd, J = 7.1, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 168.0, 165.7, 142.5, 142.1, 142.0,

128.7, 128.7, 127.6, 127.5, 127.4, 127.3, 125.1, 77.4, 61.3, 60.5, 46.0, 45.9, 14.3, 14.3; HRMS (EI): Exact mass calcd for $C_{23}H_{25}NO_4$ $[M]^+$ 379.1784. Found 379.1778.

Anal. Calcd. for $C_{23}H_{25}NO_4$: C, 72.80; H, 6.64; N, 3.69. Found C, 72.32; H, 6.62; N, 3.65.

1-Benzhydryl-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-aziridine-2-carboxylic acid ethyl ester

(4i). Following the general procedure, benzhydryl-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene) amine (**2i**) (0.203 g, 0.677 mmol) and triflic acid (19 μ L, 0.169 mmol) were stirred in propionitrile (2.2 mL) at -78°C , then ethyl diazoacetate (87 μ L, 0.813 mmol) was added dropwise to the cold solution. After stirring at -78°C for 6 h, the reaction was quenched by the addition of a saturated sodium bicarbonate solution and the reaction worked up according to the general procedure. Purification by column chromatography on silica gel (20-40-100 % ether/hexanes) afforded 214 mg (83%) of **4i** as a white solid. $R_f = 0.21$ (20% ether/hexanes); $[\alpha]_D^{25} = +89.1$ (c 1.0, CHCl_3); IR (film) 3090, 3055, 3027, 2985, 2936, 2886, 1730, 1456, 1368, 1195, 1066, 1029 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, $J = 7.7$ Hz, 3H), 7.22-7.06 (m, 7H), 4.08 (ddd, $J = 6.8, 6.8, 6.8$ Hz, 2H), 3.97 (ddd, $J = 6.2, 6.2, 6.0$ Hz, 1H), 3.64 (dd, $J = 8.4, 6.4$ Hz, 1H), 3.60 (s, 1H), 2.85 (dd, $J = 8.4, 6.0$ Hz, 1H), 2.33 (d, $J = 6.6$ Hz, 1H), 2.04 (dd, $J = 6.9, 6.8$ Hz, 1H), 1.21 (s, 3H), 1.11 (t, $J = 6.8$ Hz, 3H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 168.8, 142.4, 141.9, 128.6, 128.5, 127.9, 127.9, 126.9, 126.9, 109.3, 77.3, 73.2, 67.9, 61.1, 47.5, 42.8, 26.8, 25.2, 14.2; HRMS (CI): Exact mass calcd for $C_{23}H_{28}NO_4$ $[M+H]^+$ 382.2018. Found 382.2018.

Anal. Calcd. for $C_{23}H_{27}NO_4$: C, 72.42; H, 7.13; N, 3.67. Found C, 72.01; H, 7.34; N, 3.51.

*Relative stereochemistry was assigned by X-ray diffraction.*³

³ Pink, M.; Williams, A. L.; Johnston, J. N. unpublished work.